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Dergimizin 2025 yılı Haziran sayısını da yine her zamanki gibi büyük bir heyecanla sizler için hazırladık.

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Hepsi birbirinden değerli 16 orijinal makaleyi bu sayımızda bulunmaktadır. Neonatoloji alanında 1, obstetri-perinatoloji alanında 7 ve reprodüktif endokrinoloji- infertilite alanında 2 orjinal makaleye yer verdik. Genel jinekoloji ve jinekolojik onkoloji alanlarına ait 3'er araştırma makalesini de bu güzel sayımıza ekledik.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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Türkiye'nin güneydoğusunda üçüncü basamak yenidoğan yoğun bakım ünitesinde inhale nitrik oksit kullanım profili üzerine retrospektif bir çalışma

A retrospective study on inhaled nitric oxide use profile in a tertiary neonatal intensive care unit in southeastern Turkey

Mehmet KILIÇ[1], Halil ASLAN[1], İhsan YILDIRIM[1], Fatih İŞLEYEN[1]

[1]Yenidoğan Yoğun Bakım Ünitesi, Şanlıurfa Eğitim ve Araştırma Hastanesi, Şanlıurfa, Türkiye

ÖZ

Amaç: İnhale nitric oksit (iNO), yenidoğanın persistan pulmoner hipertansiyonu (PPHT) için terapötik bir ajan olarak kullanılan selektif bir pulmoner vazodilatördür. Bu çalışmada PPHT nedeniyle iNO tedavisi uyguladığımız term ve preterm olguları kategorize etmek, etnik kökene göre bireyler arası özellikleri ve iNO uygulamamızı değerlendirmek amaçlanmıştır.

Gereç ve Yöntemler: Çalışma 1 Ocak 2019 – 31 Aralık 2023 tarihleri arasında iNO tedavisi alan hastalardan oluşmuştur. Hastalar gestasyon haftaları, etnik köken, hastanede yatış süresive pulmoner hipertansiyon tanısının zamanına göre sınıflandırılmıştır.

Bulgular: Çalışmaya 31'i (% 42,5) kız ve 42'si (% 57,5) erkek 73 bebek alınmıştır. Hastalarımızın gestasyon haftası ortanca 37 (24-40) hafta, doğum ağırlığı ise ortanca 2800 (640-5400) gram idi. iNO tedavi süresi ortanca 120 (4-780) saat olarak saptandı. 37 hafta altında 35 (% 47,9) hasta varken >37 hafta 38 (% 52,1) hasta idi. 37 hafta altında iNO tedavisi başlama günü ortalama 6,66±11,47 gün iken >37 haftada 2,37±1,95 gün olarak saptanmıştır (p=0,026). Ortalama saturasyon değeri iNO öncesi 74,86±13,28 iken iNO sonrası 90,60±5,81 saptandı (p<0,001). Bebeklerin 53'ü (% 72,6) Türk ve 20'si (% 27,4) mülteci idi. Türk bebeklerde 29 hasta taburcu, 24 hasta eksitus iken mültecilerde ise 6 hasta taburcu ve 14 hasta eksitus oldu (p=0,059).

Sonuç: Term ve preterm bebeklerde iNO tedavisi PPHT durumunda kullanılmaktadır. Term bebeklerdeolduğu gibi pretermlerde de iNO tedavisine iyi yanıt alınmaktadır. Prematüre bebeklerde endikasyon dışı bir tedavi olduğundan iNO tedavisine başlama kararına ilişkin parametreler optimize edilerek daha iyi tedavi stratejileri geliştirilmelidir.

Anahtar Kelimeler: Yenidoğan, preterm, inhale nitrik oksit, yenidoğanın persistan pulmoner hipertansiyonu

ABSTRACT

Aim: Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator used as a therapeutic agent for persistent pulmonary hypertension of the newborn (PPHN). This study aimed to categorize term and preterm cases treated with iNO for PPHN, to evaluate inter-individual characteristics and iNO application according to ethnicity.

Materials and Methods: The study included patients who received iNO treatment between January 1, 2019 and December 31, 2023. Patients were categorized according to gestational weeks, ethnicity, length of hospital stay and time of pulmonary hypertension diagnosis.

Results: A total of 73 infants were included in the study, 31 (42.5%) were girls and 42 (57.5%) were boys. The median gestational age of our patients was 37 (24-40) weeks, and the median birth weight was 2800 (640-5400) grams. The median duration of iNO treatment was 120 (4-780) hours. There were 35 (47.9%) patients under 37 weeks and 38 (52.1%) patients above 37 weeks. The mean day of iNO treatment initiation was 6.66±11.47 days in those under 37 weeks and 2.37±1.95 days in those over 37 weeks (p=0.026). The average saturation value was 74.86±13.28 before iNO and 90.60±5.81 after iNO (p<0.001). 53 (72.6%) of the infants were Turkish and 20 (27.4%) were refugees. Among Turkish infants, 29 were discharged and 24 died, while among refugees, 6 were discharged and 14 died (p=0.059).

Conclusion: iNO therapy is used in both term and preterm infants with PPHN. A good response to iNO treatment is observed in preterms as well as in term infants. Since it is an off-label treatment in preterm infants, parameters related to the decision to initiate iNO treatment should be optimized and better treatment strategies should be developed.

Keywords: Newborn, premature, inhaled nitric oxide, persistent pulmonary hypertension of the newborn

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Sorumlu Yazar/Corresponding Author: Halil ASLAN, Yenidoğan Yoğun Bakım Ünitesi, Şanlıurfa Eğitim ve Araştırma Hastanesi, Şanlıurfa, Türkiye
E-mail: drhaslan1@gmail.com

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GİRİŞ

Yenidoğanın persistan pulmoner hipertansiyonu (PPHT), geç preterm ve term bebeklerin %10'unda görülen, kanın duktus arteriosus ve/veya foramen ovale boyunca sağdan sola şantı sonrası pulmoner vasküler direncin artması ile karakterize ciddi hipoksemiye yol açan bir hastalıktır (1). Gelişmekte olan ülkelerde inhale nitrik oksit (iNO) ve ekstrakorporeal membran oksijenasyon erişim eksikliği, mortalite ve morbiditenin artmasına, özellikle de nörogelişimsel bozulmaya yol açabilmektedir. Pulmoner hipertansiyon ile ilişkili hipoksik solunum yetmezliği olan yenidoğanların tedavisinde iNO kullanımı ile zamanında ve erken doğmuş bebeklerde ekstrakorporeal membran oksijenizasyonu ihtiyacı azalmaktadır (2). Nitrik oksit (NO) düşük miktarlarda kan akışının düzenlenmesi, trombosit reaktivitesi ve nörotransmisyon yaparken, daha yüksek NO konsantrasyonu sitotoksik ve sitostatik özelliklere sahiptir. Yenidoğanın PPHT tedavisinde iNO'nun tercih edilmesinin nedeni, sistemik vasküler tonusta bir azalma olmadan pulmoner vasküler tonusu etkileyebilmesidir (3,4).

Nitrik oksit doğal olarak oluşan ve pulmoner dolaşımın ekstrauterin hayata adaptasyonunu kolaylaştıran bir gazdır. Nitrik oksit ayrıca antiinflamatuar ve modüle edici özelliklere de sahiptir (5). Nitrik oksit molekülü; pulmoner spesifik bir vazodilatördür. Serbest bir radikal gaz olan ve inhalasyon yoluyla uygulanan NO hücre zarlarından kolaylıkla geçebilen küçük bir molekül olup, yarılanma ömrü saniyeler kadar kısadır (6). Yenidoğanlarda endojen NO sentezi, doğum, stres, oksijen artışı veya sepsis gibi olaylarla indüklenerek nitrik oksit sentaz aracılığıyla oluşur ve cGMP aracılığıyla düz kas hücrelerinde vazodilatasyona neden olur. İnhale NO, pulmoner venlerde vazodilatasyon yapmakta ventilasyon perfüzyon uyumsuzluğunu azaltarak alveollerdeki kan akışının artmasını sağlamaktadır (7). İnhale NO kullanımı PPHT olan yenidoğanlarda oksijenizasyonu iyileştirir (8). Amerika Birleşik Devletleri Gıda ve İlaç İdaresi, iNO tedavisini PPHN tanılı 34. gebelik haftasında doğan term ve preterm bebeklerde onayladı (9). Bu çalışmada yenidoğan yoğun bakım ünitesinde iNO kullandığımız term ve preterm olguları kategorize etmek ve iNO uygulamamızı değerlendirmek amaçlanmıştır.

GEREÇ VE YÖNTEMLER

Çalışma retrospektif olarak 1 Ocak 2019 – 31 Aralık 2023 yılları arasında Şanlıurfa Eğitim ve Araştırma Hastanesi yenidoğan yoğun bakım ünitesinde yenidoğanın PPHT tanısı ile iNO tedavisi uygulanan term ve preterm bebekler alınarak gerçekleştirildi. Etik onay Harran Üniversitesi Klinik Araştırmalar Etik Kurulu tarafından 15.04.2024 tarihinde verilen 24.04.27 sayılı izinle alındı. Majör konjenital, kalp ve multipl anomalileri olan bebekler çalışma dışı bırakıldı. Bebekler gestasyonel haftasına göre <37 hafta (grup I) ve ≥37 hafta (grup II) olarak iki gruba ayrıldı. İnhale NO tedavisi, ciddi solunum yetmezliği olan (FiO2 0,9 ve MAP ≥10 cm H_2O olmasına rağmen saturasyon [sPO2] <%85 olması) konvansiyonel ventilasyon sonrası yüksek frekanslı osilatuvar ventilasyon uygulamalarına yanıt vermeyen bebeklere başlandı. Tüm bebeklerde preduktal ve postduktal olarak ölçülen sPO2 farkı %10'un üzerindeydi. iNO, selektif pulmoner vazodilatasyon yaparak ekstrapulmoner sağ sol şantta azalma sağladığı ve alveolar ventilasyon perfüzyon bozukluğunu düzelttiği için iNO başlanması için ekokardiyografik inceleme şartı aranmadı. Ekokardiyografik inceleme doğuştan kalp hastalıkları tanısını dışlamak amacıyla yapıldı. Mekanik ventilasyon sırasında intratrakeal olarak sürekli iNO tedavisi uygulandı. Hastalara NO gazı mekanik ventilatör devresinin aferent koluna eklenen bir set ile verildi. İnhale NO tedavisi sırasında oluşan NO_2 gazının ölçüm değerleri ppm olarak sürekli kaydedildi. Tedaviye 20 ppm dozunda başlandı ve tedavinin 1. saatinde FiO2 değeri 0,20'den fazla düşen hastalar pozitif yanıt verenler olarak kabul edildi. Pozitif yanıt verenlerde, OI <10'a ve FiO2 <60'a ulaşana kadar tedavi 20 ppm'de tutularak sonrasında her 4-6 saatte iNO dozu kademeli azaltıldı. Bir saat boyunca tedaviye rağmen FiO2 düzeyi değişmediyse veya 0,10'dan daha az düştüyse protokole göre iNO tedavisi sonlandırıldı. Bu bebeklere magnezyum sülfat infüzyonu (200 mg/kg yüklemeyi takiben 50 mg/kg/saat infüzyon), iloprost inhalasyonu (100 ng/kg), sildenafil (3 mg/kg/gün, oral yol ile) uygulandı. Bebekler stabil olduktan sonra iNO kademeli azaltılarak kesildi. Hastalar iNO tedavisine başlama zamanına göre erken (postnatal ilk 3 günde) ve geç (postnatal 4. gün ve sonrası) olmak üzere iki gruba ayrıldı.

Persistan pulmoner hipertansiyon etiyolojisinde RDS, yenidoğanın geçici takipnesi, pnömoni, pnömotoraks, neonatal sepsis, mekonyum aspirasyon sendromu, perinatal asfiksi, konjenital diyafram hernisi, hidrops fetalis, özefagus atrezisi gibi çeşitli risk faktörleri tanımlanmıştır. Gebelik yaşına göre küçük (SGA; gebelik haftasına göre doğum ağırlığı <%10 persentil), normal (AGA; %10-90 persentil) ve gebelik haftasına göre büyük (LGA; gebelik haftasına göre doğum ağırlığı >%90 persentil) olarak hastalar sınıflandırıldı. Hasta dosyalarından ve elektronik kayıt sisteminden annenin gebelik öyküsü, doğum ile ilgili demografik özellikler, doğum öncesi steroid uygulaması, doğum haftası, doğum ağırlığı, cinsiyet, doğum şekli, 1. ve 5. dakika Apgar skoru, iNO tedavisi öncesi kan gazı parametreleri, inotrop ihtiyacı, mekanik ventilasyon süresi ve modu, iNO başlangıç zamanı, iNO tedavi süresi, iNO öncesi ve sonrası methemoglobin, sPO2 ve kalp tepe atım değerleri, sürfaktan gereksinimi, hastanede yatış süresi ve ölüm verileri geriye dönük olarak toplandı.

Verilerin istatistiksel analizleri, SPSS 20.0 (SPSS Inc., Chicago, IL, ABD) analiz programı kullanılarak yapıldı. Tüm sürekli değerler, uygun olduğu yerde medyan ve ortalama ± standart sapma olarak

sunuldu. Kategorik değerler frekans ve yüzde olarak sunuldu. İki bağımsız grubun karşılaştırılmasında kategorik değişkenler için Pearson ki-kare analizi, sürekli değişkenler için Student's t-testi, parametrik olmayan değişkenlerin karşılaştırılmasında Mann-Whitney U testi kullanılmıştır. İstatistiksel anlamlılık p<0,05 olarak belirlendi.

BULGULAR

Çalışmaya 31'i (%42,5) kız ve 42'si (%57,5) erkek olmak üzere iNO tedavisi uygulanan 73 bebek alınmıştır. Hastalarımızın gestasyon haftası ortanca 37 (24-40) hafta, doğum ağırlığı ise ortanca 2800 (640-5400) gram idi. Hastalarımız gestasyonel haftaya göre değerlendirildiğinde 37 hafta altında doğan (grup I) hasta sayımız 35 (%47,9) iken 37 hafta ve üzerinde doğan (grup II) hasta sayısı ise 38 (%52,1) idi. Bebeklerin 53'ü (%72,6) Türk ve 20'si (%27,4) mülteci idi. Toplamda 73 hastamızın 35'i taburcu olabilirken 38 hastada eksitus gerçekleşti. Grup I olarak adlandırılan 37 hafta altında doğan hastaların 12'si taburcu ve 23'ü ise eksitus oldu. Grup II olarak adlandırılan 37 hafta ve üzeri doğan bebeklerde ise 23 hasta taburcu olabilirken, 15 hastada eksitus gerçekleşti. Grup I bebeklerde, grup II bebeklere göre eksitus oranı anlamlı olarak yüksek saptandı (p=0,035). Türk bebeklerden 29 hasta taburcu olabilirken 24 hastada eksitus gerçekleşti. Mülteci bebeklerde ise sadece 6 hasta taburcu olabilirken 14 hasta eksitus oldu. Eksitus oranı mülteci bebeklerde Türk bebeklere oranla anlamlı olmasa da daha yüksek olarak gözlendi (p=0,059).

iNO tedavi süresi ortanca 120 (4-780) saat olarak saptandı. Normal spontan doğan (n:47) grupta ortalama iNO süresi 156,9±147,7 saat iken sezaryen doğum ile doğanlarda (n:26) ortalama iNO süresi 150,1±163,5 saat idi (p=0,858). Hastaların iNO tedavisi öncesi ve tedavi sonrası ortalama kalp tepe atımı, methemoglobin düzeyleri arasında anlamlı fark saptanmadı. Hastaların iNO tedavisi öncesi ortalama sPO2 değeri 74,86±13,28 iken iNO tedavisi sonrası

Tablo 1. Bebeklerin Doğum Haftasına Göre Demografik Verileri ve Vital Bulgularının Karşılaştırılması

Değişkenler	Grup	n	Ort	S	% 95 Güven Aralığı		t	p
					Alt Sınır	Üst Sınır		
iNO öncesi sPO2	< 37	35	76,23	9,78	-4,07	5,34	,269	,789
	≥ 37	38	75,59	10,22				
iNO sonrası sPO2	< 37	35	91,11	5,37	-1,74	3,75	,732	,467
	≥ 37	38	90,11	6,24				
iNO öncesi kalp tepe atımı	< 37	35	141,00	21,27	**1,38**	**24,41**	**2,233**	**,029**
	≥ 37	38	128,11	27,18				
iNO sonrası kalp tepe atımı	< 37	35	134,06	21,62	-5,01	15,24	1,007	,317
	≥ 37	38	128,95	21,45				
iNO öncesi methemoglobin	< 37	34	,69	,39	-,39	,19	-,677	,501
	≥ 37	34	,79	,77				
iNO sonrası methemoglobin	< 37	34	1,43	,52	-,56	,16	-1,099	,276
	≥ 37	34	1,63	,91				
iNO toplam tedavi süresi, saat	< 37	35	151,26	146,66	-77,87	65,54	-,171	,864
	≥ 37	38	157,42	159,52				
iNO başlama zamanı, postnatal gün	< 37	35	6,66	11,47	**,52**	**8,06**	**2,271**	**,026**
	≥ 37	38	2,37	1,95				
İnvaziv ventilasyon süresi, gün	< 37	33	15,30	16,45	-5,83	6,97	,179	,859
	≥ 37	38	14,73	9,91				
Noninvaziv ventilasyon, gün	< 37	31	2,13	3,65	-2,15	1,06	-,679	,500
	≥ 37	38	2,68	2,99				
Toplam oksijen süresi, gün	< 37	32	18,25	20,26	-9,88	6,55	-,406	,686
	≥ 37	38	19,92	13,69				
Yatış süresi, gün	< 37	35	21,26	23,82	-13,94	6,41	-,739	,463
	≥ 37	38	25,03	19,72				

iNO: inhale nitrik oksit, sPO2: saturasyon

ortalama sPO2 değeri 90,60±5,81olup iNO tedavisi sonrası sPO2 değerinde dramatik artış saptandı (p<0,001). Tüm hastalarımız inotropik ajan tedavisi aldı. İkili inotrop tedavisi 18 hastada, üçlü inotrop 15 hastada, dörtlü inotrop tedavisi ihtiyacı ise 30 hastada gözlendi.

Demografik verilere ve vital bulgulara ilişkin sonuçların bebeklerin doğum haftasına göre farklılaşıp farklılaşmadığını incelemek için hastalar değerlendirildiğinde grup I'de yer alan bebeklerin iNO tedavisi öncesi ortalama kalp tepe atımı sayısının grup II'ye göre daha yüksek olduğu saptanmıştır (p=0,029). Grup I'de iNO tedavisi başlama günü ortalama 6,66±11,47 gün iken grup II'de ise 2,37±1,95 gün olarak saptanmıştır (Tablo 1). Grup II'de grup I'e göre postnatal ilk günlerde iNO tedavisi başlama gereksinimi daha fazla olup anlamlı olarak daha düşük olduğu görülmektedir (p=0,026). Ancak diğer araştırma değişkenlerinin ortalamaları arasında anlamlı bir farklılaşma elde edilmemiştir (p>0,05).

Araştırma değişkenlerine ilişkin demografik verilerin ve iNO tedavisi öncesi alınan kan gazı parametrelerinin, bebeklerin Türk ya da mülteci olmasına bağlı olarak farklılaşıp farklılaşmadığı incelendiğinde, Türk bebeklerin yatış gün sayısı ortalamalarının mülteci bebeklerden anlamlı olarak daha yüksek olduğu görülmektedir (p=0,027). Ancak diğer araştırma değişkenlerinin ortalamaları arasında anlamlı bir farklılaşma elde edilmemiştir (p<0,05). Bulgular Tablo 2'de sunulmuştur.

Tablo 2. Bebeklerin Demografik Verileri ve iNO Tedavisi Öncesi Alınan Kan Gazı Parametrelerinin Etnik Kökene Göre Karşılaştırılması

Değişkenler	Grup	n	Ort	S	% 95 Güven Aralığı		t	p
					Alt Sınır	Üst Sınır		
pH	Türk	50	7,04	,17	-,15	,05	-1,072	,288
	Mülteci	18	7,10	,21				
pCO2, mmHg	Türk	50	69,98	24,88	-6,75	18,48	,929	,356
	Mülteci	18	64,11	16,34				
HCO3, mmol/L	Türk	50	15,12	6,34	-3,97	2,63	-,407	,686
	Mülteci	18	15,79	4,07				
Baz Açığı, mmol/L	Türk	50	-11,42	6,96	-5,35	2,52	-,717	,476
	Mülteci	18	-10,01	7,77				
Laktat, mmol/L	Türk	50	6,37	4,65	-1,64	3,68	,766	,447
	Mülteci	18	5,35	5,01				
iNO başlama zamanı, postnatal gün	Türk	53	4,77	9,22	-3,09	5,63	,583	,562
	Mülteci	20	3,50	5,18				
iNO tedavi süresi, saat	Türk	53	170,94	169,44	-18,92	139,21	1,517	,134
	Mülteci	20	110,80	82,08				
iNO öncesi sPO2	Türk	53	74,69	9,94	-9,51	,80	-1,687	,096
	Mülteci	20	79,05	9,47				
iNO sonrası sPO2	Türk	53	90,08	6,16	-4,91	1,17	-1,229	,223
	Mülteci	20	91,95	4,67				
iNO öncesi kalp tepe atımı	Türk	53	134,98	25,86	-11,11	15,47	,327	,744
	Mülteci	20	132,80	23,83				
iNO sonrası kalp tepe atımı	Türk	53	132,37	22,28	-7,99	14,72	,591	,556
	Mülteci	20	129,00	19,78				
İnvaziv ventilasyon süresi, gün	Türk	51	16,41	14,74	-1,87	12,27	1,467	,147
	Mülteci	19	11,21	7,32				
HFOV süresi, gün	Türk	24	9,13	6,35	-5,46	6,56	,188	,852
	Mülteci	17	8,57	8,44				
Noninvaziv ventilasyon süresi, gün	Türk	50	2,76	3,54	-,53	3,05	1,402	,166
	Mülteci	18	1,50	2,33				
Toplam oksijen süresi, gün	Türk	53	21,38	18,84	-,85	17,08	1,807	,075
	Mülteci	20	13,26	8,24				
Yatış süresi, gün	Türk	53	26,64	23,94	1,44	23,54	2,254	,027
	Mülteci	20	14,15	9,95				

iNO: inhale nitrik oksit, sPO2: saturasyon, HFOV: yüksek hızda titreşimli ventilasyon

Bebeklerin taburcu ya da eksitus olma oranlarının annelerin maternal bir hastalığa sahip olma durumlarına göre farklılaşıp farklılaşmadığını incelemek için analiz edildiğinde gruplar arasında anlamlı bir farklılaşma olmadığı gözlenmiştir (Tablo 3).

Hastalar pulmoner hipertansiyon durumuna göre erken ve geç pulmoner hipertansiyon olarak gruplandırıldığında 53 hasta erken PH, 20 hasta ise geç PH idi. Hastalarımızın 69 tanesi tekil gebelik sonrası doğarken 4 hasta ikiz gebelik sonrası doğmuştur. Erken PH tekil gebeliklerde daha sık gözlenirken ikiz gebelik ile doğan hastalarımızda geç PH daha sık saptandı (Tablo 4). Sürfaktan ihtiyacı açısından hastalar değerlendirildiğinde geç PH olan hastalarda erken PH olan hastalara göre daha fazla sayıda sürfaktan verilme ihtiyacı olduğu gözlendi (p<0,001).

TARTIŞMA

Yenidoğanın PPHT, hipoksemi nedeniyle yenidoğan yoğun bakım ünitesine yatırılan yenidoğanlarda yüksek mortalite ve morbidite oranlarına sahip kritik bir durumdur. Doğumda insan akciğer dolaşımı, yüksek dirençli pulmoner dolaşımdan düşük dirençli

Tablo 3. iNO Tedavisi Uygulanan Bebeklerin Taburcu veya Eksitus Olma Oranlarının Maternal Hastalık Durumlarına Göre Karşılaştırılması

Maternal Hastalık	Taburcu n (%)	Eksitus n (%)	Toplam n (%)	χ^2	p
Yok	25	23	48	8,037	,154
	52,1	47,9	100,0		
Hipertansiyon	1	3	4		p>0,05
	25,0	75,0	100,0		
Gestasyonel diyabetes mellitus	5	2	7		
	71,4	28,6	100,0		
Erken membran rüptürü	1	8	9		
	11,1	88,9	100,0		
Koryoamniyonit	1	1	2		
	50,0	50,0	100,0		
Preeklampsi	2	1	3		
	66,7	33,3	100,0		
Toplam	35	38	73		
	47,9	52,1	100		

Tablo 4. Hastaların erken veya geç pulmoner hipertansiyon durumlarının demografik veriler ile karşılaştırılması

	Erken PH (n=53)	Geç PH (n=20)	p
Gebelik durumu			
Tekil, n (%)	52 (98,1)	17 (85)	,060
Sürfaktan tedavisi			
Almadı	5 (9,4)	2 (10)	**<,001**
1 kez	25 (47,2)	2 (10)	
2 kez	23 (43,4)	10 (50)	
3 kez	0	5 (25)	
4 kez	0	1 (5)	
Taburcu/Eksitus			
Taburcu, n (%)	25 (47,2)	10 (50)	,829
Etnik köken			
Türk, n (%)	39 (73,6)	14 (70)	,759
Gestasyonel yaşa göre			
SGA	1 (1,9)	1 (5)	,428
AGA	42(79,2)	17 (85)	
LGA	10 (18,9)	2 (10)	
Doğum şekli			
Normal vajinal, n (%)	32 (60,4)	15 (75)	,285
Gestasyonel hafta			
<37 hafta, n (%)	23 (43,4)	12 (60)	,205

dolaşıma geçiş yapar. Pulmoner dolaşımda artan basıncı hızlı ve güvenilir bir şekilde teşhis edebilmemiz ve sonrasında bu durumun altında yatan nedeni belirlememiz önemlidir. Yenidoğan döneminde mekonyum aspirasyonu, sepsis, pnömoni, konjenital diyafragma hernisi, konjenital kalp defektleri, pulmoner hipoplazi ve hava yollarındaki yapısal değişiklikler nedeniyle PPHT olabilir (10). Bu karmaşık hastalık birçok komplikasyona, hatta ölüme yol açabilir (11). Srnkova ve ark. üç yıl boyunca yenidoğan ünitesinde iNO tedavisi uygulanan 11 hastayı içeren çalışmalarında 11 hastadan 5'inin (%45,5) tedavi sırasında öldüğünü bildirmişlerdir (12). Çalışmamız daha geniş seride toplam 73 hasta dahil edilerek gerçekleştirilmiş ve eksitus oranı (n:38, %52) benzer şekilde bulunmuştur.

Yenidoğanın PPHT 'nin tipik semptomları doğumdan 6-12 saat sonra ortaya çıkan solunum yetmezliği ve siyanozdur. Çoğunlukla perinatal asfiksi, düşük Apgar skoru ve amniyotik sıvıda renk değişikliği şeklinde ortaya çıkabileceği gibi herhangi bir perinatal bulgu olmadan da ortaya çıkabilir (13). Persistan pulmoner hipertansiyon tanılı yenidoğanların tedavisi sistemik hemodinamikleri iyileştirmeyi amaçlayan destekleyici tedaviden oluşur. Srnkova ve ark. çalışmalarında 11 hastanın tümünde inotropik ajan ile destek tedavisi sağlamıştır. Çoğu vakada iki veya daha fazla inotrop, bir vakada ise dörde kadar inotropik ilacın kombinasyonuyla tedavi gereksinimi bildirilmiştir (12). Çalışmamızda da hastaların tümünde inotropik ajan kullanıldı. Benzer şekilde çoğu vakada (n:63) iki veya daha fazla inotrop, 30 hastada ise dörtlü inotrop tedavisi ihtiyacı gözlendi. Mortalite sayımızın yüksek olması, kritik hasta profilimiz nedeniyle dörtlü inotrop tedavisi ihtiyacımızın yüksekliği ile açıklanabilir.

Srnkova ve ark iNO tedavisi uygulanan 11 hasta (4 preterm ve 7 term bebek) bulunan çalışmalarında hastaların 9'u sezaryen ile 2'si normal spontan yolla doğmuştur. Çalışmamızda da hastalarımızın çoğu term iken sezaryen yolla doğan hasta oranımız ise normal spontan doğuma göre daha düşük idi. Aynı çalışmada ortalama iNO tedavi süresi 42,5±32,1 (3-95) saat saptanırken çalışmamızda ortalama iNO tedavi süresi 154,5±152,5 (4-780) saat idi. Ortalama iNO tedavi süremizin daha uzun bulunması hasta profilimizin daha farklı haftalarda kritik hastaları içermesi ve mevcut çalışmanın az sayıda hasta (toplam 11 hasta) ile yapılmış olması ile ilişkili olabilir. Klinik çalışmalarda kullanılan en yüksek iNO dozu 20 ppm iken bazı çalışmalarda tedaviye yanıt alınamaması durumunda doz 40-80 ppm'e kadar artırılmıştır (12,14). Bizim çalışmamızda tedaviye başlangıç dozu olarak ve izlemde en fazla 20 ppm iNO uygulandı.

İnhale NO tedavisi pulmoner hipertansiyonu, hipoksik solunum yetmezliği olan term bebeklerde selektif pulmoner vazodilatör etki ile oksijenlenmeyi etkin bir şekilde iyileştirmektedir. Gestasyonel 34 hafta altındaki bebeklerde iNO'nun rutin kullanımını önermek için yeterli kanıt bulunmadığını bildiren çalışmalar olsa da preterm bebeklerde de iNO tedavisinin hipoksemik solunum yetmezliği, RDS ve bronkopulmoner displazide de en az term bebekler kadar etkili olabileceği bildirilmektedir (15-17). Annede ateş, akciğer hastalığı, diyabet, mekonyum boyalı amniyotik sıvı, perinatal asfiksi, fetal distres ve sepsis gibi çeşitli faktörlerin varlığı neonatal pulmoner hipertansiyona neden olabilmektedir (18). Çalışmamızda da benzer risk faktörlerine sahip annelerden doğan hastalarımızın olduğu gözlendi. Toplamda 35 prematüre hastamızın 12'si iNO tedavisi sonrası taburcu edilerek prematüre bebeklerde de iNO tedavisinin etkinlik sağladığı gözlenmiştir.

Hayvan çalışmalarında kronik akciğer hastalığında distal pulmoner arter endotelinde olduğu gibi küçük hava yolu epitelinde de NO sentaz ekspresyonunun azaldığı gösterilmiştir. Aynı zamanda sepsisi olan hipoksemik PPHT'li bebeklerde trakeal aspirat analizi ile endojen nitrik oksit üretiminde geçici bir kusur olduğu gösterilmiştir (19-21). Erken PPHT ve geç PPHT açısından hastalarımızın sürfaktan ihtiyaçları değerlendirildiğinde üç ve daha fazla sayıda sürfaktan verilme oranı geç PPHT grubunda daha fazla iken erken PPHT grubunda iki ve daha az sayıda sürfaktan alan hastaların daha fazla olduğu gözlendi. Literatürde tekrarlayan sürfaktan tedavisi ihtiyacı ile erken ve geç PPHT'nın ilişkisi hakkında çalışma bildiğimiz kadarıyla bulunmamaktadır. Geç PPHT grubunda erken PPHT grubuna göre daha fazla sayıda sürfaktan ihtiyacının olması geç PPHT hastalarının kronik akciğer hastalığı, tekrarlayan sepsis ve ventilatör ilişkili pnömoniye bağlı sekonder sürfaktan eksikliği görülme sıklığının daha fazla olması ile açıklanabilir.

Pulmoner hipertansiyon ile iNO tedavisi alan 44 hastanın dahil edildiği bir çalışmada iNO başlama zamanı gestasyonel hafta ile ilişkisi değerlendirilmiştir. Bu çalışmada >34 hafta hasta grubunda <34 hafta olan hasta grubuna göre PH tanısı yaşamın ilk günlerinde konularak erken dönemde iNO tedavisine başlanmıştır (18). Bizim çalışmamızda da benzer şekilde term hasta grubunda preterm hasta grubuna göre iNO tedavisine yaşamın ilk günlerinde başlanma gereksinimi olduğu saptanmıştır.

Literatürde farklı hedef sPO2 değerlerini karşılaştıran klinik çalışmalar kısıtlı sayıdadır. İnhale NO tedavisi uygulanan ≥34 hafta PPHT tanılı yenidoğanların alındığı bir çalışmada oksijenasyonu optimize etmek, hipoksemiyi düzeltmek için yüksek oksijen konsantrasyonlarına ihtiyaç duyulduğu fakat hiperoksemi riskinde artış gözlendiği bildirilmiştir (22). Geç preterm ve term 181 bebeğin dahil edildiği çalışmada manuel oksijen tedavisi sırasında sıklıkla hiperoksemi meydana geldiği PPHT'li bebeklerde hiperoksemi için yüksek risk konusunda klinik farkındalığın gerekliliği vurgulanmıştır.

Neonatologların çoğunun PPHT tanılı hasta takibinde hipoksemiden kaçınırken oksijen toksisitesine rağmen hiperoksemiye karşı toleranslı oldukları anket çalışmasında bildirilmiştir (23). Bizim çalışmamızda hipoksi ve hiperokside geçen süre net olarak hesaplanamasa da hasta yönetiminde hipoksinin düzeltilmesi birincil öncelik olarak hedeflenmiş hiperoksi tablosundan kaçınma ikinci planda kalmıştır. de Jager ve arkadaşları otomatik olarak oksijen kontrolünün sağlanabilmesi gibi yeniliklerin kullanımı ile oksijen toksisitesinin minimalize edilmesi, optimal oksijen titrasyonunun hedeflenmesi gerektiğini bildirmişlerdir.

Aşırı düşük doğum ağırlıklı 1732 bebekte erken hipoksemik solunum yetmezliğinin mortalite ve nörogelişimsel sonuçlar ile ilişkisinin değerlendirildiği çalışmada bebekler gestasyonel yaşa göre kilo, doğum şekli, etnik açıdan iNO tedavisi gereksinimi yönünden incelenmiştir (24). Bu çalışmada yaşamın ilk döneminde erken hipoksemik solunum yetmezliği ile iNO gereksinimi yönünden hastalar değerlendirildiğinde beyaz ırkta iNO gereksinimi daha fazla iken Afrika kökenli Amerikalılarda iNO gereksiniminin daha az olduğu, İspanyol ve diğer ırklarda ise iNO gereksiniminin benzer olduğu bildirilmiştir. Çalışmamızda hasta profili olarak daha fazla doğum ağırlığına sahip olmakla birlikte etnik açıdan İspanyol ve diğer ırklar gibi iNO tedavisi gereksiniminin erken veya geç dönemde benzer olduğu bulunmuştur.

Çalışmanın sınırlılıkları olarak retrospektif olması, iNO tedavisi verilmemiş bebeklerden oluşan bir kontrol grubunun olmaması, örneklem içerisinde aşırı düşük doğum ağırlıklı prematüre bebek sayısının oldukça az sayıda olması sayılabilir. Bu kısıtlılıklara rağmen çalışmamız PPHT'li yenidoğanlarda mevcut olan sınırlı klinik çalışma verilerine önemli bir katkı sağlayan yönleri bulunmaktadır.

Sonuç olarak iNO, term ve prematüre bebeklerde neonatal PPHT tedavisinde kullanılmaktadır. Prematüre bebeklerde endikasyon dışı bir tedavi olduğundan iNO tedavisine başlama kararına ilişkin parametreler optimize edilmelidir. Bu nedenle iNO öncesi ve sonrası parametrelerin değerlendirildiği, prospektif, geniş sayıda hasta içeren çalışmalara ihtiyaç vardır.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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Effect of cerclage suture type on pregnancy and newborn results: mersylene suture versus prolene suture

Serklaj sütür tipinin gebelik ve yenidoğan sonuçları üzerine etkisi: mersilen sütüre ve prolen sütür karşılaştırılması

Masum KAYAPINAR[1], Zafer BÜTÜN[2], Melike SAVAŞ[3]

[1]Private Clinic, Perinatology, Mersin, Türkiye
[2]Private Clinic, Perinatology, Eskisehir, Türkiye
[3]Eskişehir City Hospital, Obstetric and Gynecology, Eskişehir, Türkiye

ABSTRACT

Aim: The aim of this study is to compare pregnancy and neonatal outcomes according to the type of the suture material used in the transvaginal cerclage operation.

Materials and Methods: Demographic data regarding cerclage indications, number of weeks of gestation in cerclage, cerclage suture type (prolene, mersilene), gestational week at cerclage insertion and delivery, routes of delivery were recorded. In addition, birth weight, 1st and 5th minute APGAR scores, and neonatal intensive care unit (NICU) requirements were recorded as neonatal parameters. Patients were divided into two groups according to cerclage suture type (group 1 mersilene (n=40) or group 2 prolene (n=39)) and maternal, newborn and pregnancy outcomes were compared between these groups.

Results: Comparison of the groups in terms of age, gravidity, parity, number of miscarriages and BMI revealed significantly higher mean gravidity in group 1 compared to group 2 (P<0.05), while groups were found to be similar in terms of age, parity, number of miscarriages and BMI (P>0.05). Cesarean delivery rate was 40 % in group 1 while it was 43.6 % in groups 2, no statistical difference was determined in terms of rate of cesarean delivery (p>0.05). Similar number of newborns needed NICU admission between the two groups following delivery (17.5% versus 17.9 %p>0.05). Mean APGAR scores at 1st (6.8 versus 7.4) and 5 th (7.8 versus 8.3) min were comparable between the groups (p>0.05)

Conclusion: Although mersilene stitch is commonly preferred, data analysis revealed similar results with prolene stitch in terms of maternal and neonatal outcomes.

Keywords: Mersilene,prolene, cerclage, cervical cerclage, neonatal outcome

ÖZ

Amaç: Bu çalışmanın amacı transvajinal serklaj operasyonunda kullanılan sütür materyalinin tipine göre gebelik ve neonatal sonuçları karşılaştırmaktır.

Gereçler ve Yöntem: Serklaj endikasyonları, serklajdaki gebelik haftası, serklaj sütür tipi (prolen, mersilen), serklajın uygulandığı ve doğumdaki gebelik haftası, doğum şekli ile ilgili demografik veriler kaydedildi. Ayrıca doğum ağırlığı, 1. ve 5. dakika APGAR skorları ve yenidoğan yoğun bakım ünitesi (YYBÜ) gereksinimleri yenidoğan parametreleri kaydedildi. Hastalar serklaj sütür tipine göre iki gruba ayrıldı (grup 1 mersilen (n=40) veya grup 2 prolen (n=39)) ve bu gruplar arasında maternal, yenidoğan ve gebelik sonuçları karşılaştırıldı.

Bulgular: Gruplar yaş, gravite, parite, düşük sayısı ve VKİ açısından karşılaştırıldığında, grup 1'de ortalama gravitenin grup 2'ye göre anlamlı olarak daha yüksek olduğu (P<0.05), yaş, parite, düşük sayısı ve VKİ açısından ise grupların benzer olduğu saptanmıştır (P>0.05). Sezaryenle doğum oranı grup 1'de %40 iken grup 2'de %43.6'dır, sezaryenle doğum oranı açısından istatistiksel fark saptanmamıştır (p>0.05). Doğumu takiben iki grup arasında benzer oranda yenidoğanın YYBÜ'ye yatırılması ihtiyacı olmuştur (%17,5'e karşı %17,9 p>0,05). Ortalama APGAR skorları 1. (6.8'e karşı 7.4) ve 5. (7.8'e karşı 8.3) dakikalarda gruplar arasında benzer bulunmuştur (p>0.05)

Sonuç: Mersilen sütür yaygın olarak tercih edilmesine rağmen, veri analizi sonucu maternal ve neonatal sonuçlar açısından prolen sütür ile benzer sonuçlar elde edilmiştir.

Anahtar Kelimeler: Mersilen, prolen, servikal serklaj, neonatal sonuçlar

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Sorumlu Yazar/Corresponding Author: Zafer BÜTÜN, Hoşnudiye mah. Ayşen sokak No:28/77, 26080 Tepebaşı, Eskisehir, Türkiye
E-mail: zaferbutun@hotmail.com

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INTRODUCTION

Preterm birth (PTB) is an important factor that increases neonatal morbidity and mortality. Although there are many underlying causes of preterm birth, one of the important ones in its etiology is cervical insufficiency (1). One of the main obstetric interventions for prevention in women with cervical insufficiency is cervical cerclage (2). Cerclage has been found to be beneficial in women with a history of differences in physical examination, sonography findings indicating cervical insufficiency, and a history of second trimester miscarriage (3). While many variables are evaluated in terms of cerclage success, there are a limited number of studies that evaluate the effect of cerclage suture material on the effectiveness of cerclage in preventing premature birth and provide different results. While it has been reported that the use of different suture types does not differ in terms of prolonging the pregnancy period (4), it has also been reported that the braided polyester thread (MersileneR) suture type is more effective in prolonging the pregnancy period than other suture types (5). However, some animal and wound site studies are based on the hypothesis that bacteria will multiply more in multifilament sutures and cause infection.

It has been suggested that monofilament sutures would be less associated with infection than mersilene due to suture risk (6-8). Although these are non-absorbable stitches, their success in affecting the pregnancy period is still not known for sure. Some studies in the literature argue that thicker sutures provide greater force and greater tension, thus providing better pregnancy outcomes (9). In order to increase suture power, previous study sought to determine whether routine placement of a second suture during cervical cerclage increases its effectiveness. Analysis of the data revealed that the two-stitch approach to cervical cerclage increases cerclage height but may not increase effectiveness. (10). Some other studies aimed to determine the efficacy of different techniques, Shirodkar cerclage was compared with that of the McDonald procedure for the prevention of PTB in women with a short cervix. Authors concluded that In women with short cervical length randomly assigned to receiving cerclage, no significant difference in prevention of PTB was observed using Shirodkar or McDonald's procedures (11). On the contrary, some authors have suggested that thicker and braided sutures increase the risk of infection, may lead to changes in vaginal flora and premature birth, and therefore may increase negative neonatal outcomes (12).

The aim of this study is to compare the effectiveness of monofilament sutures (Proline™) and braided polyester thread (Mersilene™) sutures used in transvaginal cerclage and to evaluate the pregnancy and neonatal outcomes of these suture materials used in transvaginal cerclage in terms of thickness.

MATERIALS AND METHODS

Hospital records and surgical operation reports of patients who underwent transvaginal cervical cerclage in a tertiary center between 2020 and 2024 were retrospectively examined from the hospital archive and system. Eskişehir Şehir Hastanesi Etik Kurulu approval was obtained before the study (22/02/2024-ESH/GOEK 2024/86). Regardless of the indication for cerclage, pregnant women who did not have congenital anomalies and underwent transvaginal cervical cerclage were included in the study. Patients whose demographic data, cerclage (suture and indication) or newborn information could not be obtained were excluded from the study. By examining the patient's surgical operation reports and files, demographic data (age, gravida, parity), cerclage indications (ultrasound indication, prophylactic or physical examination indication), cerclage weeks, cerclage suture type (prolene, mersilene), method of cerclage application were determined. Each patient included in the study was evaluated. (McDonald, Shirodkar), weeks of birth and mode of delivery (C/S, normal spontaneous vaginal birth) were recorded. In addition, newborns' birth weights, 1st and 5th minute APGAR scores, and NICU requirements were recorded. Since the choice of stitch type was at the discretion of the gynecologist as per hospital policy, no records were kept. Regardless of the stitch type, all cerclage procedures were performed in 12-3-6-9 hours, respectively. Under regional anesthesia, the patient is placed in the dorsal lithotomy position and the vagina is prepared with betadine solution. A speculum or right-angle retractors are used to adequately visualize the cervix. The anterior lip of the cervix was gently grasped using ring polyp forceps and the vesicocervical junction was identified. Immediately anterior to this junction, a nonabsorbable suture is placed in a gathered fashion across the cervix, taking care to avoid the paracervical vessels. The stitch is then tied with a surgeon's knot in the front or back. History-based cerclage (prophylactic) was defined as cerclage performed in the absence of labor and placental abruption, in one or more second trimester pregnancy losses due to painless dilatation, or in previous pregnancies due to painless dilatation in the second trimester of the previous trimester. Cerclage based on physical examination (emergency or rescue cerclage) was defined as painless cervical dilation (minimum 1 cm) in the second trimester. Cerclage based on ultrasound finding was defined as history of spontaneous (PTB) in the current pregnancy and ultrasound finding of short CL (less than 25 mm). For the first week, 2x200 mg daily progesterone treatment was continued orally and then intravaginally. Progesterone support was continued until the cerclage stitch was removed. The patients were divided into two groups, mersilene (group 1) and prolene (group 2), according to the type of suture used. Maternal, newborn and pregnancy outcomes of the groups were compared.

Statistical Analysis

Continuous variables were represented by median (minimum-maximum), while categorical data were represented by number and percentage. Kolmogorov-Smirnov Goodness of Fit Test was used to analyze normality of continuous variables. Continuous variables were compared with the Independent Samples T Test when they had a normal distribution, and with the Mann Whitney U Test when they did not have a normal distribution. Risk factors and odds ratio values related to Mersilene use were determined by Logistic Regression Analysis (Backward: LR). Variables that were found to be significant as a result of both clinical and univariate analysis were selected and evaluated with the Multivariate Logistic Regression Model. Model fit was evaluated with the Hosmer-Lemeshow test. Comparison of categorical data was made with Chi-square Test (Fisher's Exact Test when necessary). According to previous study results, the sample size of the study population was calculated as 150 patients (α = 0.05 and study power = 80%). IBM SPSS Package Program version 22.0 was used for analyzes (IBM Corporation, Armonk, NY, USA). Statistical significance level was taken as $p<0.05$.

RESULTS

Comparison of the groups in terms of age, gravidity, parity, number of miscarriages and BMI revealed significantly higher mean gravidity in group 1 compared to group 2 ($P<0.05$), while groups were found to be similar in terms of age, parity, number of miscarriages and BMI ($P>0.05$, Table 1). No difference was determined with regard to gestational week at cerclage application, cervical length, cervical dilatation just before cerclage insertion, gestational age at cerclage removal and delivery and birth weight ($p>0.05$, Table 2). Groups were

Table 1. Demographic data of the patients.

	Cerclage type	N	Mean	Std. Deviation	P value
Age (years)	Mersylene Suture	40	31.83	6.460	
	Prolene Suture	39	29.69	5.979	0.1
Gravidity	Mersylene Suture	40	3.68	2.005	
	Prolene Suture	39	2.74	1.332	<0.05
Parity	Mersylene Suture	40	1.20	1.363	
	Prolene Suture	39	.74	1.019	0.09
Miscarriages	Mersylene Suture	40	1.45	1.648	
	Prolene Suture	39	1.00	.761	0.1
BMI (kg/m2)	Mersylene Suture	40	26.7053	3.80000	
	Prolene Suture	39	27.1457	5.54794	0.7

Table 2. The outcomes for patients according to cerclage type.

	Cerclage type	N	Mean	Std. Deviation	P Value
Gestational age at cerclage application (weeks)	Mersylene Suture	40	17.93	4.079	
	Prolene Suture	39	16.33	3.003	0.05
Cervical Length (mm)	Mersylene Suture	40	22.95	13.843	
	Prolene Suture	39	27.67	12.995	0.1
Cervical Dilatation (mm)	Mersylene Suture	40	1.05	1.584	
	Prolene Suture	39	.51	1.048	0.08
Gestational age at removal (weeks)	Mersylene Suture	40	34.63	5.021	
	Prolene Suture	39	35.46	3.776	0.4
Gestational age at delivery (weeks)	Mersylene Suture	40	34.90	5.098	
	Prolene Suture	39	35.85	3.997	0.4
Birth Weigth (gr)	Mersylene Suture	40	2545.00	905.575	
	Prolene Suture	39	2765.38	794.023	0.3

comparable in terms of subgroups established according to their number of previous deliveries (p>0.05). Groups were comparable in terms of indications for cerclage insertion (History based (23 vs. 28), emergency (13 vs. 5), ultrasound indicated (4 vs. 6), p>0.05). Cesarean delivery rate was 40 % in group 1 while it was 43.6 % in groups 2, no statistical difference was determined in terms of rate of cesarean delivery (p>0.05). Similar number of newborns needed NICU admission between the two groups following delivery (17.5% versus 17.9 %p>0.05). Mean APGAR scores at 1st (6.8 versus 7.4) and 5 th (7.8 versus 8.3) min were comparable between the groups (p>0.05)

DISCUSSION

The aim of this study is to compare the effectiveness of monofilament sutures (Proline™) and braided polyester thread (Mersilene™) in transvaginal cerclage and to evaluate pregnancy and newborn outcomes according to the thickness of these materials. In our study, comparison of the groups in terms of age, gravidity, parity, number of miscarriages and BMI revealed significantly higher mean gravidity in group 1 compared to group 2, while groups were found to be similar in terms of age, parity, number of miscarriages and BMI. No difference was determined with regard to gestational week at cerclage application, cervical length, cervical dilatation just before cerclage insertion, gestational age at cerclage removal and delivery and birth weight. Similar number of newborns needed NICU admission between the two groups following delivery. Mean APGAR scores at 1st and 5 th min were comparable between the groups.

Since McDonald cervical cerclage was first described 60 years ago as a technique to stabilize and prevent (PTB) the cervical insuffieciency, many gynecologists frequently use nonabsorbable sutures; however, there is not enough data to compare this suture type with others (13,14). Various materials have been used for cerclage. These materials include human fascia lata, Mersilene™ (Ethicon, NJ), Prolene™ (Ethicon, NJ), Tevdek™ (Teleflex, PA), and metal wires (15,16). The most commonly used are nonabsorbable monofilaments such as Mersilene™ (Thicon RS-21 or D-8113; Ethicon, NJ) (17) and prolene (18). Pregnancy outcomes of 109 pregnant women were presented according to the type of cerclage suture used, no difference was found between the pregnancy outcomes of the two groups (19).

Similar to our study, prevous study aimed to compare the effectiveness of monofilament suture (Proline™) and braided polyester thread (Mersilene™) sutures in transvaginal cerclage and to evaluate the pregnancy and neonatal results. Analysis of the data revealed that the prolene suture was applied to pregnant women with higher gravida, that the gestational age at delivery was significantly higher in the prolene suture group, and cervical lengths were lower in the mersilene suture group (20).

Another study comparing effectiveness of Mersilene tape versus alternative suture types in prolonging singleton pregnancies as well as other pregnancy and neonatal outcomes showed that Mersilene tape does not reduce the risk of preterm birth before 37, 28 or 24 weeks. Data showed that higher risk of preterm birth between 34 and 37 weeks with Mersilene tape but lower incidence before 34 weeks, higher neonatal morbidity and mortality (21).

Another data of 64 patients on this issue indicated that Mersilene, compared to Prolene, was associated with significantly lower rates of pretrm delivery at less than 24 weeks and less than 26 weeks (22).

Although mersilen sutures have traditionally been the material of choice for cerclage, prolene sutures appear to be associated with reduced PTB and improved neonatal outcomes. Although more comprehensive randomized clinical trials are needed to determine possible relationships between suture material and cerclage outcomes, prolene sutures continue to offer an option to traditional mersilene sutures (23).

Thick suture has been associated with a later gestational age at birth and a lower risk of birth and premature birth less than 34 weeks' gestation without significant increase in maternal or neonatal morbidity. In fact, thick cerclage suture was associated with lower odds of adverse maternal and neonatal outcomes, including chorioamnionitis and neonatal intensive care unit admission, compared to thin suture (24).

Monofilament suture did not reduce the rate of pregnancy loss compared with braided suture. Authors indicated that, clinicians should use the results of this trial to facilitate discussions regarding suture selection to optimize outcomes (25).

In conclusion, although mersilene stitch is commonly preferred based on previously published studies, according to our data analysis revealed similar results with prolene stitch in terms of maternal and neonatal outcomes.

Ethics Committee Approval:
Eskişehir Şehir Hastanesi Etik Kurulu approval was obtained before the study (22/02/2024-ESH/GOEK 2024/86).

Peer-review:
Externally peer-reviewed.

Author Contributions:
Z.B., M.K., M.Ş. conceived the study. and M.Ş., M.K. searched the literature and collected the data. M.K., Z.B. and M.Ş. performed the statistical analysis. Z.B., M.K., M.Ş. drafted the manuscript. Z.B., M.Ş., M.K. reviewed the manuscript. Both authors contributed to editorial changes in the manuscript. Both authors have read and approved the final paper. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work. retrospective study, patient consent was not a requisite component.

Conflict of Interest:
The authors declared that there is no conflict of interest.

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None

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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Evaluation of the effectiveness of obstetric lubricant gel in labor in nulliparous and primiparous women: a randomized controlled study

Nullipar ve primipar kadınlarda doğumda obstetrik lubrikan jelin etkinliğinin değerlendirilmesi: Randomize kontrollü çalışma

Sahin Kaan BAYDEMIR[1], Bircan YILDIRIM BAYDEMIR[2], Can Ozan ULUSOY[1], Ali GOKCE[2], Tuncay YUCE[3], Feride SOYLEMEZ[2]

[1]Ministry of Health, Etlik City Hospital, Ankara, Türkiye
[2]University of Ankara, Department of Obstetrics and Gynecology, Ankara, Türkiye
[3]Private Clinic, Gaziantep, Türkiye

ABSTRACT

Aim: Our hypothesis was that lubricating gels used at the beginning of the active phase of labor could reduce the incidence of episiotomies and shorten the duration of labor. This study aims to investigate and confirm this theory with a randomized controlled trial.

Material and Methods: A prospective randomized controlled trial was conducted at obstetrics and gynecology department of a university hospital between January 2017 and April 2017. The study included 102 nulliparous and 93 primiparous singleton pregnancies. 50 primiparous women and 47 nulliparous patients were randomly assigned to the obstetric gel group. Obstetric gel was applied to participants in the study groups at the beginning of the active phase of labor. Outcomes were episiotomy rates and duration of labor.

Results: Episiotomy rates were significantly lower in nulliparous obstetric gel group (36.1% and 63.6%, p=0.005). The duration of the active phase of the first and second stage of labor was significantly lower in the obstetrical gel groups compared to the control groups in both parities (150±86 and 203.5±134, p=0.021, 28.8±18.2 and 62.6±53.8, p<0.001 in nulliparous and 143.4±61.4 and 185.3±97.2, p=0.016, 21.5±14.8 and 36.9±34.1, p=0.006 in primiparous, respectively).

Conclusion: The application of obstetric gel shortened the duration of the active phase of the first stage of labor and the duration of the second stage of labor. In addition, we observed that episiotomy rates were reduced by the use of obstetric gel in the nulliparous group.

Keywords: Episiotomy; labor; obstetric gel; parturition; second stage of the labor

ÖZ

Amaç: Çalışmanın amacı doğumun aktif fazının başlangıcında kullanılan kayganlaştırıcı jellerin epizyotomi insidansını azaltabileceğini ve doğum süresini kısaltabileceğini göstermektir. Bu çalışma, bu teoriyi randomize kontrollü bir çalışma ile doğrulamayı amaçlamaktadır.

Gereç ve Yöntemler: Ocak 2017 ile Nisan 2017 tarihleri arasında bir üniversite hastanesinin kadın hastalıkları ve doğum kliniğinde prospektif randomize kontrollü bir çalışma olarak yürütülmüştür. Çalışmaya 102 nullipar ve 93 primipar tekil gebelik dahil edildi. 50 primipar kadın ve 47 nullipar hasta randomize edilerek obstetrik jel grubuna dahil edilmiştir. Çalışma gruplarındaki katılımcılara doğumun aktif fazının başında obstetrik jel uygulanmıştır. Sonuçlar gruplar arasında epizyotomi oranları ve doğum süresilerinin farkının değerlendirilmesidir.

Bulgular: Epizyotomi oranları nullipar obstetrik jel grubunda anlamlı olarak daha düşük olarak bulunmuştur (%36.1 ve %63.6, p=0.005). Doğumun birinci ve ikinci evresinin aktif fazının süresi her iki paritede de obstetrik jel gruplarında kontrol gruplarına kıyasla anlamlı olarak daha düşük saptanmıştır (150±86 ve 203.5 ±134, p=0.021, nulliparlarda 28.8±18.2 ve 62.6±53.8, p<0.001 ve primiparlarda sırasıyla 143.4±61.4 ve 185.3±97.2, p=0.016, 21.5±14.8 ve 36.9±34.1, p=0.006).

Sonuç: Obstetrik jel uygulaması doğumun birinci evresinin aktif fazının süresini ve doğumun ikinci evresinin süresini kısaltmıştır. Ayrıca, nullipar grupta obstetrik jel kullanımı ile epizyotomi oranlarının azaldığını gözlemlenmiştir.

Anahtar Kelimeler: Epizyotomi; doğum; obstetrik jel; parturisyon; doğumun ikinci evresi

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Sorumlu Yazar/Corresponding Author: Şahin Kaan BAYDEMİR, Ministry of Health, Etlik City Hospital, 6010 – Etlik / Ankara, Türkiye
E-mail: drkaanbydmr@gmail.com

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INTRODUCTION

The first stage and second stages of labor are the two phases of vaginal birth. The latent phase and the active phase are additional divisions of the first stage of work. The point at which there is a noticeable rise in the rate of cervical dilatation is known as the active phase of labor. Cervical dilation of 6 cm be considered the start of the active phase of labor. When the cervical dilation is complete, the second stage of labor begins and finishes with the delivery of the newborn (1). It has been demonstrated that there is an increased risk of adverse maternal and neonatal outcomes in cases of protraction and arrest disorders, including cesarean delivery, chorioamnionitis, postpartum hemorrhage, fetal acidosis, and neonatal intensive care unit (NICU) admission (2). In a retrospective study of 19,000 patients, it was shown that when the definition of prolongation of the 2nd stage of labor was increased by 1 hour, cesarean section rates decreased, but neonatal acidemia, NICU admission and 3rd-4th degree perineal injuries increased (3).

Multiple adaptive chances are needed for vaginal delivery. Vaginal delivery has been described as a potentially stressful experience by Nygaard (4). Many strategies have been put forth to lessen the traumatic impact of childbirth. Warm compresses and perineal massage have been recommended as ways to stretch and soften the perineum (5). Additionally, it has been discovered that increasing the number of midwives can aid to lessen perineal damage during labor (6). The perineum is traumatized by episiotomy in addition to the stress caused by vaginal delivery. It is no longer recommended that routine episiotomy be performed and the decision to perform an episiotomy is at the discretion of the clinician at the time of delivery. The limited use of episiotomy has been demonstrated to reduce the risk of perineal and vaginal injury (7, 8).

Reducing the trauma associated with vaginal birth has recently become a significant topic of interest. There are a limited number of studies in the literature investigating the use of lubricant gels. The effects of using lubricant gels remain unclear and continue to be a subject of debate (9). It has already been hypotized that obstetric gel could help reduce friction during labor. Thus the duration of labor may be shortened and perineal trauma may be reduced (10). Contradictory findings exist regarding the use of lubricant gels during labor. While some studies, such as those by Seval et al. (11) and Azardish et al. (9) , suggest that lubricant gels shorten labor stages and reduce episiotomy rates, a meta-analysis found no significant impact on the duration of the second stage of labor (10).

The objective of this study is to investigate and confirm the hypothesis that the application of lubricant gels at the beginning of the active phase of labor may reduce the duration of delivery and episiotomy rates The objective of this study is to investigate and confirm this hypothesis through a randomized controlled trial.

MATHERIALS AND METHODS

Pregnant women who were admitted to obstetrics and gynecology department of the university hospital for vaginal delivery between January 2017 and April 2017 were assessed for eligibility. This study was conducted in accordance with the ethical standards set by the Declaration of Helsinki. The institutional ethics committee of the university approved the study (approval no: 09-606-18) and written informed consent has been obtained from all patients. The study included nulliparous and primiparous singleton pregnancies between 37 and 41 weeks + six days of gestation and vertex presentation of the fetus with an estimated birth weight of 2000–4500 g. The study excluded multiparous pregnancies and women who had previously undergone a cesarean section, as well as those with contraindications to vaginal delivery. PG E1 or PG E2 was not used for cervical dilatation. Patients requiring medication for cervical dilatation were not included in the study. NCT number is NCT06069596. It was obtained retrospectively.

The participants were separated into two distinct categories, namely nulliparous and primiparous, on the basis of their parity status. Each cohort comprised 110 participants initially. The nulliparous and primiparous groups were randomly assigned to either the study or control group in a 1:1 ratio using a computer-generated randomization program to ensure a randomized and unbiased selection process. The randomization procedure was conducted in a double-blind manner, with the investigators responsible for the study remaining unaware of the allocation until the conclusion of the study. All participants in the study received the standard antepartum care regimen in the delivery room. A total of 25 patients were lost to follow-up during the course of the study. Consequently, obstetric lubricant gel was administered to patients in the study groups, which included 47 nulliparous and 50 primiparous patients. Clinical care of the participants was provided by same team of physicians with no changes about study protocol. Patients did not undergo routine amniotomy. However, in patients who did not have spontaneous rupture of amniotic membranes during the progression of the active phase, amniotomy was performed when cervical dilatation was 8-9 cm. Continious fetal monitoring was performed until the delivery. No patient received epidural anesthesia during labor. Maternal and fetal parameters was recorded by partograph during labor. APGAR scores were evaluated by a neonatologist who was not informed about the study and the groups. At the onset of the active phase of labor, a specially designed applicator was

used to administer obstetric lubricant gel to the vaginal canal. The study utilized a highly viscous, isotonic gel with a mildly acidic pH ranging from 6.0 to 6.7. This gel comprised hydroxyethylcellulose, propylene glycol, and glycerin. The packaging included a sterile 15 ml syringe and a flexible applicator.

The active phase of the first stage of labour was defined as starting with cervical dilation of 3–5 cm or more, in the presence of active uterine contractions (>200 Montevideo units), ending with complete cervical dilation. The second stage of labour was defined as starting when cervical dilation is complete and ending with fetal delivery. The primary outcome was duration of active phase and second stage of labor while the secondary outcomes were observation of type of the delivery (cesarean or vaginal delivery), episiotomy rates, ocytocin requirement, analgesic requirement, birth weight and APGAR scores of the newborns.

Statistical Analysis

Data analyzes were performed by using SPSS Version 21.0 (IBM Corporation, Armonk, NYC, USA). Samples were tested with Shapiro Wilk to determine normality of distributions. According to the results, non parametric tests were preferred. Continuous variables were compared with Mann Whitney U test. Categorical variables were compared with Chi square test or Fisher's exact test where appropriate. A P value of <0.05 was considered statistically significant. The sample size calculation based on previously published data (12) revealed that this study needs recruit at least 84 persons for each group to have 80% power with 5%.

RESULTS

Flowchart of this study is shown in Figure 1. Between January 2017 and April 2017, a total of 220 patients who applied for delivery participated to the study. All the participants were divided into two groups based on their parity. Nulliparous and primiparous pregnant women were randomized using a computer system. Twenty five patients were lost to follow up during the labor. The numbers of patients in the obstetric gel groups were 47 and 50, respectively (Figure 1).

There were no significant differences between the groups in terms of age, gestational age, body mass indexes, cesarean rates, oxytocin induction, bishop scores at the time of gel application and APGAR scores in both parity groups (Table 1). In nulliparous women, fetal birth weights were similar in both groups, although the fetal birth weights in primiparous control group were higher than the obstetric gel group (3418 ± 421 grams and 3245 ± 383 grams, p=0.042, respectively). While, episiotomy rates were significantly lower in nulliparous obstetric gel group (36.1% and 63.6%, p=0.005, respectively), there was no significant difference in primiparous group (36% and 29.1%, p=.449, respectively). The duration of the active phase of the first stage and the second stage of the labor were significantly lower in obstetric gel groups compared to the control groups in both parity (150±86 mins and 203.5±134 mins, p=0.021, 28.8±18.2 mins and 62.6±53.8 mins, p<0.001 in nulliparous, and 143.4±61.4 mins and 185.3±97.2 mins, p=0.016, 21.5±14.8 mins and 36.9±34.1 mins, p=0.006 in primiparous, respectively). APGAR scores were similar across

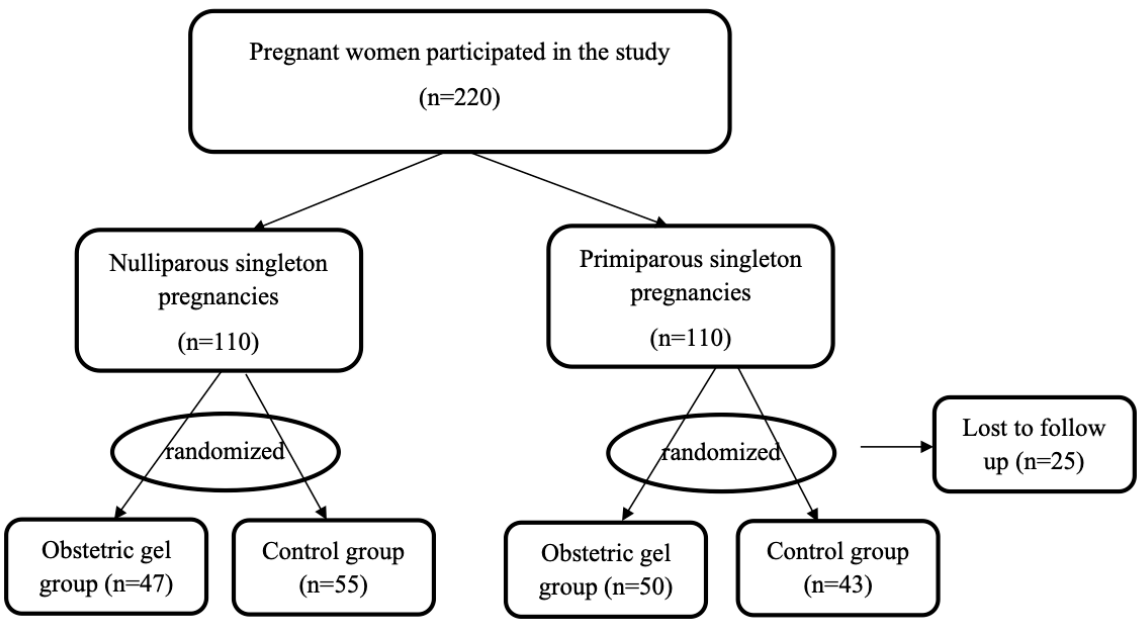

Figure 1. Flow chart of the study

Table 1. Patients characteristics and outcome variables of the study population

	Nulliparous			Primiparous		
	Obstetric gel group (n=47)	Control group (n=55)	P value	Obstetric gel group (n=50)	Control group (n=43)	P value
Age, years, mean ± SD	26.7±4.7	26.4 ±5.1	0.917	26.9±5.1	27.7±4.7	0.759
Gestational age, days, mean ± SD	273.4±6.1	271.7±5.8	0.892	271.1±4.3	275.5±8.3	0.436
BMI, kg/m², mean ± SD	30.66±4.44	29.96±4.11	0.410	29.73±4.30	31.33±4.49	0.084
Cesarean section, n(%) -fetal distress -failure to progress	6(12.7%) 3(6.3%) 3(6.3%)	12(21.8%) 5(9.0%) 7(12.8%)	0.231	2(4%) 2(4%) 0	4(7.2%) 3(5.2%) 1(2%)	0.470
Episiotomy rates, n(%)	17(36.1%)	35(63.6%)	**0,005**	18(36%)	16(29.1%)	0.449
Ocytocin induction, n(%)	22 (46.8%)	27(49.1%)	0.818	15(30%)	19(34.5%)	0.619
Bishop score*, mean ± SD	9.76±0.86	9.65±0.88	0.524	9.66±0.86	9.69±0.96	0.851
Duration of the active phase of the first stage, min, mean ± SD	150±86	203.5±134	**0.021**	143.4±61.4	185.3±97.2	**0.016**
Duration of the second stage, min, mean ± SD	28.8±18.2	62.6±53.8	**<0.001**	21.5±14.8	36.9±34.1	**0.006**
Fetal weight, g, mean ± SD	3284±448	3250±377	0.793	3245±383	3418±421	**0.042**
APGAR 1, mean ± SD	7.32±1.47	7.48±0.9	0.472	7.85±0.91	7.55±0.88	0.529
APGAR 5, mean ± SD	8.95±0.97	8.96±0.47	0.692	9.26±0.44	9.01±0.75	0.524

*Bishop score at the time of gel application
‡ Mann-Whitney U, T test or Chi-square test SD: Standard deviation

all groups. No side effects were observed with the use of obstetric lubrican gel.

DISCUSSION

The findings of the present study demonstrated that the duration of the active phase of the first stage of labor and the duration of the second stage of labor were shorter in the obstetric gel groups. Additionally, the rate of episiotomy was found to be significantly lower in the obstetric gel group among nulliparous women.

A limited number of studies have been published on this topic. In a randomized controlled trial (RCT) published by Schaub et al. in 2008, it was demonstrated that the application of the obstetric gel resulted in a notable reduction in the duration of the second stage of labor (12). Although the use of lubrican gel resulted in a reduction in the duration of the first stage of labor and the total duration of labor, these findings were not statistically significant. Additionally, the author indicated that the incidence of perineal tears was lower in the group that received the obstetric gel. No adverse effects were observed. Aydın et al. also reported similar findings. The durations of the first and second stages of labor were found to be shorter in the obstetric gel group compared to the control group (13). In an RCT conducted by Seval et al. in 2017, it was observed that the mean duration of the second stage of labor was significantly shorter in the obstetric gel group compared to the control group, regardless of the number of previous pregnancies (45±34 minutes and 58±31 minutes, respectively; p=.005) (14). Among nulliparous women, the mean duration of the second stage of labor was found to be shorter in the study group compared to the control group (53±52 mins and 83±42 mins, respectively; p = 0.003). However, no statistically significant difference was observed between the two groups in multiparous women with regard to the duration of the first and second stages of labor. Additionally, the authors indicated that the 5-minute APGAR scores of the study group were significantly higher than control group. No significant difference was observed in the duration of the active phase of the first stage of labor. In a recent RCT, Azarkish et al. investigated the effects of an obstetric gel on the length of labor and perineal trauma in primiparous women (9). The study reported that the mean duration of the total length of labor, the first stage, and the second stage were significantly shorter in the obstetric gel group compared to the control group in primiparous women. Furthermore, the authors have indicated that perineal health was notably superior in the obstetric gel group. The percentage of women who underwent episiotomy and experienced perineal trauma was significantly lower in the obstetric gel group compared to the control group. Additionally the authors stated that the mean duration of the first stage of labor was reported to be 141.64±77.89 minutes in the obstetric gel group

and 190.02±117.60 minutes in the control group. Furthermore, the duration of the second stage of labor was 37.62±18.24 in the study group and 43.69±16.24 in the control group. A systematic review and meta-analysis published in 2022 demonstrated that the utilization of lubricant gel was associated with a reduction in the occurrence of perineal trauma, the administration of episiotomy, and second-degree perineal laceration, in addition to a shorter second stage of labor (15) .

In contrast with these findings, Ashwal et al. reported no reduction in the durations of the stages of labor following the administration of an obstetric gel. The mean lengths of the active and second stages of labor were 157 minutes and 48 minutes, respectively, in the obstetric gel group and 219 minutes and 56 minutes, respectively, in the control group (16). The authors noted that these differences did not achieve statistical significance. In the cited study, the groups were randomly assigned, regardless of the number of previous pregnancies. The Ashwal et al. study included both nulliparous and multiparous women in its groups. One hypothesizes that a significant difference would have been identified between the groups had the groups been divided in accordance with parity. Furthermore, the authors indicated that while the obstetric gel group exhibited lower rates of grade II perineal tears and episiotomy compared to the control group, there were no statistically significant differences between the groups in terms of rates of episiotomy and grade II perineal tears. Furthermore, Aquino and colleagues published a meta-analysis that included three studies that are referenced in this article. The authors indicated that the application of obstetric gel does not result in a reduction in the length of labor. However, the authors also stated that the use of lubricant gel could potentially reduce perineal trauma by reducing friction through a purely physical effect, thereby decreasing the opposing force during vaginal birth (10). Furthermore, the study indicated that the rates of operative vaginal births and cesarean sections did not differ between the obstetric gel and control groups. Additionally, the use of obstetric gel did not result in a reduction in the duration of the second stage of labor. In a recently published expert opinion, the authors posit that perineal massage and stretching of the perineum with a water-soluble lubricant gel during the second stage of labor are associated with an increased rate of intact perineum and a decreased rate of severe perineal trauma and episiotomy. The authors recommend perineal massage as a technique to reduce severe perineal trauma during the second stage of labor (17). It was reported that perineal massage was associated with a 51% reduction in the incidence of severe perineal trauma and a 44% reduction in the requirement for episiotomy (18). It is nevertheless recommended that obstetric gel should not be used as a lubricating gel in the absence of perineal massage (17).

The present study findings indicate that the obstetric gel did not affect the rates of cesarean section. However, the length of the active phase of the first stage of labor and the length of the second stage of labor were shorter in the obstetric gel group. A prospective randomized controlled study with different groups, such as an obstetric gel group, an obstetric gel group with perineal massage, and a control group, may provide greater clarity. Additionally, the rate of episiotomy was found to be significantly lower in the obstetric gel group among nulliparous women.

Study Limitations

Our study has several limitations. One limitation was the degree of standardization of the methodology. To maximize standardization, all patients were consistently monitored and received gel application by the same team. However, a higher level of standardization could have been achieved if all interventions and follow-ups were performed by a single specialist. The lower mean birth weight of the infants in the obstetric gel group, as compared to the control group, among primiparous pregnant women may have influenced the study results in a manner that favored the study group. This represents a potential limitation of the study. Our study also has several strengths. The present study was a prospectively designed randomized controlled trial with group allocation based on patient parity.

CONCLUSION

In the present study, we have found that the application of obstetric gel shortened the duration of the active phase of the first stage of the labor and the duration of the second stage of the labor. In addition, we have observed that episiotomy rates were reduced by using obstetric gel in nulliparous group.

Conflict of Interest

The authors declared no conflict of interests.

Ethics Committee Approval:

The institutional ethics committee of the university approved the study (Ankara University Ethics Committee) and written informed consent has been obtained from all patients.

NCT number is NCT06069596. It was obtained retrospectively.

The study was presented as an oral presentation at EBCOG-TJOD 2017 in Turkey.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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Clinical use of PGE2 (dinoprostone) and cervical ripening balloon catheter during delivery induction in patients with a Bishop score of ≤4 with vertex presentation

Bishop skoru ≤4 olan vertex geliş hastalarda doğum indüksiyonunda PGE2 (dinoproston) ve servikal olgunlaştırıcı balon kateterin klinik kullanımdaki yeri

Hakkı ŞERBETÇİ[1], Melih VELİPAŞAOĞLU[1], Hüseyin Mete TANIR[1]

[1]Department of Obstetrics and Gynecology, Osmangazi University Faculty of Medicine, Eskişehir, Türkiye

ABSTRACT

Aim: We aimed to compare the clinical use of PGE2 (dinoprostone) and cervical ripening balloon catheter for delivery induction in patients with a Bishop score of ≤4 with vertex presentation.

Material and Methods: This study was retrospectively conducted and included the induction of labor between January 2014 and January 2017 at Eskisehir Osmangazi University, Department of Obstetrics and Gynecology. There was a total of 60 patients in the study and 30 patients were given dinoprostone and 30 patients were given birth by double balloon catheter. We compared the clinical results of the patients. Multivariable regressions were used to identify odds of induction success.

Results: There was no significant difference between the demographic characteristics of the patients. When the clinical results of the patients were compared, there was no difference between the vaginal delivery rate and the delivery time between the two groups. The duration of active labor in the balloon catheter group was statistically significantly longer (p = 0.036). The amount of postpartum hemorrhage in the balloon catheter group was also significantly higher (p = 0.008).

Conclusion: The ideal agent to be used in cervical pregnancy is still a controversial issue. In this regard, more work needs to be done with the patient.

Keywords: PGE2, Double balloon catheter, induction of labor, cervical ripening

ÖZ

Amaç: Bu çalışmada Bishop skoru ≤4 olan vertex geliş hastalarda doğum indüksiyonunda PGE2(dinoproston) ve servikal olgunlaştırıcı balon kateterin klinik kullanımdaki yerini karşılaştırmak amaçlandı.

Gereçler ve Yöntem: Bu çalışma retrospektif yapılmış olup Eskişehir Osmangazi Üniversitesi Kadın hastalıkları ve Doğum Anabilim Dalında Ocak 2014 -Ocak 2017 tarihleri arasında yapılan doğum indüksiyonlarını kapsamaktadır. Çalışmada toplam 60 hasta mevcut olup 30 hastaya dinoproston ile 30 hastata ise çift balon katater ile doğum indüksiyonu yapılmıştır. Hastaların klinik sonuçları karşılaştırılmıştır. İndüksiyon sonucuna etki edebilecek faktörler lojistik regresyon modeli ile analiz edildi.

Bulgular: Hastaların demografik özellikleri arasında anlamlı fark yoktu. Hastaların klinik sonuçları karşılaştırıldığında ise her iki grup arasında vajinal doğum oranı ve doğum süreleri arasında fark saptanmadı. Balon katater grubunda aktif doğum eylemi süresi istatistiksel olarak anlamlı ölçüde uzun saptandı (p=0,036). Balon katater grubunda postpartum kanama miktarı anlamlı ölçüde fazlaydı (p=0,008).

Sonuç: Servikal olgulaşmada kullanılacak ideal ajan hala güncel bir tartışma konusudur. Bu konuda daha fazla hastayla yapılacak çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: PGE2, Çift balon katater, doğum indüksiyonu, servikal olgunlaşma

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Sorumlu Yazar/Corresponding Author: Hakkı ŞERBETÇİ, Department of Obstetrics and Gynecology, Osmangazi University Faculty of Medicine, Odunpazarı, Eskişehir, Türkiye
E-mail: leo.trakya@gmail.com

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INTRODUCTION

Induction of labour is a fundamental practice in modern obstetrics. The intravenous administration of oxytocin for the purpose of inducing labour is currently the most commonly employed method (1). In this regard, intravaginal PGE2, which represents one of the most recently introduced methods for labour induction in clinical practice, is being employed with increasing frequency (2, 3).

Induction of labour with a balloon catheter, which is a mechanical method, is a relatively novel technique, and there is a paucity of studies on the subject in the literature. In a study in which clinical experiences obtained with balloon catheter were compared with the existing literature, it was reported that the use of a balloon catheter for induction resulted in a lower rate of caesarean section than other induction methods (4).

In a separate evaluation, it is asserted that the utilisation of a balloon catheter during the induction phase offers a number of advantages, including simplicity, cost-effectiveness and the absence of significant adverse systemic effects (5). Furthermore, a study comparing the use of prostaglandin, oxytocin and balloon catheter applications concluded that induction with a balloon catheter resulted in a reduction in caesarean section rates and a shorter duration of labour (6). In one study, it was shown that tachysystole and uterine hyperstimulation developed at higher rates with the use of prostaglandin compared to balloon catheterisation and that the use of prostaglandin in addition to balloon catheterisation did not provide additional benefit (7).

In the light of these findings, the aim of this study was to compare the clinical outcomes of patients who underwent balloon catheterisation and PGE2 (dinoprostone) administration.

There are studies directly comparing the results of balloon catheterisation and PGE2 (dinoprostone) administration. In our study, we aimed to compare the effect of balloon catheter and dinoprostone on cervical maturation and clinical outcomes in patients with Bishop score ≤4.

MATERIALS AND METHODS

This study was designed as a retrospective observational study comprising women with term pregnancies who underwent induction of labour between January 2014 and January 2017 at the Department of Obstetrics and Gynaecology, Eskisehir Osmangazi University. The study population was divided into two groups: the first group (n=30) underwent cervical ripening with a balloon, while the second group (n=30) underwent cervical ripening with dinoprostone.

Vaginal bleeding, multiple pregnancy, anomalies of presentation, contraindications for vaginal delivery (placenta previa, genital herpes, genital chonduloma), caesarean section or uterine surgery, estimated fetal weight of 4500 g or more were excluded.

The demographic characteristics (age, gravida, etc.) and obstetric ultrasonography findings of all patients selected for the study and control groups were recorded on special forms. The patients were then taken to the gynaecological table, where the genital area, vagina and cervix were examined. Bishop scoring was performed for each patient. Patients with a Bishop score of ≤4 were included in the study, while patients with a Bishop score above 4 were excluded.

Among 60 pregnant women, 30 pregnant women underwent cervical ripening balloon and the other 30 pregnant women underwent cervical ripening and dilatation with dinoprostone. After obtaining informed consent from both groups, cervical ripening and dilatation with cervical ripening balloon in one group and cervical ripening and dilatation with dinoprostone in the other group were performed. Each balloon of the double-balloon cervical ripening balloon was inflated with 80 ml saline. After the procedure, both groups of pregnant women were compared in terms of the time between the start of induction and delivery, need for additional oxytocin, duration of active labour (from 4cm opening to delivery), uterine hyperstimulation, mode and outcome of delivery, rate of caesarean section due to fetal distress in labour, rate of non-progressive labour, amount of postpartum haemorrhage, postpartum APGAR scores 1, 5, minutes, rates of amniotic fluid with meconium and reasons for induction. The weight of blood-soaked objects is calculated to estimate the loss of blood in millilitres.

Statistical Package for the Social Sciences (SPSS) for Windows 24.0 was used for statistical calculations and comparisons. The conformity of the data to normal distribution was tested by Shapiro-Wilk test. Pearson exact chi-square, Pearson chi-square, Continuity correction chi-square and Fisher exact chi-square tests were used in statistics. Independent samples t test was used for parametric samples. In addition, non-parametric Spearman correlation coefficient was used. Data were presented as arithmetic mean and standard deviation and $p<0.05$ was considered statistically significant.

RESULTS

There was no statistically significant difference between the demographic characteristics of the study and control groups (Table 1).

While 13 (43%) of the patients in the balloon catheter group delivered vaginally, 18 (60%) of the patients in the dinoprostone group delivered vaginally. 17 (56.7%) of the patients in the balloon catheter group and 12 (40%) of the patients in the dinoprostone group underwent caesarean section. There was no significant difference in the rates of caesarean section (p=0.301) (Table 2).

In the balloon catheter group, 5 (16.6%) of the pregnant women underwent caesarean section for fetal distress and 10 (33.3%) for non-progressive labour; in the probe group, 3 (10%) of the pregnant women underwent caesarean section for fetal distress and 9 (30%) for non-progressive labour. Although the number of pregnant women undergoing caesarean section for non-progressive labour was higher in the balloon group than in the dinoprostone group, the difference was not statistically significant (p=0.1). Although the number of pregnant women who underwent caesarean section for fetal distress was higher in the balloon group than in the dinoprostone group, no statistically significant difference was found. (p=0.706). 2 patients in the balloon catheter group underwent caesarean section for unexplained vaginal bleeding. Placental abruption was suspected.

No uterine hyperstimulation was observed in both double balloon catheter and dinoprostone groups. It was also observed that there was no statistically significant difference between the postnatal apgar scores and birth weights of both groups in the study (Table 3).

The mean amount of postpartum haemorrhage was 318±219 ml in the balloon catheter group and 201±60 ml in the dinoprostone group. The balloon catheter group was found to be significantly higher among the postpartum haemorrhage amounts (p=0.008). In the balloon catheter group, three out of 30 patients experienced a uterine atony complication. Conversely, no instances of uterine atony were observed in the dinoprostone group. However, no statistically significant difference was identified between the two groups in terms of uterine atony (p=0.237).

The incidence of meconium-stained amniotic fluid detected during labour was one case in the dinoprostone group and no instances of meconium-stained amniotic fluid were observed in the balloon catheter group. No statistically significant difference was observed between the two groups in terms of meconium-stained amniotic fluid (p=0.1).

Table 1. Demographic comparison of the patient groups

	Labour Induction Form		P value
	Baloon Cathater	**Dinoprostone**	
Number of Patients	30	30	-
Age	28.76±6.10	26.23±3.87	0,061
Gravidity	1(1-7)	1(1-11)	0.689
Parity	1(0-3)	1(0-10)	0.629
Gestational week of birth	38.4±1.2	37.8±0.9	0.051

*p<0.05 was considered statistically significant

Table 2. Comparison of balloon catheter and dinoprostone groups in terms of delivery modes and C/S indications

		Labour Induction Form		P value
		Baloon Cathater	**Dinoprostone**	
Type of birth	Vaginal	13(%43,3)	18(%60)	0.301
	Cesarean	17(%56,7)	12(%40)	
Indications for C/S				
	Fetal distress	5(%16,6)	3(%10)	0.706
	Non-progressive labor	10(%33,3)	10(%30)	0.1
	Placental abruption	2(%11)	0	0,077

*p<0.05 was considered statistically significant

Table 3. Comparison of groups in terms of labor duration and clinical outcomes

	Labour Induction Form		P value
	Baloon Cathater	Dinoprostone	
Apgar 1st minute	9(8-9)	9(8-9)	0,606
Apgar 5th minute	10(9-10)	10(9-10)	0,985
Birth weight	2899±519	2971±490	0.556
Postpartum haemorrhage (ml)	318±219	201±60	**0.008**
Duration of labor (hour)	16.50 ± 8.35	13.75 ± 8.52	0.212
Duration of active labour (hour)	6.54 ± 4.08	4.45 ± 1.73	0.036

*p<0.05 was considered statistically significant

The mean time between the induction of labour and the onset of labour was 16.50 ± 8.35 hours in the balloon catheter group and 13.75±8.52 hours in the dinoprostone group. No statistically significant difference was observed between the two groups (p=0.212). A comparison of the duration of active labour revealed that it was 6.54±4.08 hours in the balloon catheter group and 4.45±1.73 hours in the dinoprostone group. The duration of active labour in the balloon catheter group was found to be significantly longer than that observed in the dinoprostone group (p=0.036) (Table 3).

DISCUSSION

Medical or obstetric complications during pregnancy may require cervical ripening and induction of labour. Induction of labour is required in approximately 20-30% of all pregnancies (8, 9). There are numerous techniques that may be employed to induce labour. In term pregnancies, if the onset of labour is not occurring in a normal manner and a caesarean section is not indicated, it is necessary to facilitate the ripening of the cervix. A variety of methods have been employed for this purpose. In the present era, prostaglandin derivative drugs are frequently employed for the purpose of cervical maturation and labour induction. Oxytocin is a safe and effective agent for the induction of uterine contractions. Nevertheless, the efficacy of this approach is frequently contingent upon the condition of the cervix at the outset of labour induction (1).

In a study comparing balloon catheter and misoprostol in the literature, the amount of postpartum haemorrhage was found to be similar with both methods (10). In our study, balloon catheter application caused a significant increase in the amount of postpartum haemorrhage compared to induction with dinoprostone. The reason for this was the development of uterine atony and consequently postpartum haemorrhage in 3 patients in the balloon catheter group. There is no study in the literature showing a relationship between balloon catheter and uterine atony.

In a prospective randomised controlled trial of 210 patients comparing dinoprostone and double balloon catheter, the rate of uterine tachysystole was significantly higher in the dinoprostone group (11). The reason why uterine tachysystole was not observed in our study may be due to the relatively small number of patients.

A comparison of the patients in the study revealed that eight individuals in the dinoprostone group and 13 in the balloon group received oxytocin for a mean duration of 3.87±2.58 and 4.34±1.99 hours, respectively, to facilitate labour induction. No significant difference was observed in the need for additional oxytocin between the two groups. In a separate study comprising a larger patient cohort, it was observed that the requirement for supplementary oxytocin was markedly elevated in the double balloon catheter group relative to the dinoprostone group during labour induction in women with a Bishop Score below 6 (12).

When the duration of active labour was compared, it was calculated as 6.54±4.08 hours in the balloon catheter group and 4.45±1.73 hours in the dinoprostone group. The duration of active labour in the balloon catheter group was significantly longer than that in the dinoprostone group (p=0.036). In contrast, in a study conducted with nulliparous women with a Bishop Score below 6, it was found that the duration of labour with double balloon catheter was shorter than in the dinoprostone group (13). However, more studies with a larger number of patients are needed in this field.

It is known that a mature cervix is associated with an increased amount of oxytocin receptors in the myometrium. Therefore, although multiparous patients give birth faster, the lack of increase in the amount of postpartum uterine atony and bleeding may also be related to this situation. It is also possible to obtain the effects mentioned above with direct protoglandin administration,

but uterine tachysystole is a condition that should be carefully observed during labour induction. If this condition is observed, induction should be stopped or the dose should be reduced, but oral or vaginal misoprostol administration is not easily reversible. In addition, one study showed that increasing the dose of prostoglandin administered did not change the success of labour induction, although it shortened the duration of labour (14). In the light of these data, the balloon method, which is more physiological and relatively easier to reverse, may be a more rational choice.

Although it was not calculated in this study, the lower cost of balloon application, especially considering that it is reusable, can be considered as a reason for preference compared to other methods.

In our study, no significant difference was observed between the 1st and 5th minute APGAR scoring of the newborns in both groups and it is thought that the balloon catheter does not have a negative effect on postnatal outcomes.

The principal objective of this study was to assess the utilisation and clinical efficacy of a balloon catheter, which is not a commonly employed device in our country. The balloon catheter appears to be a viable option in terms of reusability and cost-effectiveness. The markedly elevated incidence of postpartum haemorrhage in comparison to dinoprostone can be attributed to the occurrence of uterine atony observed in the balloon catheter cohort. Further studies with larger patient populations are required to fully demonstrate the clinical efficacy of this approach in our country. If the findings of larger studies confirm that induction with a balloon catheter results in fewer systemic side effects, a lower incidence of caesarean section, and reduced costs, it could be offered as the preferred method for inducing labour in suitable patients.

Ethics Committee Approval

The study protocol received approval from the relevant institutional ethics committee on 30/06/2017 (reference number 201).

Author Contributions

H.S.: Conception and design of the study; analysis and interpretation of the data and writing-review. M.V.: Conception and design of the study; analysis and interpretation of the data. M.T: Methodology, supervision.

Conflict of Interest

The authors have no conflicts of interest revelant to this article.

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Evaluation of prenatal invasive testing complications in a tertiary care centre

Üçüncü basamak merkezde prenatal invaziv test komplikasyonlarının değerlendirilmesi

Zafer BÜTÜN[1], Masum KAYAPINAR[2], Ece AKÇA SALIK[3], Gökalp ŞENOL[4], Kamuran SUMAN[5]

[1]Private Clinic, Perinatology, Eskisehir, Türkiye
[2]Private Clinic, Perinatology, Mersin, Türkiye
[3]Eskişehir City Hospital, Obstetric and Gynecology, Eskişehir, Türkiye
[4]Hitit University, Erol Olçok Education and Research Hospital, Clinic of Perinatology, Çorum, Türkiye
[5]Afyonkarahisar Hospital, Afyonkarahisar, Türkiye

ABSTRACT

Aim: Invasive tests such as amniocentesis or chorionic villus sampling (CVS) are associated with an increased risk of miscarriage, testing should be done with caution in pregnancies considered to be at high risk for aneuploidies and other genetic disorders. The aim of our study is to present the complications that develop after invasive prenatal tests such as amniocentesis, cordocentesis and chorionic villus sampling.

Materials and Methods: A retrospective observational study was conducted covering a period of 3 years and 1 month, involving 282 pregnant women at high risk of genetic disorders who underwent invasive prenatal testing such as chorionic villus sampling, amniocentesis, or cordocentesis.

Results: A statistically significant difference was found in at least one group in terms of gestational age at delivery, birth weight, current week and pregnancy risk among amniocentesis, cvs and cordocentesis groups ($p<0.05$). The average birth weight of the amniocentesis group (3099.04 ± 688.21) was found to be higher than the cvs group (2172.42 ± 1551.06). The risk of screening test for amniocentesis (0.0038±0.0063) and cordocentesis groups (0.001±0.0023) was found to be higher than the cvs group (0.0058±0.0061) The rate of USG anomaly in the cordocentesis group (73.2%) was found to be different from the Amniocentesis group (42.8%) and cvs group (12.1%). The rate of termination was found to be higher in the CVS (33.3%) and cordocentesis (31.7%) groups compared to the amniocentesis (4.3%) group.

Conclusion: Complication rates including bleeding, redness at the wound site, fetal bradycardia, amniotic fluid leakage, chorioamnionitis, miscarriage were similar among group.

Keywords: Amniosentesis, chorionic villus sampling, cordosentesis, invasive prenatal testing, complications

ÖZ

Amaç: Amniyosentez veya koryon villus örneklemesi (CVS) gibi invaziv testler artmış düşük riski ile ilişkilidir, anöploidiler ve diğer genetik bozukluklar açısından yüksek riskli olduğu düşünülen gebeliklerde test dikkatli yapılmalıdır. Çalışmamızın amacı, amniyosentez, kordosentez ve koryon villus örneklemesi gibi invaziv prenatal testlerden sonra gelişen komplikasyonları sunmaktır.

Gereçler ve Yöntem: Yüksek genetik bozukluk riski taşıyan ve koryon villus örneklemesi, amniyosentez veya kordosentez gibi invaziv prenatal testler uygulanan 282 gebeyi kapsayan ve 3 yıl 1 aylık bir süreyi kapsayan retrospektif gözlemsel bir çalışma gerçekleştirilmiştir.

Bulgular: Amniyosentez, cvs ve kordosentez grupları arasında doğumdaki gebelik yaşı, doğum ağırlığı, mevcut hafta ve gebelik riski açısından en az bir grupta istatistiksel olarak anlamlı fark bulundu ($p<0.05$). Amniyosentez grubunun ortalama doğum ağırlığı (3099,04±688,21) CVS grubundan (2172,42±1551,06) daha yüksek bulunmuştur. CVS, amniyosentez (0,0038±0,0063) ve kordosentez gruplarında (0,001±0,0023) tarama testi riski cvs (0,0058±0,0061) grubuna göre daha yüksek bulunmuştur. Kordosentez grubundaki USG anomali oranı (%73,2), amniyosentez grubu (%42,8) ve CVS grubundan (%12,1) farklı bulunmuştur. Terminasyon oranı CVS (%33,3) ve kordosentez (%31,7) gruplarında amniyosentez (%4,3) grubuna kıyasla daha yüksek bulunmuştur.

Tartışma: Kanama, yara yerinde kızarıklık, fetal bradikardi, amniyon membran rüptürü, koryoamniyonit, düşük gibi komplikasyon oranları gruplar arasında benzer olarak bulunmuştur.

Anahtar Kelimeler: Amniyosentez, koryon villus örneklemesi, kordosentez, invaziv prenatal testler, komplikasyon

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Sorumlu Yazar/Corresponding Author: Zafer BÜTÜN, Hoşnudiye mah. Ayşen sokak No:28/77, 26080 Tepebaşı/Eskisehir, Türkiye
E-mail: zaferbutun@hotmail.com

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INTRODUCTION

Amniocentesis is a medical procedure used to collect fetal cells from the amniotic fluid in order to identify chromosomal abnormalities in the fetus. The procedure is typically performed after sixteen weeks, with the assistance of ultrasound, this prenatal diagnostic technique can be beneficial for families when there are concerns about genetic disorders (1,2). Prenatal diagnosis is obtained through amniocentesis (3,4). It allows for early detection of any chromosomal issues, enabling parents and healthcare providers to prepare for the birth and plan for the child's future health and care needs. Certain indications may lead a healthcare provider to recommend amniocentesis. These include maternal age over 35 years, a family history of genetic conditions, previous pregnancies with abnormalities, or ultrasound findings indicating potential issues with the fetus. The procedure may also benefit women who test positive for genetic abnormalities in first or second trimester screening tests (1,5,6) .

While amniocentesis can provide crucial information, it is an invasive procedure that carries risks for both the mother and fetus. Therefore, it is vital for healthcare professionals to offer thorough counseling about the reasons for the procedure, its risks, benefits, and limitations. Although the risks are generally small, any potential complications should be discussed openly with expectant mothers. (7,8). Over recent years, there has been a notable rise in the number of pregnant women undergoing invasive prenatal diagnostic procedures, such as amniocentesis and chorionic villus sampling. Advances in these techniques now allow for earlier scheduling of procedures, which can lead to quicker diagnoses (9). A primary concern about these invasive methods is the risk of miscarriage and fetal loss (10). There has also been interest in understanding any potential fetal complications resulting from these procedures. (11). While studies on maternal complications address the psychological impact of prenatal tests, other complications after invasive prenatal tests have not been adequately investigated (12).

Research indicates that there may be connections between amniocentesis and issues such as prenatal bleeding, placental abruption, and leakage of amniotic fluid. (12,13). The likelihood of such complications appears to rise when amniocentesis is performed in the early stages of pregnancy (14). Similar risks have been associated with chorionic villus sampling as well. However, some studies have reported no significant increase in pregnancy complications (15,16). The interpretation of these findings requires careful consideration, as there are limited reports addressing maternal complications, and many studies lack proper control groups (17).

The purpose of this study is to determine whether amniocentesis and chorionic villus sampling, when routinely performed for pregnancies with low-risk indications, lead to an increased risk of maternal complications. This includes issues like bleeding during pregnancy, placental abruption, complications related to the amniotic membranes, complications affecting labor, and birth-related issues compared to women who have not undergone these procedures.

MATERIAL AND METHODS

This was a retrospective observational study conducted on patients who underwent prenatal invasive testing between July 2020 and July 2023. After ethical approval (22/11/2023- ESH/GOEK 2023/63R) was obtained to conduct this study, all pregnant women at high risk for genetic disorders who underwent invasive prenatal testing such as chorionic villus sampling, amniocentesis, or cordocentesis were included in this study. A total of 282 consecutive women were selected from the database according to our inclusion and exclusion criteria. The invasive procedures were conducted by a single operator (Z.B) at a single medical centre.

• Inclusion criteria: Patients receiving diagnostic intervention due to positive biochemical/ultrasonographic/both screening or positive history of genetic disorder in previous child or known mutation, with or without family history of genetic syndrome. Genetic diagnostic testing was offered to patients with a combined risk >1/1000.

• Exclusion Criteria: Patients were excluded from the study if they underwent interventions for reasons other than those specified, such as fetal reduction, fetal blood transfusions, fetal therapy. Additionally, those who opted out of invasive testing were not included. A single practitioner conducted a comprehensive ultrasound examination, followed by a detailed consultation with the patient and their family. During this consultation, the necessity, risks, and potential complications of prenatal invasive tests were discussed, as well as alternative options, including their relative benefits and drawbacks. Informed consent was obtained in writing from all participants prior to the procedure. All interventions were performed using a transabdominal approach under sterile conditions. A 22G spinal needle was used for amniocentesis, while a 20G spinal needle was utilized for chorionic villus sampling and cordocentesis, with ultrasound guidance applied through a free-hand technique by the same individual. Following the procedures, all patients received prophylactic oral antibiotics and progesterone support, with anti-D injections administered as needed. The ultrasound examination and invasive procedures were conducted

using a transabdominal curved transducer, either 3.5–5 MHz or 2–9 MHz, on a GE Voluson E8 system.

This retrospective study gathered data from departmental records regarding maternal age, reasons for the invasive tests, family history of genetic syndromes, ultrasound findings from the current examination, and results of the tests. Additionally, information on both early and late complications related to the procedures—such as miscarriage, infections, amniotic fluid leakage, fetal injury, and fetal loss were also recorded and analyzed using SPSS version 22.0.

RESULTS

A statistically significant difference was found in at least one group in terms of birth week, birth weight, current week and pregnancy risk between amniocentesis, cvs and cordocentesis groups ($p<0.05$). In the pairwise comparisons made;

The mean of the amniocentesis group at birth week (37.5±3.72) was found to be higher than the cvs group (29.58±12.31). Summary of some of the categoric and continuous variables among groups were summarized in Table 1 and 2.

The average birth weight of the amniocentesis group (3099.04±688.21) was found to be higher than the cvs group (2172.42±1551.06).

All groups were found to be different in terms of the current week. The highest mean was found in the cordocentesis group (25.98±2.65), followed by the amniocentesis group (19.59±2.62) and the lowest mean in the cvs group (12.55±0.51) (Table 3).

The risk of screening test for amniocentesis (0.0038±0.0063) and cordocentesis groups (0.001±0.0023) was found to be higher than the cvs group (0.0058±0.0061). A higher biochemical risk does not necessarily correspond to an increased likelihood of chromosomal abnormalities. In our study, only 19% of fetuses with a nuchal

Table 1. Invasive test groups and complications rates

	Groups	n	%
Invasive test	Amniocentesis	208	73.8%
	CVS	33	11.7%
	Cordocentesis	41	14.5%
Indication	Increased risk at screening test	74	26.2%
	Fetal structural anomaly	123	43.6%
	Fetal structural anomaly and increased risk for screening test	85	30.1%
Bleeding	No	280	99.3%
	Yes	2	0.7%
Hyperemia	No	276	97.9%
	Yes	6	2.1%
Bradycardia	No	279	98.9%
	Yes	3	1.1%
Amnion leakage	No	281	99.6%
	Yes	1	0.4%
Chorioamnionitis	No	281	99.6%
	Yes	1	0.4%
Miscarriage	No	281	99.6%
	Yes	1	0.4%
Termination	No	249	88.3%
	Yes	33	11.7%
Route of delivery	Vd	184	65.2%
	Cs	98	34.8%
Fetal sex	Girl	185	65.6%
	Boy	97	34.4%

Table 2. Demographic data of patients

	n	Mean	SS	Min	Max
Gestational age at delivery (weeks)	282	36.16	6.3	12	41
	282	2903.97	973.54	20	4230
Age (years)	282	29.53	5.71	17	45
Height (cm)	282	162.28	5.48	150	178
Weight (kg)	282	69.65	13.15	45	113
Gravidity	282	2.28	1.51	1	12
Parity	282	1.02	1.11	0	8
Weeks	282	19.69	4.22	12	32
Risk	282	0.0036	0.006	0.0001	0.0476
BMI (kg/m2)	282	26.44	4.74	16.26	42.44

Table 3. Pregnancy and delivery data of the three invasive test groups

	Intervention	n	Mean	SS	Mean Rank	p
Gestational age at delivery (weeks)	Amniocentesis	208	37.5	3.72	150.58	**0.001**
	Cvs	33	29.58	12.31	96.74	
	Cordocentesis	41	34.66	6.21	131.44	
Birth weight (grams)	Amniocentesis	208	3099.04	688.21	151.5	**0.002**
	Cvs	33	2172.42	1551.06	106.55	
	Cordocentesis	41	2503.17	1215.94	118.89	
Age (years)	Amniocentesis	208	29.89	5.62	145.72	0.302
	Cvs	33	29.06	6.09	135.03	
	Cordocentesis	41	28.07	5.7	125.29	
Height (cm)	Amniocentesis	208	162.27	5.77	141.83	0.775
	Cvs	33	161.88	5.44	133.15	
	Cordocentesis	41	162.66	3.9	146.54	
Weight (kg)	Amniocentesis	208	70.09	13.58	143.34	0.492
	Cvs	33	66.39	11.46	125.7	
	Cordocentesis	41	70.02	12.12	144.88	
Bmi	Amniocentesis	208	26.6	4.82	143.23	0.66
	Cvs	33	25.39	4.45	129.36	
	Cordocentesis	41	26.49	4.6	142.5	
Gravide	Amniocentesis	208	2.26	1.44	142.18	0.875
	Cvs	33	2.36	2.03	134.98	
	Cordocentesis	41	2.32	1.46	143.32	
Parite	Amniocentesis	208	1.03	1.1	142.91	0.542
	Cvs	33	0.85	1	127.8	
	Cordocentesis	41	1.15	1.28	145.39	
Weeks	Amniocentesis	208	19.59	2.62	138.72	**<0.001**
	Cvs	33	12.55	0.51	17	
	Amniocentesis	41	25.98	2.65	255.79	
Risk	Cvs	208	0.0038	0.0063	139.54	**<0.001**
	Cordocentesis	33	0.0058	0.0061	197	
	Amniocentesis	41	0.001	0.0023	0.0002	0.0006

translucency measurement above the 95th percentile were found to have chromosomal abnormalities. Similarly, 21% of fetuses in the study that presented with an absent nasal bone were diagnosed with trisomy 21.

A proportional difference was observed in at least one group of the Amniocentesis, Cvs and Cordocentesis groups according to the indication for invasive testing ($p<0.001$). In the pairwise comparison, no difference was seen in the rate of combined test risk in the three

Table 4. Differences between the three groups according to fetal invasive tests

	Category	Amniocentesis		Cvs		Cordocentesis		p
		n	%	n	%	n	%	
Indication	High risk for combined test	57	27,4%[a]	11	33,3%[a]	6	14,6%[a]	**<0,001**
	Fetal anomaly	89	42,8%[a]	4	12,1%[b]	30	73,2%[c]	
	Both	62	29,8%[a]	18	54,5%[b]	5	12,2%[a]	
Bleeding	No	207	99,5%	32	97,0%	41	100,0%	0,241
	Yes	1	0,5%	1	3,0%	0	0,0%	
Hyperemia at scar	No	204	98,1%	32	97,0%	40	97,6%	0,651
	Yes	4	1,9%	1	3,0%	1	2,4%	
Bradycardia	No	207	99,5%	33	100,0%	39	95,1%	0,093
	Yes	1	0,5%	0	0,0%	2	4,9%	
Amnion leakage	No	207	99,5%	33	100,0%	41	100,0%	0,999
	Yes	1	0,5%	0	0,0%	0	0,0%	
Choriamnionitis	No	207	99,5%	33	100,0%	41	100,0%	0,999
	Yes	1	0,5%	0	0,0%	0	0,0%	
Miscarriage	No	207	99,5%	33	100,0%	41	100,0%	0,999
	Yes	1	0,5%	0	0,0%	0	0,0%	
Termination	No	199	95,7%	22	66,7%	28	68,3%	**<0,001**
	Yes	9	4,3%[a]	11	33,3%[b]	13	31,7%[b]	
Route of delivery	Vd	118	56,7%	30	90,9%	36	87,8%	**<0,001**
	Cs	90	43,3%[a]	3	9,1%[b]	5	12,2%[b]	
Sex	Girl	135	64,9%	22	66,7%	28	68,3%	0,908
	Boy	73	35,1%	11	33,3%	13	31,7%	

groups. All rates were found to be different in those performed for USG anomaly. The rate of USG anomaly in the Cordocentesis group (73.2%) was found to be different from the Amniocentesis group (42.8%) and CVS group (12.1%). The rate of those performed for both risk and USG findings in the CVS group (54.5%) was found to be higher than in the Amniocentesis (29.2%) and Cordocentesis groups (12.2%).

The rate of termination was found to be higher in the CVS (33.3%) and cardocentesis (31.7%) groups compared to the Amniocentesis (4.3%) group. Distribution of complications following three different procedures was presented in Table 4.

DISCUSSION

In this study, we aimed to analyze the complications that arise after invasive prenatal procedures such as amniocentesis, cordocentesis, and chorionic villus sampling. We discovered that the rate of pregnancy termination was significantly higher in the CVS group (33.3%) and the cordocentesis group (31.7%) compared to the amniocentesis group, which had a termination rate of only 4.3%. Additionally, the rate of cesarean sections was higher in the amniocentesis group (43.3%) compared to the cordocentesis (12.2%) and CVS groups (9.1%).

Amniocentesis involves piercing the membranes, whereas chorionic villus sampling (CVS) does not. This distinction could help explain why there is a greater risk of complications related to the amniotic sac following amniocentesis, while such risks are less associated with CVS. Research has found a notable connection between amniocentesis and the leakage of amniotic fluid after the procedure (18). These studies documented pregnancy complications from the moment the procedure was performed until delivery. One particular study conducted in Canada found that early amniocentesis was linked to a higher risk of fetal loss and the development of talipes equinovarus (19). The association between invasive procedures and unusual birth outcomes has not been extensively documented, with the exception of a British study that noted an increased incidence of dysfunctional labor following amniocentesis (20). The

higher incidence of instrumental vaginal deliveries observed in the amniocentesis group, along with a similar increase in the chorionic villus sampling group, aligns with the findings of abnormal birth types linked to invasive procedures. However, prior studies have not indicated any association between these invasive techniques and the frequency of instrumental deliveries (21).

In a systematic meta-analysis, Akolekar indicated that the risk of miscarriage related to the procedures of amniocentesis and chorionic villus sampling was significantly lower than what had been previously reported, with figures of 0.11% for amniocentesis and 0.22% for CVS (22). Guidelines for invasive procedures indicate that the risks associated with amniocentesis include fetal loss (ranging from 0.1% to 1%), amniotic fluid leakage (between 1% and 2%), and chorioamnionitis (less than 1%). After undergoing amniocentesis, the likelihood of amniotic fluid leakage remains elevated for up to 24 weeks, although spontaneous closure of the membranes is frequently observed (23). Factors such as less experience, multiple interventions, bloody amniotic fluid, and the presence of fetal abnormalities can elevate the risk of fetal loss. According to the literature, the complication rates associated with chorionic villus sampling vary, showing fetal loss rates between 0.2% and 2%, and about 10% for vaginal bleeding. Additionally, the risk of fetal loss increases with repeated needle insertions and if the procedure is performed at a gestational age of less than 10 weeks.

The incidence of fetal loss following transcervical chorionic villus sampling (CVS) is noted to be elevated, with rates reported around 2.5%. A previous study indicated that a single operator conducted over 145 procedures annually, totaling 433 procedures over three years, without experiencing any major complications. During the subsequent eight weeks post-amniocentesis, CVS, or cordocentesis, no complications including amniotic fluid leakage, chorioamnionitis, or fetal loss were reported in any cases. Among the CVS procedures where the placenta was situated, only three instances of vaginal bleeding (0.7%) were documented, a figure significantly lower than what the literature typically indicates. The success rate for obtaining samples was 100% in a single session and 99.3% in a single attempt. Overall, a lower complication rate was observed in their study compared to existing literature, likely attributed to the fact that all procedures were performed by a single fetal medicine consultant with 20 years of extensive experience, adhering to stringent protocols for pre- and post-procedure care. Such a minimal complication rate is typically achievable only after navigating a considerable learning curve (24). According to the literature, the rates of failure to culture amniocyte or trophoblastic cells following amniocentesis and chorionic villus sampling (CVS) are reported to be 0.1% and 0.5% respectively. In a prior study, culture failure occurred in 2 cases (0.46%) of the total, both of which involved patients who underwent chorionic villus sampling for biochemical screening that was positive for trisomy 21, despite having normal fluorescence in situ hybridization (FISH) results. Notably, none of the patients required reoperation. (25)

A systematic review has revealed considerable variation in the rates of pregnancy loss and complications following both amniocentesis and chorionic villus sampling (CVS). For amniocentesis specifically, data on pregnancy loss within 14 days post-procedure indicated no significant variability, with a pooled loss rate of 0.6%. However, the risk of fetal loss tends to rise with longer follow-up periods, increasing from 0.6% within 14 days to 1.9% for overall pregnancy loss. While these percentages can be useful for general guidance, they do not account for the inherent background risk, which means they do not fully address the additional risks associated with the procedures. Notably, the baseline risk for women undergoing CVS will typically be higher than that for those undergoing amniocentesis, as amniocentesis is usually performed later in pregnancy, when the likelihood of spontaneous miscarriage is reduced. It seems reasonable to conclude that this distinction is a significant factor contributing to the elevated miscarriage rates observed in women who undergo CVS (26).

A review of the literature on amniocentesis included control groups to assess background risk. The pooled findings revealed a 25% relative increase in total pregnancy loss following amniocentesis and a 46% rise in pregnancy loss before 24 weeks of gestation. However, these results were notably heterogeneous, leading to wide confidence intervals that were not statistically significant. The absolute risk difference between the cases and controls was found to be comparable, indicating that the risk of pregnancy loss during the second trimester and overall fetal loss increases by approximately 0.6% after amniocentesis. Furthermore, the use of non-randomised control groups may introduce significant bias, as they typically do not allow for a direct comparison between the two groups (27). The significant differences observed in complication rates are surprising, especially considering that all studies were conducted under ultrasound guidance by well-trained personnel. The rates of amniocentesis procedures that required multiple needle insertions ranged from 0.2% (representing 9 out of 3,696 cases) to 2.8% (58 out of 2,068 cases) and 2.9% (7 out of 240 cases) (28).

In conclusion, cesarean sections was significantly higher in the amniocentesis group (43.3%) compared to the cordocentesis group (12.2%) and the chorionic villus sampling (CVS) group (9.1%). However, the complication rates including issues such as bleeding, redness at the wound site, bradycardia, amniotic fluid leakage,

chorioamnionitis, and miscarriage were found to be similar across all groups.

Ethics Committee Approval:
Ethical approval (22/11/2023- ESH/GOEK 2023/63R) was obtained to conduct this study.

Conflict of Interest
The authors declare no conflict of interest.

Author Contributions
Z.B., M.K., E.A.S. conceived the study. and G.Ş., K.S. searched the literature and collected the data. M.K., E.A.S. and G.Ş. performed the statistical analysis. Z.B., M.K., K.S. drafted the manuscript. Z.B., G.Ş., K.S. reviewed the manuscript. Both authors contributed to editorial changes in the manuscript. Both authors have read and approved the final paper. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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Gebe okuluna katılan gebeler ile katılmayan gebelerin prenatal bağlanmaları arasındaki fark

Difference between prenatal attachment of pregnant women who attended pregnancy school and those who did not attend pregnancy school

Ayça K. KÜÇÜKYURT[1], Gülnihal ARTUĞ CANSIZLAR[2]

[1]Istanbul Training and Research Hospital, Istanbul, Türkiye
[2]Department of Women's Health and Gynecologic Nursing, Florence Nightingale Faculty of Nursing, Istanbul University-Cerrahpasa, Istanbul, Türkiye

ÖZ

Amaç: Gebelik döneminde bebeğin sağlıklı gelişimi, doğum öncesi bağlanma düzeyiyle yakından ilişkilidir. Bu çalışmada, Sağlık Bakanlığı'nın Gebe Okulu Eğitim Programı kapsamında verilen, 5 hafta süren, her biri 120 dakika olan online eğitimlerin prenatal bağlanma düzeyine etkisi incelenmiştir. Çalışmanın amacı, bu eğitime katılan ve katılmayan gebelerin prenatal bağlanma düzeyleri arasındaki farkı belirlemektir.

Gereçler ve Yöntem: Çalışma, son test kontrol gruplu yarı deneysel bir tasarıma sahiptir. Sağlık Bakanlığı'nın Gebe Okulu Eğitim Programı'na uygun olarak hazırlanan 5 haftalık eğitim, deney grubunda yer alan 30 gebe üzerinde uygulanmıştır. Kontrol grubu ise programa katılmayan 30 gebeden oluşmaktadır. Toplam 60 gebeye Kişisel Bilgi Formu (PIF) ve Prenatal Bağlanma Envanteri (PBE) uygulanmıştır.

Bulgular: Elde edilen bulgular, vaka ve kontrol gruplarındaki katılımcıların yaşadığı bölge, eşlerin eğitim durumu ve gebelik haftasının prenatal bağlanma ile istatistiksel olarak anlamlı bir ilişki içinde olduğunu göstermiştir ($p < 0,05$).

Sonuç: Vaka ve kontrol gruplarındaki katılımcıların yaşadığı bölge, eşlerin eğitim düzeyi, gebelik haftası ve eğitim programına katılımın prenatal bağlanma düzeyi üzerinde istatistiksel olarak anlamlı etkisi olduğu görülmüştür. Gebe Okulu Eğitim Programı'nın yaygınlaştırılması ve erişim imkanlarının artırılması önerilmektedir.

Anahtar Kelimeler: Doğum öncesi bakım, anne-fetus ilişkisi, sağlık eğitimi.

ABSTRACT

Aim: The healthy development of a baby during pregnancy is greatly affected by prenatal attachment. Within the scope of the Pregnancy School Training Program of the Ministry of Health, the training lasted 5 weeks; each training session was conducted online for 120 minutes, and this program provided the training content. This study aims to reveal the difference between the prenatal attachment levels of pregnant women who participated in the training in the program and those who did not.

Materials and Methods: Materials and Methods: This semi-experimental study used a post-test control group design. Sixty pregnant women participated: 30 in the experimental group and 30 in the control group. Data were collected using the Personal Information Form (PIF) and the Prenatal Attachment Inventory (PAI).

Results: When the comparisons made in our study were examined, it was seen that the region where the participants in the case and control groups lived, the education level of their spouses, and the week of pregnancy had a statistically significant relationship with prenatal attachment ($p < 0,05$).

Conclusion: It was observed that the region where the participants in the case and control groups lived, the educational status of the spouses, the week of pregnancy, and attendance at pregnancy school had a statistically significant relationship with prenatal attachment. It is recommended that the Pregnancy School Education Program be increased.

Keywords: Prenatal care, maternal-fetal relations, health education.

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Sorumlu Yazar/Corresponding Author: Ayça K. KÜÇÜKYURT, Obstetrician and Gynecologist, Istanbul Training and Research Hospital, Istanbul, Türkiye
E-mail: aycakubat72@gmail.com

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GİRİŞ

Gebelik, kadınların hayatında keyifli ve eşsiz bir dönemdir (1). Gebelik sırasında anne ve bebek arasında ilk ilişkinin temelleri atılmakta olup, bu ilişki "prenatal bağlanma" olarak tanımlanmaktadır (2). Prenatal dönemde güvenli bağlanma, bebeğin ruhsal ve fiziksel sağlığının gelişimi açısından büyük önem taşımaktadır (3). Prenatal bağlanmayı etkileyen faktörler arasında gebelik semptomları, primipar veya multipar olma, bebek hareketlerini hissetme, sigara/alkol kullanımı, sağlık davranışlarındaki değişiklikler, gebeliğin planlanması, eşlerin ilgi ve desteği ile perinatal dönem ve bebek bakımına ilişkin bilgi alma yer almaktadır (4).

Kartal ve Karaman'ın çalışmasında, doğuma hazırlık eğitimine katılan kadınların prenatal bağlanma düzeylerinin olumlu yönde etkilendiği belirtilmiştir (5). Perinatal dönemde verilen eğitimler, gebe ve ailesinin fiziksel ve psikososyal ihtiyaçlarını karşılarken, doğuma hazırlık süreçlerine de katkı sağlamaktadır (6). 2013 yılından itibaren doğuma hazırlık eğitimlerinde standardizasyon sağlanmış olup, bu eğitimler Sağlık Bakanlığı tarafından belirlenen içerik ve süreye uygun şekilde düzenlenmektedir (7).

Doğuma hazırlık eğitimleri, çiftlerin gebelik, doğum ve doğum sonrası döneme dair bilgilendirilmesini, doğumun nasıl yönetileceği, doğum ağrısını nasıl kontrol edeceklerini öğrenmelerini, bilinçli doğum yapmalarını ve ebeveynlik rollerine hazırlanmasını amaçlayan yapılandırılmış özel eğitimlerden oluşmaktadır (8). Ülkemizde normal doğuma teşvik politikaları olmasına rağmen, doğuma hazırlık eğitimleri ile ilgili çalışmalar sınırlıdır. Bu çalışmanın amacı, gebe okuluna katılan ve katılmayan gebelerin prenatal bağlanma düzeyleri arasındaki farkı incelemektir.

GEREÇLER VE YÖNTEM

Araştırma, son Test Kontrol Gruplu yarı deneysel bir tasarıma sahiptir. Araştırmaya dahil edilecek kişi sayısını belirlemek amacıyla güç (power) analizi yapıldı ve testin gücü G*Power 3.1 programı kullanılarak hesaplandı. Literatürde benzer bir çalışma olarak Kartal ve Karaman'ın (2018) "Doğuma Hazırlık Eğitiminin Gebelerde Prenatal Bağlanma ve Depresyon Riski Üzerine Etkisi" başlıklı araştırmasında, Prenatal Bağlanma Ölçeği farkına ilişkin etki büyüklüğü (effect size) 0.76 olarak belirlendi (5).

Çalışmanın gücünün %95'in üzerine çıkması için, %5 anlamlılık düzeyinde ve 0.76 etki büyüklüğünde her bir grupta 27 kişi olmak üzere toplamda 54 kişiye ulaşılması hedeflendi. Kayıplar göz önünde bulundurularak deney grubu ve kontrol grubunda yer alacak kişi sayısı deney ve kontrol grubuna 30 gebe toplamda 60 katılımcı dahil edildi. Katılımcıların randomizizasyonu, Random.org kullanılarak gerçekleştirildi.

Çalışma, kadın hastalıkları ve doğum kliniğine (KHDK) rutin kontrollerini yaptırmak amacıyla başvuran gebeler üzerinde yürütüldü. Araştırma izni ilgili etik kurul komitesi tarafından 08.04.2022 tarihli ve No:110 karar numarasıyla onaylandı.

Eğitim Programı

Eğitim programı, Sağlık Bakanlığı'nın Gebe Okulu Eğitim Programı kapsamında 5 hafta süren ve eğitim içeriği bu programa uygun olarak gerçekleştirilmiştir. Her bir eğitim 120 dakika ve interaktif online olarak gerçekleştirilmiştir.

1. Oturum: Gebelik ve Beslenme, Üreme Anatomisi, Hormonlar ve Adet Döngüsü, Döllenme, Dış Gebelik, İkiz Gebelik, Gebelikte Fizyolojik Değişiklikler, Gebelikte Sigara, Alkol, İlaç Kullanımı, Gebelikte Hijyen, Kıyafet Seçimi, Gebelikte ve Çalışma Hayatı, Gebelikte Cinsellik, Gebelikte Kontrol Zamanları, Gebelikte Hormonal Değişiklikler, Bebeğin Anne Karnında Gelişimi Gebelikte Beslenme, Gebelikte Egzersiz, Gebelikte Tehlike Belirtileri.

2. Oturum: Doğuma Hazırlık Felsefeleri, Doğum Eyleminin Belirtileri, Doğum Çantası Hazırlama, Doğum İçin Hastaneye Gelindiğinde Yapılacaklar, Normal Doğum, Perine Masajı (Uygulamalı), Müdahaleli Doğumlar, Doğumun Fizyolojik Dengesi, Doğum Ağrısı ile Baş Etmede İlaçsız Yöntemler, Nefes Teknikleri (Uygulamalı), Dokunma ve Masaj Teknikleri (Uygulamalı), Aromaterapi.

3. Oturum: Anne Sütü ve Emzirme, Anne Sütünün Özellikleri ve Yararları, Memelerin Yapısı, Emzirmenin Yararları, Emzirme Mekanizması, Emzirme Tekniği (Uygulamalı), Anne Sütünü Azaltan/Arttıran Faktörler, Sütün Yettiği Nasıl Anlaşılır, Emzirirken Çıkabilecek Sorunlar ve Çözümler, Süt Nasıl Sağılır ve Saklanır, Meme Bakımı, Emzirme ve İlaç Kullanımı.

4. Oturum: Bebek Bakımı Yenidoğana Doğumdan Hemen Sonra Yapılan Uygulamalar, Yenidoğan Tarama Testleri, Aşı Uygulamaları, Yenidoğanın Özellikleri/Görünümü, Yenidoğan Refleksleri, Yenidoğan Döneminde Görülen Sorunlar, Göbek Bakımı, Bebek Banyosu (Uygulamalı), Bebek Giyimi (Uygulamalı), Alt Değiştirme (Uygulamalı), Tırnak Kesimi, Bebek Masajı (Uygulamalı), Gaz Çıkarma (Uygulamalı), Doğum Sonu Dönemde Anne Bebek Bağlanması, Bebeğin Odası, Yenidoğan Güvenliği, Bebeğin Nüfus İşlemleri, Sağlam Çocuk Kontrolleri

5.Oturum: Lohusalık ve Aile Planlaması, Lohusalık Dönemi, Doğum Sonu Annede Meydana Gelen Fizyolojik Değişiklikler, Doğum Sonu Annede Meydana Gelen Psikolojik Değişiklikler, Doğum Sonu Tehlike İşaretleri, Doğum Sonu Günlük Yaşam, Doğum Sonu Güvenli Egzersiz, Doğum Sonrası Gebelikten Korunma.

Veri Toplama Formu

Gebeleri tanıtan Bireysel Bilgi Formu ve Prenatal Bağlanma Envanteri olmak üzere iki form kullanılmıştır.

Bireysel Bilgi Formu

Gebenin sosyodemografik (eğitim durumu, çalışma durumu, ekonomik durum, aile tipi), obstetrik ve şu anki gebelik özelliklerini (gebelik sayısı, yaşayan çocuk sayısı, planlanmış gebelik, şu anki gebelik haftası) içeren sorulardan oluşmaktaydı.

Prenatal Bağlanma Envanteri

Prenatal Bağlanma Envanteri (The Prenatal Attachment İnventory) 1993 yılında Mary Muller tarafından geliştirilmiştir. Gebelik boyunca kadınların yaşadıkları düşünceleri, duyguları, durumları açıklamak ve bebeğe prenatal dönemdeki bağlanma düzeylerini belirlemek amacıyla geliştirilen ölçek 21 maddeden oluşmaktadır. Her madde 1 ile 4 arasında puan alabilen dörtlü likert tiptedir. Ölçekten en az 21 en fazla 84 puan alınabilmektedir. Gebenin aldığı puanın artması bağlanma düzeyinin de arttığını göstermektedir. 1: Hiçbir zaman, 2: Bazen, 3: Sık sık, 4: Her zaman şeklinde puanlanmıştır (9).

Verilerin Toplanması

5 hafta süren eğitim programına aksatmadan katılımını sağlayan gebelere ve rutin kontrollerini yaptırmak amacıyla polikliniğe gelen, gebe okulu eğitimine katılmayan gebelere, Bireysel Bilgi Formu ve Prenatal Bağlanma Envanteri uygulandı.

İstatistik Analizi

Araştırmada elde edilen verilerin tanımlayıcı istatistiklerin de ortalama, standart sapma, medyan, en düşük ve en yüksek değerler ile frekans ve oranlar kullanılmıştır. Verilerin normal dağılıma uygunluğu Kolmogorov-Smirnov testi ile değerlendirilmiştir. Nicel bağımsız değişkenlerin analizinde, dağılımın normal olmadığı durumlarda Mann-Whitney U testi uygulanmıştır. Nitel bağımsız değişkenlerin analizinde ise Ki-kare testi kullanılmış, ancak test koşullarının sağlanamadığı durumlarda Fisher testi tercih edilmiştir. İstatistiksel analizler SPSS 28.0 programı ile gerçekleştirilmiştir.

BULGULAR

Çalışmaya katılan kadınların yaş ortalaması 28 olup, katılımcıların %82,3'ü kentsel bölgede yaşamaktadır. Eğitim durumlarına bakıldığında, katılımcıların %34,6'sı ortaokul, %32,7'si lise ve %30,8'i lisans mezunudur. Katılımcı eşlerinin eğitim düzeyi ise en yüksek oranda %41,5 ile lise mezunu olarak belirlenmiştir. Gebelerin %94,7'si doğal yollarla gebe kalmış ve %80'i gebeliği istemektedir. Doğum öncesi bakım (DÖB) alma oranı %96,5 olarak saptanmıştır (Tablo 1).

Tablo 1. Demografik Özellikler

		Min-Mak			Medyan	Ort.±ss/n-%		
Yaş		16,0	-	42,0	28,0	28,8	±	5,9
Prenatal Bağlanma Puanı		32,0	-	82,0	62,0	60,4	±	12,7
Gebelik Haftası		20,0	-	32,0	26,0	32,7	±	5,1
						n		**%**
Yaşadığı Bölge	Kentsel					51		82,3%
	Kırsal					9		17,6%
Eğitim Durumu	Ortaokul					21		34,6%
	Lise					19		32,7%
	Ön lisans					2		1,9%
	Üniversite					18		30,8%
Eşin Eğitim Durumu	İlkokul					12		22,7%
	Lise					26		41,5%
	Üniversite					22		35,8%
Gebe Kalma Şekli	Doğal					57		94,7%
	Tedavi İle					3		5,2%
Gebelik İsteme	(-)					10		20%
	(+)					50		80%
Gebelik Eğitimi	(-)					30		56,6%
	(+)					23		43,4%
DÖB Alma	(-)					2		3,4%
	(+)					58		96,5%

DÖB: Doğum Öncesi Bakım

Tablo 2. Vaka ve Kontrol Grubunun Demografik Özelliklerinin Karşılaştırılması

		Kontrol Grubu (-)					Vaka Grubu (+)				p	
		Ort.±ss/n-%			Medyan		Ort.±ss/n-%			Medyan		
Yaş		27,8	±	4,7	27,0		30.1	±	7,0	28,0	0,263	m
Gebelik Haftası		31,3	±	4,6	32,0		34,6	±	5,3	36,0	**0,002**	m
Prenatal Bağlanma Puanı		55,9	±	14,3	58,0		63,8	±	10,3	66,0	***0,034***	m
		n		%			N		%			
Yaşadığı Bölge	Kentsel	28		93,3%			23		69,6%		***0,022***	X^2
	Kırsal	2		6,7%			7		30,4%			
Evlilik Yaşı		21,7	±	8,7	24,0		21,4	±	5,3	22,0	0,322	m
Eşin Yaşı		31,9	±	7,0	30,0		32,5	±	6,4	31,0	0,522	m
Eğitim Durumu												
Ortaokul		8		27,6%			11		47,8%		***0,009***	X^2
Lise		8		27,6%			11		47,8%			
Ön lisans		1		3,4%			0		0,0%			
Üniversite		13		44,8%			8		4,4%			
Eşin Eğitim Durumu												
Ortaokul		3		10%			10		39,1%		***0,014***	X^2
Lise		13		43,3%			13		43,5%			
Üniversite		15		46,7%			7		17,4%			
Gebe Kalma Şekli	Doğal	29		96,7%			28		92,8%		0,573	X^2
	Tedavi İle	1		3,3%			2		7,1%			
Gebeliği İsteme	(-)	5		16,7%			5		16,7%		0,396	X^2
	(+)	25		83,3%			25		83,3%			
DÖB Alma	(-)	1		3,4%			1		3,4%		1,000	X^2
	(+)	29		96,6%			29		96,6%			

X^2 Ki-kare test / m Mann-Whitney u test
DÖB: Doğum Öncesi Bakım

Kontrol grubundaki katılımcıların yaş ortalaması 27, yaşadığı bölge %93,3 ile kent, evlilik yaşı ortalaması ise 24 olarak hesaplanmıştır. Kontrol grubunda katılımcıların eğitim durumu %44,8 ile lisans mezunu olanlar arasında yoğunlaşmıştır. Eşlerin eğitim düzeyi ise %46,7 ile lisans mezunu olarak belirlenmiştir. Kontrol grubundaki gebelerin gebelik haftası ortalama 26 hafta olarak bulunmuştur. Katılımcıların %96,6'sı doğum öncesi bakım almış ve prenatal bağlanma puanı ortalaması 58 olarak tespit edilmiştir (Tablo 2). Vaka grubundaki katılımcıların yaş ortalaması 28, yaşadığı bölge %69,6 ile kent, evlilik yaşı ortalaması ise 22 olarak belirlenmiştir. Katılımcıların eğitim düzeyi açısından dağılımı %47,8 ile ortaokul ve lise mezunları arasında yoğunlaşmıştır. Eşlerin eğitim düzeyi ise %43,5 ile lise mezunu olanlar arasında en yüksek orandadır. Vaka grubundaki gebelerin gebelik haftası ortalama 36 hafta olarak hesaplanmıştır. Katılımcıların %96,6'sı doğum öncesi bakım almış ve prenatal bağlanma puanı ortalaması 66 olarak bulunmuştur (Tablo 2).

Vaka ve kontrol grubunda yer alan katılımcıların yaşadığı bölgenin, eşlerin eğitim düzeyinin ve gebelik haftasının prenatal bağlanma ile istatistiksel olarak anlamlı bir ilişki gösterdiği belirlenmiştir ($p<0,05$) (Tablo 2).

TARTIŞMA

Doğum sonrası dönemde annelik rolüne uyum sağlamada ve anne-bebek bağının oluşumunda prenatal dönemin önemi büyüktür. Çalışmamızda prenatal bağlanmanın eğitim durumu, yaşadığı bölge, eşlerin eğitim düzeyi ve gebelik haftası gibi faktörlerle istatistiksel olarak anlamlı bir ilişki gösterdiği tespit edilmiştir. Literatürde prenatal bağlanmanın çeşitli sosyo-demografik faktörlerden etkilendiği belirtilmektedir. Özkan Koç ve ark. (2020), prenatal bağlanmanın yaş, eğitim düzeyi ve gebelik sayısıyla ilişkili olduğunu

bildirmiştir (10). Ayrıca, çalışmamızda eşlerin eğitim düzeyinin ve yaşanılan bölgenin prenatal bağlanma üzerinde anlamlı bir etkisinin bulunması, bu bulguları destekler niteliktedir.

Gebelik sürecinde doğum öncesi eğitim, gebelerin güçlenmesini, gebelik ve doğum süreçleriyle daha iyi başa çıkmalarını ve doğum sonrası döneme daha iyi uyum sağlamalarını desteklemektedir (11, 12). Literatürde, prenatal bağlanmanın annenin bebeğini birey olarak algılaması, bebek hareketlerini hissetmesi ve doğum öncesi hazırlık yapmasıyla ilişkili olduğu belirtilmiştir (13). Bilgin ve ark. (2020) çalışmasında, doğum öncesi eğitim alan gebelerin prenatal bağlanma düzeylerinin arttığı bildirilmiştir (14). Çalışmamızda da gebe okuluna düzenli katılım sağlayan gebelerin prenatal bağlanma düzeylerinin, eğitime katılmayanlara göre anlamlı şekilde daha yüksek olduğu bulunmuştur. Ayrıca gebelik haftası ilerledikçe prenatal bağlanma düzeyinin artması, annenin bebeğine olan ilgisinin ve merakının doğuma yaklaştıkça yoğunlaştığını göstermektedir.

Prenatal bağlanma ile gebelik haftası arasındaki pozitif ilişki, Teixeira ve ark. (2016) gebelik haftası arttıkça anne-fetüs bağının güçlendiğini bildiren çalışmasıyla uyumludur (15). Çalışmamızda kontrol grubundaki gebelerle karşılaştırıldığında, vaka grubunda prenatal bağlanmanın daha yüksek olduğu ve bunun gebelik haftasıyla ilişkili olduğu belirlenmiştir.

Eşlerin eğitim düzeyi, annenin prenatal bağlanma sürecinde önemli bir faktör olarak ortaya çıkmaktadır. Üstünsöz ve ark. (2010) çalışmasında, prenatal bağlanma ile eşlerin eğitim düzeyi arasında pozitif bir korelasyon bulunmuştur (16). Çelik ve ark. (2020) yüksek riskli gebelerle yaptığı çalışmada da benzer şekilde eşlerin eğitim düzeyi prenatal bağlanma ile anlamlı bir ilişki göstermiştir (17). Bizim çalışmamızda da eşlerin eğitim düzeyinin prenatal bağlanma ile arasında anlamlı bir ilişki olduğu görülmüştür.

Kentsel ve kırsal bölgelerde yaşayan gebeler arasındaki prenatal bağlanma düzeyine ilişkin sonuçlar literatürde farklılık gösterebilmektedir. Örneğin, Majeed ve ark. (2022), kentsel bölgelerde yaşayan gebelerin prenatal bağlanma düzeylerinin kırsal bölgelerde yaşayanlara göre daha yüksek olduğunu belirtmiştir (18). Ancak Bernad ve ark. (2024) çalışmasında yaşadığı bölgenin prenatal bağlanma üzerinde etkili olmadığı bildirilmiştir (19). Çalışmamızda yaşadığı bölgenin prenatal bağlanma üzerinde anlamlı bir etkisi bulunmuş, ancak bu durumun vaka ve kontrol gruplarındaki dağılımdan kaynaklanmış olabileceği değerlendirilmektedir.

Çalışmamız literatürdeki bulgularla uyumlu olarak prenatal bağlanmanın eğitim düzeyi, yaşadığı bölge, gebelik haftası ve eşlerin eğitim düzeyi gibi faktörlerden etkilendiğini göstermektedir. Bu sonuçlar, doğum öncesi eğitimlerin gebelerin prenatal bağlanma düzeyini artırmak ve gebelik sürecine daha iyi uyum sağlamalarını desteklemek açısından önemini vurgulamaktadır.

SONUÇ

Çalışmamızda anne ve bebek arasında güvenli bağlanma açısından prenatal dönemde gebelik okuluna başvuran ve katılımını tamamlayan gebeler ile böyle bir eğitim almayan gebeler arasında bir fark olup olmadığını araştırmaya çalıştık. Bu konuda literatür incelendiğinde benzer çalışmalar yapılmış olup oradaki sonuçlarla bizim elde ettiğimiz sonuçları tartışma kısmında karşılaştırdık. Gebelerin prenatal bağlanmalarını kıyaslama amacıyla ucuz, kolay ulaşılabilir ve non-invaziv bir yöntem olarak Prenatal Bağlanma Ölçeğindeki sorular ile gebelere anket yapılmıştır. Sonuçlarımızda vaka ve kontrol grubunda yer alan katılımcıların yaşadığı bölge, eşlerin eğitim durumunun, gebelik haftasının ve gebe okuluna katılıma devamın prenatal bağlanma ile istatistiksel olarak anlamlı ilişkisi olduğu görülmüştür.

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Retrospective evaluation of patients who underwent myomectomy during cesarean section

Sezaryen sırasında myomektomi yapılan hastaların retrospektif değerlendirilmesi

Hüseyin Aytuğ AVŞAR[1], Onur YAVUZ[2], Can ATA[3], Tevfik Berk BİLDACI[4], Selçuk ERKILINÇ[5]

[1]Tınaztepe Galen University Faculty of Medicine, İzmir, Türkiye
[2]Dokuz Eylul University School of Medicine, İzmir, Türkiye
[3]Buca Seyfi Demirsoy Training and Research Hospital, İzmir, Türkiye
[4]Izmir Democracy University Faculty of Medicine, OB/GYN Department, Türkiye
[5]Izmir Democracy University Faculty of Medicine, Oncology Department, Türkiye

ABSTRACT

Aim: To evaluate the obstetric and neonatal outcomes of patients who underwent myomectomy at the time of cesarean section (C/S).

Materials and Methods: A total of 480 patients aged 19-45 who presented to the gynecology and obstetrics clinic between 2018-2023, underwent pregnancy follow-up and C/S delivery in our hospital, and met the inclusion criteria were included in our study. Myomectomy was performed during C/S in 220 patients included in the study, and it was not performed in 260 patients. Age, number of pregnancies, abortion status, fetal weight at birth, Apgar scores, C/S indication, myoma localization, and hemoglobin values of all patients were compared retrospectively.

Results: The number of abortions was significantly higher in the myomectomy (+) group ($p<0.001$). Mean gestational age at birth was significantly lower in the myomectomy (+) group ($p=0.020$). Operation time and hospital stay were significantly higher in the myomectomy (+) group ($p<0.001$). Myoma size was significantly higher in the myomectomy (+) group ($p<0.001$). Postoperative hemoglobin value was significantly lower in the myomectomy (+) group ($p<0.001$). Change in hemoglobin value was significantly higher in the myomectomy (+) group ($p<0.001$). 5th minute Apgar score was significantly lower in the myomectomy (+) group ($p=0.022$). Fetal weight at birth was significantly lower in the myomectomy (+) group ($p=0.046$).

Conclusion: C/S-myomectomy can be performed safely by an experienced gynecologist. We believe that myomectomy generally does not cause a significant increase in maternal morbidity and mortality. A detailed discussion of the risks associated with the patient should be conducted. Large population and prospective studies are needed to clarify the long-term risks and benefits.

Keywords: Birth, cesarean section, hysterectomy, myomectomy

ÖZ

Amaç: Çalışmamızın amacı sezaryen (C/S) sırasında myomektomi yapılan hastaların obstetrik ve neonatal sonuçlarını değerlendirmektir.

Gereçler ve Yöntem: Çalışmamıza 2018-2023 yılları arasında kadın hastalıkları ve doğum polikliniğine başvuran, gebelik takibi ve sezaryen doğumu hastanemizde yapılan, dahil edilme kriterlerine uyan 19-45 yaş arası toplam 480 hasta dahil edildi. Çalışmaya dahil edilen 220 hastaya sezaryen sırasında myomektomi uygulandı, 260 hastaya ise uygulanmadı. Tüm hastaların yaş, gebelik sayısı, abortus durumu, doğumdaki fetal ağırlık, Apgar skorları, sezaryen endikasyonu, myom yerleşimi, hemoglobin değerleri retrospektif olarak karşılaştırıldı.

Bulgular: Myomektomi (+) grubunda abortus sayısı anlamlı yüksek saptandı ($p<0.001$). Doğumda ortalama gebelik yaşı myomektomi (+) grubunda anlamlı düşük saptandı ($p=0.020$). Myomektomi (+) grubunda operasyon süresi ve hastanede kalış süresi anlamlı yüksek saptandı ($p<0.001$). Myomektomi (+) grubunda myom boyutu anlamlı yüksek saptandı ($p<0.001$). Myomektomi (+) grubunda postoperatif hemoglobin değeri anlamlı düşük saptandı ($p<0.001$). Myomektomi (+) grubunda hemoglobin değerindeki değişim anlamlı yüksek saptandı ($p<0.001$). Myomektomi (+) grubunda 5. dakika Apgar skoru anlamlı düşük saptandı ($p=0.022$). Myomektomi (+) grubunda doğumda fetal ağırlık anlamlı düşük saptandı ($p=0.046$).

Sonuç: C/S-myomektomi deneyimli bir jinekolog tarafından güvenli bir şekilde yapılabilir. Myomektominin genellikle maternal morbidite ve mortalitede önemli bir artışa neden olmadığına inanıyoruz. Hastayla ilişkili riskler hakkında ayrıntılı bir tartışma yapılmalıdır. Uzun vadeli riskler ve faydaları açıklığa kavuşturmak için geniş popülasyonlu ve prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Doğum, histerektomi, myomektomi, sezaryen

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Sorumlu Yazar/Corresponding Author: Hüseyin Aytuğ AVŞAR, Tınaztepe Galen University Faculty of Medicine, İzmir, Türkiye
E-mail: aytugavsar@hotmail.com

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INTRODUCTION

Uterine myomas, commonly known as uterine fibroids, are the most common benign gynecologic tumors (1,2). Most leiomyomas are asymptomatic and may not require any treatment, but some are associated with symptoms such as heavy menstrual bleeding, pelvic pain, and constipation and may lead to reproductive problems such as recurrent miscarriage and abruptio placentae (3). The incidence of uterine leiomyomas during pregnancy varies between 1.6% and 10.7% depending on the trimester of evaluation, and is more common depending on maternal age (4). Continuing to increase Cesarean section (C/S) rates and increasing pregnancy rates at advanced maternal age may increase the likelihood that obstetricians will detect myomas during C/S (5,6).

C/S-myomectomy should be considered with caution because of concerns about persistent bleeding requiring hysterectomy and increased postoperative morbidity. Roman et al. suggested that myomectomy could be performed at the time of C/S delivery in selected patients (7). Such an approach may have several benefits, including avoiding another surgery (8). Appropriate management of newly identified or previously known leiomyomas at the time of C/S delivery requires a multifactorial approach.

The aim of study was to evaluate the obstetric and neonatal outcomes of patients who underwent myomectomy at the time of C/S delivery.

MATERIALS AND METHODS

The present study was designed as a retrospective cross-sectional study. The study was designed according to the Helsinki Declaration and signed informed consent forms were obtained from all patients. The study was initiated after receiving ethics committee approval numbered 2024/224 dated 31/01/24 from the Buca Seyfi Demirsoy Training and Research hospital ethics committee. A total of 480 patients aged 19-45 who presented to the gynecology and obstetrics clinic between 2018-2023, underwent pregnancy follow-up and C/S delivery in our hospital, and met the inclusion criteria were included in our study. Myomectomy was performed during C/S in 220 patients included in the study, and it was not performed in 260 patients. All of myomas were confirmed pathologically. Its dimensions were calculated pathologically as half the sum of width and length.

Inclusion criteria for these women were: being over 18 years old, no history of uterine atony, documentation of uterine myoma during pregnancy by antepartum ultrasonography or intraoperative findings, presence of C/S delivery, availability of preoperative and postop laboratory values in the database. Patients were included in the study if they had no evidence of antepartum hemorrhage (e.g. due to placenta previa or abruption), had not undergone another procedure (e.g. cystectomy or planned hysterectomy), and had no evidence of coagulopathy. While the case group consisted of patients who underwent myomectomy during C/S delivery, the control group consisted of patients who were documented to have myomas during pregnancy and gave birth by C/S without myomectomy. Age, gravidity, parity, BMI (body mass index), abortion, gestational age at birth, fetal weight at birth, 1st and 5th minute Apgar scores, C/S indication, myoma location, number and size, preoperative and postoperative hemoglobin values, hemoglobin difference and postoperative transfusion needs of all patients was evaluated and it was investigated whether there was a difference between the groups. Preoperative blood preparation was decided on a patient-by-patient basis according to the localization and size of the myoma. Statistical analysis was performed by SPSS version 26.0 (IBM Inc., Chicago, IL, USA). The normality of the distribution was evaluated with Kolmogorov-Smirnov. Not normally distributed parameters were analyzed with the Mann-Whitney U test. Chi-square test and Fisher precision test were used in the analysis of categorical data. The quantitative data of the patients were demonstrated as mean ± Standard-Deviation (SD) and (minimum-maximum). Qualitative data were presented as numbers and percentages (%). Results were evaluated at a 95% confidence interval (CI). The p value considered statistically significant was <0.05.

RESULTS

The number of abortions was significantly higher in the myomectomy (+) group than in the myomectomy (-) group ($p<0.001$) (Table 1).

The mean gestational age at birth was found to be significantly lower in the myomectomy (+) group than in the myomectomy (-) group ($p=0.020$). The operation time in the myomectomy (+) group was significantly higher than in the myomectomy (-) group ($p<0.001$). The duration of hospital stay in the myomectomy (+) group was found to be significantly higher than in the myomectomy (-) group ($p<0.001$). Myoma size was significantly higher in the myomectomy (+) group than in the myomectomy (-) group ($p<0.001$). Postoperative Hb value was found to be significantly lower in the myomectomy (+) group than in the myomectomy (-) group ($p<0.001$). The decrease in hemoglobin value was found to be significantly higher in the myomectomy (+) group than in the myomectomy (-) group ($p<0.001$) (Table 2).

Table 1. Comparison of demographic data according to the presence of myomectomy

Variables	Myomectomy (+) group (n=220)	Myomectomy (-) group (n=260)	p
	(min-max)		
Age (year)	31 (18-43)	31.5 (19-45)	0.910
BMI (kg/m2) (mean±SD)	24.4±2.7	25.2±2.6	0.380
Smoking (n, %)	50 (22.7%)	60 (23%)	0.760
Gravidity	2 (1-8)	2 (1-7)	0.920
Parity	2 (1-6)	2 (1-5)	0.240
Abortion	0 (0-7)	0 (0-4)	<0.001

*Continuous variables without a normal distribution were presented as medians (minimum-maximum) and with normal distribution as mean ± standard deviations. Categorical variables were presented as numbers (percentages). *BMI: Body mass index,

Table 2. Comparison of obstetric data according to the presence of myomectomy

Variables	Myomectomy (+) group (n=220)	Myomectomy (-) group (n=260)	p
	(min-max)		
Gestational age at birth (week)	39 (29-41)	39 (32-41)	0.020
Operation time (min)	82 (66-112)	54 (46-74)	<0.001
Hospital stays (day)	1 (1-4)	1 (1-3)	0.028
Indications for C/S, % *Previous C/S* *Cephalopelvic disproportion* *Fetal distress* *Malpresentation* *Non-progressive labor* *Macrosomia* *Placental abruption* *Severe preeclampsia*	 53.6 - (118/220) 17.3 - (38/220) 11.4 - (25/220) 9.1 - (20/220) 7.7 - (17/220) 0 - (0/220) 0.5 - (1/220) 0.5 - (1/220)	 57.7 - (150/260) 16.5 - (43/260) 10.8 - (28/260) 8.8 - (23/260) 5 - (13/260) 0.8 - (2/260) 0.4 - (1/260) 0 - (0/260)	0.620
Myoma location, % *Incision* *Intramural* *Subserous*	 53.6 - (118/220) 1.8 - (4/220) 44.5 - (98/220)	 55 - (143/260) 0.8 - (2/260) 44.2 - (115/260)	0.520
Number of myomas	1 (1-2)	1 (1-2)	0.840
Myoma size (cm)	3 (1-7)	2.5 (2-3.5)	<0.001
Preop Hb (gr/dL)	12 (8.7-14.7)	11.9 (8.6-14.1)	0.240
Postop Hb (gr/dL)	11 (7.3-13.8)	11.4 (7.7-13.6)	<0.001
ΔHb (preop -postop) (gr/dL)	0.9 (0.1-4)	0.4 (0.1-2.8)	<0.001
Blood Transfusion, %	9 - (20/220)	7.3 - (19-260)	0.360

*Continuous variables without a normal distribution were presented as medians (minimum-maximum). Categorical variables were presented as numbers (percentages). *C/S: Cesarean section, *Hb: hemoglobin

Table 3. Comparison of neonatal data according to the presence of myomectomy

Variables	Myomectomy (+) group (n=220)	Myomectomy (-) group (n=260)	p
	(min-max)		
1st minute Apgar score	8 (4-8)	8 (4-9)	0.820
5th minute Apgar score	9 (4-9)	9 (6-9)	0.022
Fetal weight at birth (grams)	3360 (1180-4460)	3400 (1520-5010)	0.046

*Continuous variables without a normal distribution were presented as medians (minimum-maximum).

The 5th minute Apgar score was significantly lower in the myomectomy (+) group than in the myomectomy (-) group (p=0.022). Fetal weight at birth was found to be significantly lower in the myomectomy (+) group than in the myomectomy (-) group (p=0.046) (Table 3).

DISCUSSION

Most obstetricians make a patient-based decision after careful evaluation regarding myomectomy during C/S due to massive hemorrhage, persistent bleeding and consequently increased risk of hysterectomy. In our study, abortion rate, operation time, hospital stays, myoma size and ΔHb value were found to be significantly higher in the myomectomy (+) group compared to the myomectomy (-) group. In the myomectomy (+) group, gestational age at birth, postop Hb value, 5th minute Apgar score and fetal weight at birth were found to be significantly lower than the myomectomy (-) group.

The most important risk of performing myomectomy during a C/S is bleeding. Many obstetricians avoid performing myomectomy during a C/S due to unstoppable bleeding and the necessity of hysterectomy (9). Gbadebo et al. state that myomectomy can be performed safely during a C/S if patients are selected appropriately (10). However, if myomas are not removed, complications such as preterm birth, intrauterine growth restriction, placenta previa, and postpartum hemorrhage may not be prevented in future pregnancies. However, the safety of C/S-myomectomy for large myomas has not been extensively evaluated (11). In the study by Kwon et al., although the mean myoma size was larger in the C/S-myomectomy group compared with the non-myomectomy group, no statistically significant differences were found in neonatal weight, gestational age at birth, hemoglobin changes, and days of hospital stay (11). In our study, the mean birth weight and 5th minute Apgar score were significantly lower in the myomectomy (+) group than in the myomectomy (-) group. It was thought that these results might be due to lower gestational age and intramural myomas causing fetal growth restriction.

In Kaymak et al.'s study, 40 cases who underwent myomectomy during C/S were examined and intraoperative bleeding was observed in 5 patients (12). However, there are studies showing that myomectomy performed during C/S causes severe, uncontrollable bleeding that can be terminated by hysterectomy (13). Most obstetricians have been taught not to perform myomectomy during C/S delivery due to the risks of uncontrolled bleeding, massive hemorrhage, and hysterectomy. A meta-analysis by Song et al. showed that the outcomes of patients who underwent C/S-myomectomy were not significantly different from those who underwent C/S delivery alone. The meta-analysis revealed that blood loss and transfusion requirements were not significantly different between the two groups (14). In the study by Park et al., when myomectomy and control group patients with similarly sized myomas were compared in terms of surgery time, it was found that the myomectomy group had a longer surgery time (15). In the study by El-Refaie et al., when the myomectomy group and the control group were compared, no significant difference was found in terms of the amount of blood transfusion and postoperative hemoglobin level, while the surgery time and hospital stay were found to be significantly longer in the myomectomy group than in the control group (8). In our study, while the postoperative Hb level was found to be significantly lower in the myomectomy (+) group, the hospital stay was found to be significantly higher.

There is no clear consensus in the current literature regarding the criteria for selecting suitable candidates for C/S-myomectomy. Kim et al. advocated the idea of surgery for myomas inaccessible areas such as subserosal or pedunculated myomas (13). Roman et al. suggested that intramural myomectomies should be performed carefully in their study (7). Hassiakos et al. suggested that intramural myomas in the fundus, myomas located proximal to the fallopian tubes, and myomas located in the cornua may not be good candidates for removal during C/S delivery because this may affect subsequent fertility (16). In the study by Zhao et al., the rate of subserous myomas was significantly higher in the C/S-myomectomy group than in the control group, while the rates of cervical and intramural myomas were lower in the C/S- myomectomy group than in the control group. This suggests that myomectomy is performed more frequently in those with subserous myomas, and cervical and intramural myomas should be avoided during C/S (17). Radmila et al. suggested that pedunculated and subserous myomas can be removed, and intramural and multiple myomas should be avoided (18). Celal et al. suggested that surgery should be avoided in intramural myomas (19). In our study, serous myomas were observed to be common in both groups, and a tendency was observed to perform myomectomy in myomas in this region, taking into account the myoma diameter.

In the study conducted by Sakinci et al., no statistically significant difference was found between the groups in terms of pre- and postoperative Hb values or blood transfusion rates (20). In the study conducted by Güler et al., no statistically significant difference was found between the two groups in terms of mean Hb change in the cesarean myomectomy groups (21). In the study conducted by Simsek et al., it was reported that the mean difference in postoperative hemoglobin and hemoglobin change

was significantly different between women who had cesarean myomectomy and women who had cesarean delivery without cesarean myomectomy (22). Pergialiotis et al.'s meta-analysis included 19 studies with a total of 3,900 women. Of these, 2,301 women had myomectomy at the time of cesarean delivery and 1,599 had only cesarean delivery. Women who had concurrent myomectomy had a slight decrease in hemoglobin compared with those who had only cesarean delivery (23). Although it is known that cesarean myomectomy in other cases generally should be avoided, observational data suggest that it is possible without a high risk of life-threatening events as long as the surgeon has appropriate expertise, appropriate patients are selected (eg, symptomatic pedunculated fibroids), and blood products are available. In meta-analyses of mostly retrospective studies of patients with fibroids undergoing cesarean, those undergoing concomitant myomectomy had greater drops in hemoglobin (mean difference 0.25 to 0.27 mg/dL), an approximately 40 percent increase in use of blood transfusion, and longer hospital stay (23, 24). In our study, ΔHb level was found to be significantly higher in the myomectomy (+) group than in the myomectomy (-) group. In our study, although the need for transfusion did not increase, it was found that delta hemoglobin increased. Therefore, when making a decision for cesarean myomectomy, the patient's need for transfusion and the adequacy of the center where the transfusion will be performed should be taken into consideration. The factors affecting bleeding are multifactorial and occur both from the incision site and from myomectomy. However, it is very difficult to measure the amount of bleeding separately for these factors. In more than half of the patients who underwent C/S myomectomy, the myomas were removed because they were in the incision line and were preventing the baby from being born. Pedunculated myomas with a low risk of bleeding consist of cases that are discussed with the patient before the caesarean section and are performed voluntarily in order to prevent a second operation.

Various methods have been tried to prevent hemorrhage during C/S-myomectomy. The most common application in the literature is intraoperative and postoperative high-dose oxytocin application (14). Some authors argued that specific operative techniques such as tourniquet, uterine artery ligation and purse-string suture are helpful in limiting intraoperative bleeding during C/S-myomectomy (25-27). Although we have not used the techniques described in our patients, double-layer sutures, bimanual uterine massage, and intraoperative and postoperative uterotonic agents have been effective in hemostasis in all of our patients, regardless of myoma size. Leaving uterine myomas in situ during C/S delivery may seem like a good strategy to prevent intraoperative complications. However, this may be a short-term perspective and does not properly account for long-term risks. Among 22 patients who underwent C/S delivery, a study by AbdRabbo et al reported a mean 34% increase in myoma volume over a 38-month follow-up period. 40.9% of these patients underwent myomectomy or hysterectomy within 38 months due to their symptoms (28). Overall, uterine myomas are the most common indication for hysterectomy in the United States. According to the National Center for Women's Health Information, approximately 175,000 hysterectomies are performed annually for myomas, and their economic impact is significant (29). Given the possibility of reoperation for recurrent myomas, it may be a more cost-effective course of action to make a patient-based decision and remove the myomas at the time of C/S delivery. Despite the long operation time and hospital stay, the reason for its cost-effectiveness may be the avoidance of an additional myomectomy operation throughout life.

The retrospective design and small sample size of our study can be shown as a limitation of the study. However, the evaluation of many maternal and fetal parameters and the evaluation of an objective parameter such as ΔHb data can be shown as a strength of the study.

CONCLUSION

When we evaluate the results of our study and the literature, myomectomy during C/S can be performed safely by an experienced gynecologist. We believe that myomectomy during C/S does not generally cause a significant increase in maternal morbidity and mortality. A detailed discussion should be made about the risks associated with the patient. The risks will depend on the size and location of the myoma, and most risks are similar to those of C/S delivery. However, the long-term risks and benefits, especially in terms of future pregnancies, are not yet clear. Large population or reliable prospective studies are needed to clarify these issues.

Ethics Committee Approval:
The study was initiated after receiving ethics committee approval numbered 2024/224 dated 31/01/24 from the Buca Seyfi Demirsoy Training and Research Hospital Ethics Committee.

Conflict of Interest
The authors declare no conflict of interest.

Author Contributions
Surgical and Medical Practices and Writing were handled by H.A.A. and S.E.; Concept and Design were handled by O.Y.; Data Collection and Literature search were handled by H.A.A. and C.A.; Analyses were handled by T. B.B.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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Son trimester gebelerde rekto-vajinal florada Grup B Streptokok taşıyıcılığı sıklığının ve antibiyotik duyarlılığının araştırılması

Evaluation of Group B Streptococcal carrier prevalanace and antibiotic susceptibility in recto-vaginal flora of third trimester pregnant women

Mehmet Can KEVEN[1], Hacı Öztürk ŞAHİN[2], Ali İsmet TEKİRDAĞ[3]

[1]T.C. Sağlık Bakanlığı Eskişehir Şehir Hastanesi, Perinatoloji Kliniği, Eskişehir, Türkiye
[2]T.C. Sağlık Bakanlığı Bursa Şehir Hastanesi, Jinekoloji Onkoloji Kliniği, Bursa, Türkiye
[3]T.C. Sağlık Bakanlığı Kanuni Sultan Süleyman Eğitim Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İstanbul, Türkiye

ÖZ

Amaç: Son trimester gebe kadınlarda rekto-vajinal Gurup B Streptokok kolonizasyon sıklığını, kolonizasyon sıklığına etkili olduğu düşünülen risk faktörlerinin kolonizasyon sıklığına etkisini ve antibiyotik duyarlılığını araştırmak.

Gereçler ve Yöntem: T.C. Sağlık Bakanlığı Bakırköy Doğumevi Kadın ve Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi doğumhanesine kabul edilen 500 anne adayından başvuru anında rektal ve vajinal kültür örnekleri alındı. Alınan kültür örnekleri Cerrahpaşa Tıp Fakültesi Çocuk Hastalıkları Hastanesi Mikrobiyoloji laboratuvarında değerlendirildi.

Bulgular: Çalışmaya alınan anne adaylarından toplam 41 (%8,2) kadında rekto-vajinal Gurup B Streptokok kolonizasyonu saptandı. Anne yaşı, gebelik sayısı, doğum sayısı, evlilik süresi, sigara kullanımı, eğitim durumu, erken doğum eylemi, gebelikte penisilin grubu antibiyotik kullanımı gibi faktörlerle rektovajinal Gurup B Streptokok kolonizasyon sıklığı arasında anlamlı bir ilişki izlenmedi. Yaptığımız çalışmada anne adaylarının kültür ve antibiyotik duyarlılık tetkikleri doğum sonrası 4. gün sonuçlanmıştır. Bu dönemde yenidoğanda ve anne de antibiyotik kullanım endikasyonu yoktu. Yenidoğanda gelişebilecek sepsis, pnömoni ve menenjit açısından bebekler ve gelişebilecek pelvik inflamatuar hastalık, koryoamnionit, endometrit, sepsis ve yara yeri infeksiyonu için anneler yakın takibe alındı; anne ve bebeklerin hiçbirinde bu infeksiyöz komplikasyonlara rastlanılmadığı gözlendi. Üretilen Grup B Streptokok suşlarının antibiyotik direnç paternleri incelendiğinde penisilin, vankomisin, kloramfenikol, siprofloksasin ve seftriaksona %100 duyarlılık, eritromisine %95, klindamisine %87, tetrasikline 15% duyarlılık saptandı.

Sonuç: Toplumumuzda anne adaylarında rekto-vajinal Gurup B Streptokok kolonizasyon sıklığını araştırmaya yönelik stratejilerin rutin uygulamaya geçilmesi anne ve bebekte mevcut potansiyel risklerin kontrol altına alınmasını sağlayabilir.

Anahtar Kelimeler: Gebelik, Gurup B Streptokok, rekto-vajinal flora, son trimester

ABSTRACT

Aim: To evaluate the prevalance and antibiotic susceptibility of group B streptococcus in the recto-vaginal flora samples of third trimester pregnant women, to investigate the effect of possible risk factors on colonization and to assess antibiotic susceptibility.

Materials and Methods: Recto-vaginal culture samples were collected from 500 pregnant women admitted to Maternity Clinic of Turkish Ministry of Health Bakırköy Women's Health Training and Research Hospital. The samples were analysed at Division of Pediatric Microbiology Cerrahpasa Medical Faculty .

Results: Group B Streptococcus colonization was detected in a total of 41 women (8.2%) among the participants. There was no significant relationship between factors such as maternal age, gravidity, parity, duration of marriage, smoking, education level, preterm labor, penicillin antibiotic use during pregnancy and the frequency of recto-vaginal Group B Streptococcus colonization. Culture antibiogram results were obtained on postpartum day 4. There was no indication for antibiotic use in the neonates and mothers during this period, but these infants and mothers were followed closely and no complications such as meningitis, sepsis and pneumonia developed in these neonates, and no infectious complications such as pelvic inflammatory disease, endometritis, sepsis and wound infection occurred in the mothers. 100% sensitivity to penicillin, vancomycin, chloramphenicol, ciprofloxacin and ceftriaxone, 95% sensitivity to erythromycin, 87% to clindamycin and 15% to tetracycline were detected.

Conclusion: Routine implementation of national strategies to investigate the prevalence of recto-vaginal Group B Streptococcus colonization in pregnant women can help to control the potential risks for both the mother and the neonate.

Keywords: Group B Streptococcus, pregnancy, recto-vaginal fl ora, third trimester

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Sorumlu Yazar/Corresponding Author: Mehmet Can KEVEN, T.C. Sağlık Bakanlığı Eskişehir Şehir Hastanesi, Perinatoloji Kliniği, Eskişehir, Türkiye
E-mail: cankeven@yahoo.com

Çevrimiçi Erişim/Available online at: https://dergipark.org.tr/tr/pub/jgon

GİRİŞ

İnsanların genitoüriner ve gastrointestinal sistemlerinde normal flora üyesi olarak bulunan Streptococcus agalactiae (Grup B Streptokok)'nın insanda oluşturduğu infeksiyon olguları, 1930'lu yıllardan itibaren yayınlanmaya başlanmıştır. Amerika Birleşik Devletlerinde 1970'1i yıllarda %20-50 mortalite ile seyreden neonatal infeksiyonlara yol açması ile dikkatler bu mikroorganizmanın üzerinde toplanmış ve yenidoğanda oluşabilecek infeksiyonları önlemeye yönelik olarak American College of Obstetricians and Gynecologist ve The Center Disease Control and Prevention tarafından stratejiler geliştirilmiştir. Grup B Streptokok (GBS) yenidoğanda menenjit ve sepsiste esas etyolojik faktördür. Ayrıca erişkinlerde doğum sonu endometrit, maternal üriner sistem infeksiyonları, doğum öncesi, doğum ve doğum sonrası bakteriyemi, korioamnionit ve lohusa infeksiyonlarının da başlıca etkenidir (1). Yapılan çalışmalarda yenidoğanda GBS infeksiyon riskinin maternal rekto-vajinal GBS kolonizasyon yoğunluğu ile direk ilişkili olduğu saptanmıştır (2). Ülkemizde, %1,63-37,2 gibi geniş bir aralıkta rekto-vajinal GBS kolonizasyonu olduğunu bildiren çalışmalar vardır (3,4,5,6,7,8). GBS rekto-vajinal kolonizasyonuna bağlı olarak her 1000 doğumdan 0,7-3,7 arasında yenidoğan infeksiyonu gelişebilmekte ve bu infeksiyonların %90 'ının ilk 24 saatte, %95'inin yaşamın ilk üç gününde görüldüğü bildirilmektedir (9).

Bu çalışma ile Sağlık Bakanlığı Bakırköy Doğumevi Kadın ve Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi doğumhanesine kabul edilen gebelerde rekto-vajinal GBS kolonizasyon sıklığını, kolonizasyon sıklığında etkili faktörleri ve üretilen GBS'ların antibiyotik direnç paternlerinin ortaya konması amaçlanmıştır.

GEREÇ VE YÖNTEM

Bu çalışma hastanemiz etik kurulunun 04.12.2003 gün ve 9 sayılı kararına uygun olarak başlatıldı. Aralık 2003- Mart 2004 tarihleri arasında Sağlık Bakanlığı Bakırköy Doğumevi Kadın ve Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi doğumhanesine doğum için gelen 500 anne adayı çalışma kapsamına alındı. Sancı şikayeti ve randevulu sezaryan ile doğum için TC Sağlık Bakanlığı Bakırköy Doğumevi Kadın ve Çocuk Hastalıkları Eğitim Araştırma Hastanesi doğumhanesine yatırılan gebeler, bilgilendirilmiş onamlarının alınması ardından yaş, gravida, parite, gebelik haftası, yaşayan çocuk sayısı, eğitim durumu, evlilik süresi, iş, sigara alışkanlığı, herhangi bir sebeple gebelikte penisilin grubu antibiyotik alıp almadığı sorgulandı ve gebelerin doğum şekilleri takip edilerek kayıt edildi.

Gebelerin doğumhaneye kabulünde ilk muayenede litotomi pozisyonunda muayene masasına yatırılan anne adayından steril eküvyon ile vajinal ve rektal örnekler ayrı olarak alındı. Alınan örnekler streptokokların canlılığının devamı için kan, nalidik asit ve gentamisin ilave edilmiş, Todd-Hewitt agar sıvı besiyerine ekilmesinin ardından; besiyerleri ortam sıcaklığında Cerrahpaşa Tıp Fakültesi Çocuk Kliniği Mikrobiyoloji laboratuvarına nakledildi. Streptococcus agalactiae bacitracin sensitivitesi ve pozitif CAMP testi (Cristie, Atkins, Munch-Peterson) ile identifikasyonu ardından, API metodu (Automation Pour Identification) ile rapid ID,32 Strep (BioMerieux, France) kullanılarak izole edildi. Grup tayini, Slidex strepto-kit A, B, C, D, E, F, G (BioMerieux) kullanılarak Lancefield precipitin metodu ile yapıldı.

Antibiyotik duyarlılık testi ulusal komite tarafından belirlenen klinik laboratuar standartlarına göre 5% koyun kanlı agar içeren Müller Hinton Agarda disk difüzyon metodu ile penisilin G, kloramfenikol, vankomisin, eritromisin, tetrasiklin, seftriakson, klindamisin, siprofloksasin karşı yapıldı.

İstatistik analizler için SPSS 16 (Chicago, SPSS Inc) program kullanıldı. Ki kare testi kullanılarak gebelerde rekto-vajinal grup B streptokok taşıyıcılık sıklığına anne yaşı, gravida, parite, gebelik haftası, eğitim durumu, evlilik süresi, iş durumu, gebelikte herhangi bir sebeple penisilin grubu antibiyotik alıp almadığı ve sigara kullanımının etkisi araştırıldı. Üretilen grup B streptokoklarda antibiyotik direnç paternleri ortaya konuldu.

BULGULAR

Aerop koşullarda kültür yapılan örneklerden 26(%5,2) kadında vajina, 29 (%5,8) kadında rektal 14 (%2,8) kadında ise hem rektal hem vajinal toplam 41(%8,2) kadında GBS üremesi oldu.

Çalışmaya alınan gebelerin yaş ortalaması 26,11'di. Bu hastaların gravite ortalaması 2,98, parite ortalaması 0,846 olarak izlendi. Gebelerin ortalama evlilik süreleri 5 yıldı (Tablo 1). Gebelerin öğrenim durumuna bakıldığında 42 (%8) lise, 42 (%8) ortaokul, 369 (%74) ilkokul mezunu, 47 (%9) gebe ise eğitimsizdi. Hamile kadınların 445'i (%89) ev hanımı 55'i (%11) işçi olarak çalışmaktaydı. Gebelerin 476'sının (%95) sigara kullanım hikayesi yokken; 24 tanesi (%5) sigara kullanmaktaydı. Gebelerin 472'si (%94,4) 36 hafta ve üzeri, 24 tanesi (%4,8) 32-36 hafta, 4 tanesi (%0,8) 26-32 idi. Anne adaylarının 328'i (%66) vajinal, 178'i (%34) ise C/S ile doğum yaptı.

Bizim çalışmamızda anne yaşı, gebelik sayısı, doğum sayısı, eğitim durumu, evlilik süreleri, gebelik süresince herhangi bir nedenle tam

Tablo 1. Grup B Streptokok taşıyıcılığı yönünden yaş grupları, gebelik sayıları, doğum sayıları, evlilik sürelerini içeren demografik özellikler.

	En küçük	En Fazla	Ortalama
Yaş	17	42	26,11
Gebelik Sayısı	1	9	2,1
Doğum Sayıları	0	7	0.85
Evlilik Süresi	1	23	5,4

kür penisilin tedavisi almış olmak (Tablo 2), sigara kullanımı (Tablo 3), erken doğum eylemi (Tablo 4) açısından doğumhaneye yatırılan olgular arasında GBS rekto-vajinal taşıyıcılık için risk artışına yol açan faktör saptanmadı.

Gebelerden izole edilen grup B streptokoklara penisilin, eritromisin, kloramfenikol, vankomisin, siprofloksasin, klindamisin, seftriakson, tetrasiklin ile disk difüzyon yöntemi ile antibiyotik duyarlılığı araştırıldı (Tablo 5). Elde ettiğimiz GBS suşlarının antibiyotik

Tablo 2. Grup B streptokok taşıyıcılığı yönünden gebeliğin herhangi bir döneminde herhangi bir nedenle tam kür penisilin grubu antibiyotik kullananlarla kullanmayanlar arasında taşıyıcılık açısından herhangi bir istatiksel fark izlenmedi.

Antibiyotik	Üreme yok	Üreme var	Total	P değeri
Kullanım yok	407	34	441	
Kullanım var	52	7	59	**0.308**
Total	459	41	500	

Tablo 3. Grup B streptokok taşıyıcılığı yönünden sigara içenlerle içmeyenler arasında istatiksel bir fark izlenmemiştir.

Sigara	Üreme yok	Üreme var	Total	P Değeri
Kullanım yok	431	40	471	
Kullanım var	28	1	29	**0.498**
Total	459	41	500	

Tablo 4. Grup B streptokok taşıyıcılığı yönünden erken doğum eylemi olanlarla olmayanlar arasında istatiksel bir fark izlenmedi.

Erken Doğum Eylemi	Üreme yok	Üreme var	Total	P Değeri
Yok	430	39	469	
Var	29	2	31	**1**
Total	459	41	500	

Tablo 5. İzole edilen grup B streptokok suşlarının antibiyotik duyarlılık sonuçları

Toplam Üretilen Grup B Suşu Sayısı:41	Duyarlı Suş Sayısı	Yüzde (%)	Dirençli Suş Sayısı	Yüzde (%)
Penisilin	41	100	0	0
Kloramfenikol	41	100	0	0
Eritromisin	39	95,8	2	4,2
Vankomisin	41	100	0	0
T etrasiklin	6	15	35	85
Seftriakson	41	100	0	0
Siprofloksasin	41	100	0	0
Klindamisin	36	87	5	13

direnç paternleri incelendiğinde tetrasikline karşı yüksek direnç (%85), eritromisine (%4,2) ve klindamisine (%13) karşı gelişmekte olan direnç penisilin, vankomisin, kloramfenikol, seftriakson ve siprofloksasine tam duyarlılık gözlendi.

Yaptığımız çalışmada anne adaylarının kültür ve antibiyotik duyarlılık tetkikleri doğum sonrası 4. gün sonuçlanmıştır. Bu dönemde yenidoğanda ve anne de antibiyotik kullanım endikasyonu yoktu. Yenidoğanda gelişebilecek sepsis, pnömoni ve menenjit açısından bebekler ve gelişebilecek pelvik inflamatuar hastalık, koryoamnionit, endometrit, sepsis ve yara yeri infeksiyonu için anneler yakın takibe alındı; anne ve bebeklerin hiçbirinde bu infeksiyöz komplikasyonlara rastlanılmadığı gözlendi

TARTIŞMA

Grup B streptokok tarafından insanda oluşturulmuş ilk infeksiyon olgusu 1930'lu yıllarda bildirilmesine rağmen; 1964 yılında yapılan ilk perinatal GBS çalışmasına kadar klinisyenler bu organizma hakkında hemen hemen hiçbir şey bilmemekteydi. 1970'1i yıllarda %20-50'lere varan mortalite oranları ile seyreden dramatik neonatal infeksiyonlara yol açtığının saptanması; maternal uterin infeksiyon ve sepsisinde en önemli etyolojik faktörlerinden biri olması bu mikroorganizmanın öneminin anlaşılmasını sağlamış ve bu konuda gittikçe artan sayıda çalışmalar yapılmaya başlanmıştır (1).

GBS gebe kadınlarda sadece rekto-vajinal kolonizasyona yol açmayıp aynı zamanda amnios sıvısına geçerek anne ve fetusta infeksiyon riskini arttırmakta; gebede prematür doğuma, erken membran rüptürüne, düşük doğum tartısına yol açabilmektedir (1).

Yenidoğanda ise erken ve geç başlangıçlı infeksiyonlarına yol açabilmektedirler. Erken başlangıçlı infeksiyonlarda yenidoğana geçiş çoğunlukla doğum esnasında doğum kanalında olurken; in utero asandan yolla da geçiş olabilmektedir. Geç başlayan infeksiyonda ise vertikal geçiş ve nazokomiyal geçiş söz konusudur (1).

Yenidoğanda bu kadar yüksek mortalite ve morbidite ile seyreden GBS infeksiyonlarının erken tanınması ve önlemeye yönelik ulusal programlar gerekliliği açıktır. Klinik deneyler travay esnasında IV penisilin ya da ampisilin uygulanmasının yenidoğanda GBS bağlı infeksiyon gelişimini önlemede son derece etkiliyken; prenatal dönemde rekto-vajinal GBS genital kolonizasyonunu eradike etmeye yönelik kemoproflaksinin yenidoğanı infeksiyondan korumada etkisiz kaldığını göstermiştir. 1996 yılında The Center Disease Control and Prevention, The AmericanAcademy of Pediatrics ve American College of Obstetricians and Gynecologist erken başlangıçlı hastalığı önlemeye yönelik ilkeler yayınlamışlardır. Buna göre erken başlangıçlı hastalığı önlemek için 35-37 gebelik haftalarındaki kadınların rekto-vajinal GBS kolonizasyonu açısından taranması ve travay esnasında bu hastalara antibiyotik proflaksisi yapılması önerilmiştir. Risk faktörlerine dayalı yaklaşıma göre ise 37 haftadan önce fetal zarların açılması, fetal zarların açılması ile doğum arasında geçen sürenin 18 saat veya daha fazla sürmesi ve travayda 38°C veya daha yüksek ateş gibi bir veya daha fazla risk faktörü olan gebelerde koruyucu olarak antibiyotik verilmesi önerilmektedir. Ancak yapılan çalışmalar göstermiştir ki kültürel örneklerle rekto-vajinal GBS taşıyıcılığını taramaya dayalı yaklaşımın uygulanması sayesinde erken başlangıçlı hastalığa yakalanma oranlarının ABD, Kanada, İngiltere başta birçok ülkede düştüğü ve sadece risk faktörlerinin varlığına dayalı yöntemden daha başarılı olduğu gözlenmiştir (1).

Amerika Birleşik Devletlerin de Terry ve arkadaşları 1995-1998 yılları arasında 608 gebe kadın üzerinde yaptıkları çalışmada rekto-vajinal GBS kolonizasyon sıklığı %4-40 arasında değişmekteydi ve Afrika kökenli Amerikalılarda, beyaz, lspanyol ve Asya kökenli Amerikalılara göre daha yüksek oranda kolonizasyon saptanmıştır. Ayrıca çalışmada yaş, kilo, parite, ilaç kullanımı ile rekto-vajinal GBS kolonizasyonu sıklığı arasında ilişki yoktu ama sigara içenlerde kolonizasyonun anlamlı olarak yüksek olduğu saptamışlardır (12). 1998'de Stoll BJ ve ark yaptığı bir çalışmada gelişmekte olan ülkelerde yapılmış 24 çalışma sonucunda Ortadoğu ve Kuzey Afrikada %22, Asia (Pasifik) %19, Güney Afrika %19, Hindistan ve Pakistan %12 ve Güney Amerika %14 gebe kadınlarda rekto-vajinal GBS kolonizasyon sıklığı saptanmıştır (10). Arjantin'de 28-38 hafta arasında olan 259 gebe üzerinde 2003 yılında yapılan bir çalışmada %18 rekto-vajinal GBS kolonizasyonu saptanmıştır (11).

El-Kersh ve ark 2002 yılında Suudi Arabistan'da yaptıkları çalışmada 28 haftadan büyük 217 gebe kadından 867 vajina ve rektal kültür alınmış 66 kadında (%30,4) GBS üremiş, 33 (%50) gebede hem vajinal hem de rektal üreme, 22 (%33) vajinal kültürde üreme, 11 (%17) rektal kültürde üreme saptanmış (13).

Lewin ve arkadaşları 1981 yılında 722 gebede gebeliklerinin farklı dönemlerinde GBS yönelik rekto-vajinal kültürler almışlar; gebelerdeki kolonizasyon oranının %19 olduğu ve taşıyıcılık saptanan gebelerinde %51'de kendiliğinden taşıyıcılığın kaybolduğu izlenmiş (14). İzolasyon yöntemleri, gebelik sayısı, gebeliğin farklı dönemlerinde kültür örneklerinin alınmış olması, yaş, sosyokültürel ve coğrafik farklılıklar, farklı etnik gruplardan olmak kolonizasyon sıklığında sorumlu olan değişkenlerdir.

Ülkemizde bugüne kadar yapılmış çalışmalarda %1,63-37,2 arasında rekto-vajinal GBS kolonizasyon oranları saptanmıştır. Saçar'ın 1983 yılında yaptığı çalışmada rekto-vajinal GBS

kolonizasyon oranı %37,2 saptamış olmasına karşın; çalışma 51 gebeyle sınırlıydı ve mikroorganizmaların gruplandırılmasında sadece lateks aglutinasyon testi kullanılmıştır (3). Güvenal ve arkadaşlarının saptadığı rekto-vajinal GBS kolonizasyon oranı %1,63 olup bu oran büyük olasılıkla sadece vajen arka forniksi ve serviksten kültür alınması ile alakalıdır (4).

Gökalp ve arkadaşlarının 1986'da, 100 hamile kadında yaptıkları çalışmada annelerde %7 oranında rekto-vajinal GBS kolonizasyonu saptamışlardır (5).

1999 yılında Zeynep Kamil hastanesinde 240 hamile kadın vajinal örneklemesinde gebelerin 20'sinde (%8,3) GBS kolonizasyonu saptanmıştır. Yaş ve gebelik sayısı ile kolonizasyon oranı arasında anlamlı ilişki saptanmamıştır (6). Ancak sigara içenlerde kolonizasyonun anlamlı olarak yüksek olduğu saptamışlardır (12).

Arıbaş ve arkadaşları tarafından Konya'da 1998 yılında yapılan bir çalışmada Vajen arka forniks ve serviksten kültür alınmış ancak GBS üremesi saptamamışlar (7). 1997 yılında Yavuz ve arkadaşları tarafından Van'da yapılan çalışmada 97 gebeden rektum, vajen ve serviksten kültür alınmış toplam 5 (%5,15) hastada kolonizasyon saptanmıştır (8).

Bizim çalışmamızda Sağlık Bakanlığı Bakırköy Doğumevi Kadın ve Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi doğum kliniğine kabul edilen 500 anne adayında 26 (%5,2) kadında vajinal, 29 (%5,8) kadında rektal, 14 (%2,8) kadında ise hem rektal hem vajinal toplam 41 (%8,2) kadında kültürlerde GBS kolonizasyonu saptandı

Anthony ve arkadaşlarının yaptıkları çalışmada 20 yaş altındaki gebelerde rekto-vajinal GBS kolonizasyonun daha sık olduğunu ifade etmişlerdir (29). Arısoy ve arkadaşları ise yaptıkları çalışmada yaşla beraber rekto-vajinal GBS kolonizasyonunun arttığını ifade etmişlerdir (15). Bizim yapmış olduğumuz çalışmada yaşla ve evlilik süresi ile rekto-vajinal GBS taşıyıcılığı arasında istatiksel bir fark izlenmemiştir.

Rekto-vajinal GBS kolonizasyonu ile gebelik sayısı ve parite arasında ilişkiyi inceleyen birçok çalışma yapılmıştır. Başlangıçta gebelik sayısı ve parite artışının rekto-vajinal GBS kolonizasyonu arttırdığı ileri sürülse de özellikle son yıllarda yapılan birçok çalışmada istatiksel olarak böyle bir ilişki olmadığını ifade edilmektedir (1). Anthony ve arkadaşlarının yaptıkları çalışmada gebelik sayısı artışının rekto-vajinal GBS taşıyıcılığını pozitif yönde etkilediğini hatta 3'den fazla doğum yapanlarda %30 taşıyıcılık olduğunu ileri sürmüşlerdir (15). Hammound ve arkadaşları 2'den fazla paritenin rekto-vajinal GBS kolonizasyonu için risk faktörü olduğunu ifade etmişlerdir (16). Bizim yaptığımız çalışmada ise gebelik sayısı ve parite ile rekto-vajinal GBS kolonizasyonu arasında anlamlı bir istatiksel fark izlenmemiştir.

Gebeliklerinin herhangi bir döneminde herhangi bir sebeple (genellikle idrar yolu infeksiyonu) GBS tedavisinde primer kullanılan ilaçlardan birini tam kür kullanan grupla kullanmayan grup arasında doğumhaneye kabul edildikleri anda rekto-vajinal GBS kolonizasyonu açısından istatiksel fark izlenmedi. Bu durum GBS rektal ve vajinal geçici ve aralıklı kolonizasyon yapabildiği ve doğumdan 1-5 hafta önce kolonizasyon araştırmalarının yapılması ve önlemlerin buna göre alınması gerektiği klasik bilgisi ile uyumludur (1).

Hastanemize başvuran anne adaylarının %94'ü sigara kullanmamaktaydı. Sigara kullanımı açısından rekto-vajinal GBS taşıyıcılığı incelendiğinde sigara içenlerle içmeyenler arasında istatiksel bir fark saptanmadı.

Tarama yaptığımız gebelerin %6'sı prematüre doğum yapmıştı; çalışmamızda erken doğum eylemi ve rekto-vajinal GBS kolonizasyonu arasında istatiksel anlamlı bir fark izlenmedi. Ancak vaka sayısının azlığı nedeniyle bu konuda daha ileri çalışmaların yapılması uygundur.

GBS antibiyotik rezistans paternlerine ülkemizde ve dünyada bakıldığında tetrasikline yüksek oranda direnç; buna karşın eritromisin ve klindamisine artan oranda direnç geliştiği ancak penisilinlere, vankomisin, 1. ve 2. kuşak sefalosporinlere karşı herhangi bir direncin söz konusu olmadığı ifade edilmektedir (17). Bizim yaptığımız çalışmada da elde ettiğimiz suşların antibiyotik rezistans paternleri literatürle uyumluydu ve penisilin, vankomisin, kloramfenikol, siprofloksasin ve seftriaksona %100 duyarlılık, eritromisine %95, klindamisine %87, tetrasikline %15 duyarlılık saptandı. Buda tedavide hala ilk seçeneğin penisilin ve türevleri olduğu klasik bilgisiyle uyumludur (18, 19. 20).

Yaptığımız çalışmada anne adaylarının doğum sonrası rekto-vajinal GBS kültür ve antibiyotik duyarlılık sonuçları 4. gün sonuçlanmıştır bu dönemde yenidoğana ve anne de antibiyotik kullanım endikasyonu yoktu. Yenidoğanda gelişebilecek sepsis, pnömoni ve menenjit açısından bebekler ve gelişebilecek pelvik inflamatuar hastalık, koryoamnionit, endometrit, sepsis ve yara yeri infeksiyonu için anneler yakın takibe alındı; anne ve bebeklerin hiçbirinde bu komplikasyonlara rastlanılmadığı gözlendi. Bu durumun sebebinin hastanemizde doğum esnasında 38°C üzerinde ateş, fetal zarların 12 saatin üzerinde açıldığı durumlar, 37. haftanın altında su gelişi olan olgular gibi yüksek riskli gebelere antibiyotik tedavisi başlamamıza, bir kısım bebeğin doğumu başlamayan ve su gelişi olmayan randevulu eski sezaryan olgusu olması ve rekto-vajinal GBS taşıyıcısı olgu sayımızın az olması nedeniyle olduğu kanısındayız.

Yenidoğanlarda erken başlangıçlı GBS hastalığın önlenmesine yönelik olarak, ACOG Haziran 2019 da yeni bir kılavuz yayınladı. GBS hala yenidoğan infeksiyon önde gelen sebebidir ve erken başlangıçlı hastalık için GBS, maternal gastrointestinal sistem ve genitoüriner sistem kolonizasyonu pirimer risk faktörüdür. Maternal taşıyıcı kadınların 50% de geçiş genellikle doğumda ya da membranların rüptürü sonrasın da vertikal olarak yenidoğana olmakta ve antibiyotik proflaksi olmadığında %1-2 yenidoğanda erken başlangıçlı hastalık gelişmektedir. Diğer risk faktörleri arasında doğum haftasının 37'nin altında olması, düşük doğum kilosu, uzamış membran rüptürü, intraamniotik infeksiyon, genç anne yaşı ve siyah ırktan olmak yer alır. GBS erken başlangıçlı hastalık önlenmesine yönelik olarak evrensel 36-37 hafta prenatal rekto-vajinal kültür taraması yapılmalı, doğru örnekler toplamalı, pozitif olgulara intrapartum antibiyotik proflaksisi yapılmalı ve çocuk doktorları ile yakın koordinasyon halinde olunmalıdır. Membranları sağlam travay öncesi sezaryan olgularına antibiyotik proflaksi önerilmez (21). 2005 yılında yaptığımız çalışmadan bu yana hala ülkemizde riske dayalı yaklaşımla hastalara antibiyotik tedavisi uygulanmakta olup gebelerde rekto-vajinal kültür GBS taramasına yönelik stratejiler geliştirilmemiştir.

2016 yılında Alp ve ark'larının yaptığı çalışmada 500 kadın GBS kolonizasyonu açısından taranmış; taranan kadınların 68 (%13,6)'da GBS üremesi saptanmış, gebe olmayanlarında GBS taşıyıcılığı %16,5 iken, gebelerde %9,8 olduğu görülmüştür. Gebe kadınlarda GBS taşıyıcılığı açısından fark olmamakla beraber; olguların 55 tanesinde tetrasiklin direnci, 16 tanesinde eritromisin ve klindamisin direnci, 13 tanesi levofloksasin direnci vardır (22). 2004 yılında yaptığımız çalışmadan bu yana aradan geçen sürede terasiklin direnci sebat ederken artan oranda eritromisin, klindamisin ve quinolon gurubu antibiyotik direnci izlenmiştir.

Rekto-vajinal GBS kolonizasyon sıklığı ülkeler, bölgeler ve çalışma standartlarındaki farklılıklara bağlı olarak değişen oranlarda izlenmektedir. Yaptığımız çalışmada yaş, gebelik sayısı, parite sayısı, evlilik süresi, sigara kullanımının, eğitim durumu, gebelikte GBS etkili antibiyotik kullanımı, erken doğum eylemi gibi faktörlerin rekto-vajinal GBS kolonizasyon sıklığını etkilemediği izlendi. Elde ettiğimiz GBS suşlarının antibiyotik direnç paternleri incelendiğinde tetrasikline karşı yüksek direnç, eritromisine ve klindamisine karşı gelişmekte olan direnç penisilin, vankomisin, kloramfenikol, seftriakson ve siprofloksasine tam duyarlılık gözlendi. Bu sonuçlar ülkemizde ve dünyada yapılan çalışmalarla uyumludur ve GBS infeksiyonlarda hala ilk tercihin penisilin ve türevleri olduğunu göstermektedir. Ayrıca hastanemize başvuran anne adaylarındaki rekto-vajinal GBS kolonizasyon sıklığı aynı amaca yönelik ülkemizde geçmişte yapılan çalışmaların verileriyle paralel olarak izlendi.

SONUÇ

Rekto-vajinal GBS kolonizasyon sıklığında, bizim çalışmamızdan önceki yıllarda ve sonraki yıllarda herhangi bir değişiklik izlenmemiştir. Bu bize geçmiş yıllara oranla toplumumuzun artmış bir riske maruz kalmadığı izlenimi verse de son trimester gebelerde rekto-vajinal kolonizasyonun belirlenmesine yönelik doğru kültür antibiyogram çalışmaları, intrapartum antibiyotik stratejilerinin rutine geçirilmesi ve çocuk doktorları ile yakın koordinasyon ile potansiyel neonatal mortalite ve morbiditenin önemli oranda kontrol altına alınabileceği düşüncesindeyiz.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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Ultrasound-guided Veress needle insertion in laparoscopic surgery: safety and efficacy evaluation

Laparoskopik cerrahide ultrasonografik radyolojik görüntüleme rehberliğinde Veress iğnesi girişi

Mevlut BUCAK[1], Serhan Can ISCAN[2], Evrim ERDEMOGLU[3]

[1]Department of Perinatology, Ankara Etlik City Hospital, Ankara, Turkiye
[2]Department of Gynecologic Oncology, Isparta City Hospital, Isparta, Turkiye
[3]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Suleyman Demirel University, Isparta, Turkiye

ABSTRACT

Aim: In laparoscopic surgery, abdominal access is one of the most critical steps with significant risk of complications, especially in high-risk patient groups. The Veress needle is a widely used technique for this access; however, serious complications can occur during its blind insertion. The aim of this study was to evaluate the safety and efficacy of ultrasound-guided Veress needle insertion.

Materials and Methods: This randomized prospective study was conducted at Suleyman Demirel University Faculty of Medicine. The 100 study participants were randomly assigned to receive ultrasound-guided or blinded Veress needle insertion. In both groups, insertion attempts, time, and complications were assessed. Student's t-test, Mann-Whitney U test and chi-square test were used for statistical analysis.

Results: In 88% of the ultrasound-guided accesses, success was achieved on the first attempt, while this rate was 82% with the conventional method (p=0.40).Total access time was shorter with ultrasound guidance with 92.6 ± 14.2 seconds compared to 100.4 ± 15.3 seconds with the conventional method (p=0.01). No major complications were observed in either group; there was no statistical difference in complications.

Conclusion: This study demonstrates that ultrasound-guided Veress needle insertion is a potential alternative to the traditional blind method and improves insertion time. However, the results cannot be generalized with certainty as there was no statistically significant difference in the study. A larger sample size and multicenter studies are needed to confirm the findings.

Keywords: veress needle, laparoscopic entry tecnique, ultrasound guide

ÖZ

Amaç: Laparoskopik cerrahide abdominal giriş, özellikle yüksek riskli hasta gruplarında önemli komplikasyon riski taşıyan en kritik aşamalardan biridir. Veress iğnesi, bu girişte yaygın olarak kullanılan bir tekniktir; ancak kör uygulanması sırasında ciddi komplikasyonlar meydana gelebilir. Bu çalışmanın amacı, ultrason rehberliğinde Veress iğnesi yerleştirmenin güvenilirliğini ve etkinliğini değerlendirmektir.

Gereçler ve Yöntem: Bu randomize prospektif çalışma, Süleyman Demirel Üniversitesi Tıp Fakültesi'nde gerçekleştirildi. Çalışmaya katılan 100 hasta, rastgele iki gruba ayrıldı: Birinci grup, geleneksel kör Veress iğnesi yerleştirme yöntemiyle; ikinci grup ise ultrason rehberliğinde Veress iğnesi yerleştirme yöntemiyle işlem gördü. Her iki grupta giriş denemesi sayısı, giriş süresi ve komplikasyon oranları gibi parametreler değerlendirildi. İstatistiksel analizler için Student's t-testi, Mann-Whitney U testi ve ki-kare testi kullanıldı.

Bulgular: Ultrason rehberliğinde yapılan girişlerin %88'inde ilk denemede başarı sağlanırken, geleneksel yöntemde bu oran %82 olarak bulundu (p=0.40). Toplam giriş süresi ultrason rehberliğinde 92,6 ± 14,2 saniye ile daha kısa iken, geleneksel yöntemde bu süre 100,4 ± 15,3 saniye olarak bulundu (p=0.01). Her iki grupta da büyük komplikasyonlar gözlenmedi; komplikasyon açısından da istatiksel bir fark bulunmamıştır.

Sonuç: Bu çalışma, ultrason rehberliğinde yapılan Veress iğnesi yerleştirmenin, geleneksel kör yönteme göre potansiyel bir alternatif olduğunu ve giriş süresini iyileştirdiğini göstermektedir. Ancak, çalışmada istatistiksel olarak anlamlı fark bulunmaması nedeniyle, sonuçlar kesin olarak genellenememektedir. Daha geniş örneklem büyüklüğü ve çok merkezli çalışmalarla bulguların doğrulanmasına ihtiyaç vardır.

Anahtar Kelimeler: Veress iğnesi, laparoskopik giriş tekniği, ultrason rehberliği

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Sorumlu Yazar/Corresponding Author: Mevlut BUCAK, Division of Maternal-Fetal Medicine, Department of Obstetrics, Gynecology and Reproductive Sciences, University of Maryland School of Medicine, 22 South Greene Street Suite P6H301 Baltimore, MD, 21201, USA
E-mail: mevlutbucak@gmail.com

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INTRODUCTION

Laparoscopic surgery has become a widely used procedure in gynecology for both diagnostic and therapeutic purposes. However, gaining access to the abdominal cavity remains one of the most challenging aspects of laparoscopy (1,2). The Veress needle technique is the most commonly used method by gynecologists to create a pneumoperitoneum before trocar placement (3,4). However, serious complications may occur during blind application of this technique and these complications may have significant negative effects on the patient's health outcomes and quality of life (5,6). At least 50% of all complications occurring during laparoscopic surgery are related to the abdominal access stage, with complication rates ranging from 0.1% to 1.3% (7,8).

Ultrasound guidance has attracted attention as a method that has the potential to reduce the risks of complications during Veress needle placement. This potential benefit of ultrasound guidance may contribute to the prevention of serious complications such as major vascular injuries and gastrointestinal damage by increasing the probability of correct needle placement (9). Although, in the current literature, there is evidence of the advantages of using ultrasound guidelines in surgeries, the number of research papers analyzing the outcomes of the use of such a method when placing Veress needles is low. This study is one of the first studies to evaluate the clinical efficacy and complication rates of ultrasound guidance in relation to the goal of providing a potentially safer method for creating pneumoperitoneum in laparoscopic gynecologic procedures.

Our hypothesis is that ultrasound-guided Veress needle insertion may reduce access-related complications rates compared with the conventional blind procedure. The aim of the study was to compare the complication incidences of ultrasound-guided Veress needle placement with the conventional blind procedure.

MATERIALS AND METHODS

It is a randomized prospective study carried out on patients undergoing laparoscopic surgery at Obstetrics and Gynecology Clinic of Süleyman Demirel University Faculty of Medicine Hospital from April 2018 to January 2020. In this context, the study was initiated with the approval of the Ethics Committee of Süleyman Demirel University Faculty of Medicine and was conducted in accordance with the ethical principles of the Declaration of Helsinki (Ethics Committee Approval Number: 16042019-140).

Regarding sample size, one hundred patients who were listed for elective laparoscopic surgery were recruited in the study. Patients were randomly selected from a population with a homogeneous distribution in terms of demographic characteristics such as age, gender, ethnicity and socioeconomic status. The participants in the study were post-surgery women with age 18 and above, who sought for a laparoscopic surgery at the Hospital of Süleyman Demirel University Faculty of Medicine and who agreed to the surgical operations with signed consent. Patients who declined to join the surgeries, those with history of abdominal adhesions during past operations and other severe complications probable during surgeries were not considered for the study.

This study was a randomized controlled design comparing two different Veress needle insertion techniques. Patients were divided into groups by simple random sampling and the insertion procedures were performed by the same surgeon to minimize bias due to procedural variability. In Group I, the Veress needle was inserted classically by lifting the anterior abdominal wall with laundry clamps placed to the right and left of the umbilicus; in Group II, it was inserted under the guidance of a General Electric Pro 200 ultrasonography device (GE Healthcare, Milwaukee, WI, USA) without lifting the anterior abdominal wall. Correct needle placement was confirmed in both groups by aspiration test, hanging drop test, and initial entry pressure less than 10 mmHg. Subsequently, the intra-abdominal pressure was inflated to 20 mmHg and a 10 mm trocar was inserted through the umbilicus. After trocar insertion, complications such as vascular, intestinal, gastric and omentum injuries were recorded with a 0-degree laparoscope. Measures such as verification of Veress needle access, success of access attempts and surgical complications were evaluated for both groups.

The data obtained were analyzed using SPSS 23.0 (Statistical Package for Social Sciences). Student's t-test was used for the analysis of normally distributed continuous data and Mann-Whitney U test was used for non-normally distributed continuous data. Chi-square test was used to analyze categorical data. All analyses were performed at 95% confidence interval and 5% significance level. Missing data were analyzed using the listwise deletion method. A p-value of less than 0.05 was used to establish statistical significance for all tests.

RESULTS

This study included 100 patients to evaluate the safety and efficacy of ultrasound-guided Veress needle placement compared to conventional Veress needle placement. When the demographic data of the groups were analyzed, it was observed that there was no significant difference between the two groups in terms of height,

weight and body mass index (BMI). However the age parameter was found to be lower in Group II and this difference was statistically significant (p=0.03) (Table 1).

When evaluated in terms of previous surgical history, no significant difference was found between the two groups in terms of number of operations and types of surgery. Although the number of patients who underwent laparoscopic surgery was higher in Group II, this difference was not statistically significant (p=0.21). Similarly, no significant difference was observed between the two groups in terms of surgical incisions and previous upper and lower abdominal surgeries (Table 2).

Between groups, the number of successful Veress needle insertions was similar. Both groups had similar median access numbers. First attempt failure rates and alternative access methods were similar between groups. Changing the entry point usually fixed the failure to access (Table 3).

Table 1. Comparison of Demographic Data Between Groups

Parameter	Group I (n=50)	Group II (n=50)	p-value
Age (mean±SD)	41.82 ± 11.933	36.92 ± 10.307	0.03
Height (mean±SD)	161.24 ± 5.906	160.16 ± 6.319	0.37
Weight (median, range)	71.5 (42-101)	67 (45-109)	0.38
BMI (kg/m²) (mean±SD)	27.24 ± 5.326	27.19 ± 16.088	0.96
BMI Categories (%)			
Underweight (<18.5)	4% (2/50)	6% (3/50)	0.64
Normal (18.5-24.9)	40% (20/50)	42% (21/50)	0.85
Overweight (25-29.9)	36% (18/50)	34% (17/50)	0.79
Obese (≥30)	20% (10/50)	18% (9/50)	0.76

SD = Standard Deviation BMI = Body Mass Index

Table 2. Comparison of Surgical History Between Groups

Parameter	Group I (n=50)	Group II (n=50)	p-value
Number of Previous Surgeries (median, range)	1 (0-3)	2 (0-3)	0.507
Previous Laparoscopic Surgery (chi-square test)	8%	16%	0.21
Vertical Incision in Previous Surgery (chi-square test)	2%	4%	0.55
Horizontal Incision in Previous Surgery (chi-square test)	44%	32%	0.21
Previous Abdominal Surgeries			
Lower Abdominal Surgery	50% (25/50)	40% (20/50)	0.31
Upper Abdominal Surgery	10% (5/50)	14% (7/50)	0.54
Both Upper and Lower Abdominal Surgery	4% (2/50)	6% (3/50)	0.64
Surgical Complication Rates	12% (6/50)	10% (5/50)	0.78
Adhesions from Previous Surgeries	24% (12/50)	18% (9/50)	0.46

Table 3. Number of Successful Veress Needle Insertions

Parameter	Group I (n=50)	Group II (n=50)	p-value
Number of Successful Veress Needle Insertions			
Median (range)	1 (1-2)	1 (1-3)	0.921
Alternative Insertion Methods Used in Case of First Attempt Failure			
Direct Trocar Insertion	10% (5/50)	8% (4/50)	0.73
Open Laparoscopy (Hasson Technique)	6% (3/50)	4% (2/50)	0.65
Remedial Strategies Used in Failed Insertions			
Changing Insertion Point	12% (6/50)	10% (5/50)	0.75
Additional Skin Incision	4% (2/50)	2% (1/50)	0.55

Table 4. Details of Insertion Attempts and Minor Complications During Insertion

Parameter	Group I (n=50)	Group II (n=50)	p-value
Number of Attempts			
1st Attempt (% Success)	82% (41/50)	88% (44/50)	0.40
2nd Attempt (% Success)	18% (9/50)	10% (5/50)	0.25
3rd Attempt (% Success)	0% (0/50)	2% (1/50)	0.31
Total Insertion Time (seconds)	100.4 ± 15.3	92.6 ± 14.2	0.01
Minor Complications During Insertion			
Omental Injury	4% (2/50)	6% (3/50)	0.64
Gas Leakage	6% (3/50)	8% (4/50)	0.55

SD = Standard Deviation BMI = Body Mass Index

In terms of complications, major complications (bowel injury, vascular injury, gastric injury) were not observed in both groups. In terms of minor complications, the rates of omental injury and gas leakage were similar in both groups. Although the rate of omental injury was slightly higher in Group II, this difference was not statistically significant (p=0.64) (Table 4).

Looking at the details of the entry trials, the success rate in the first trial was 88% in Group II and 82% in Group I. In the second attempt, the success rate was 18% in Group I and 10% in Group II. In the third attempt, the success rate was 2% in Group II, while no success was observed in Group I. Total access time was shorter in Group II and this difference was statistically significant (p=0.01) (Table 4). As shown in the figures, patients with a surgical history showed decreased Veress needle insertion success in both groups (Figure 1 and Figure 2). This was particularly evident in patients with multiple surgeries.

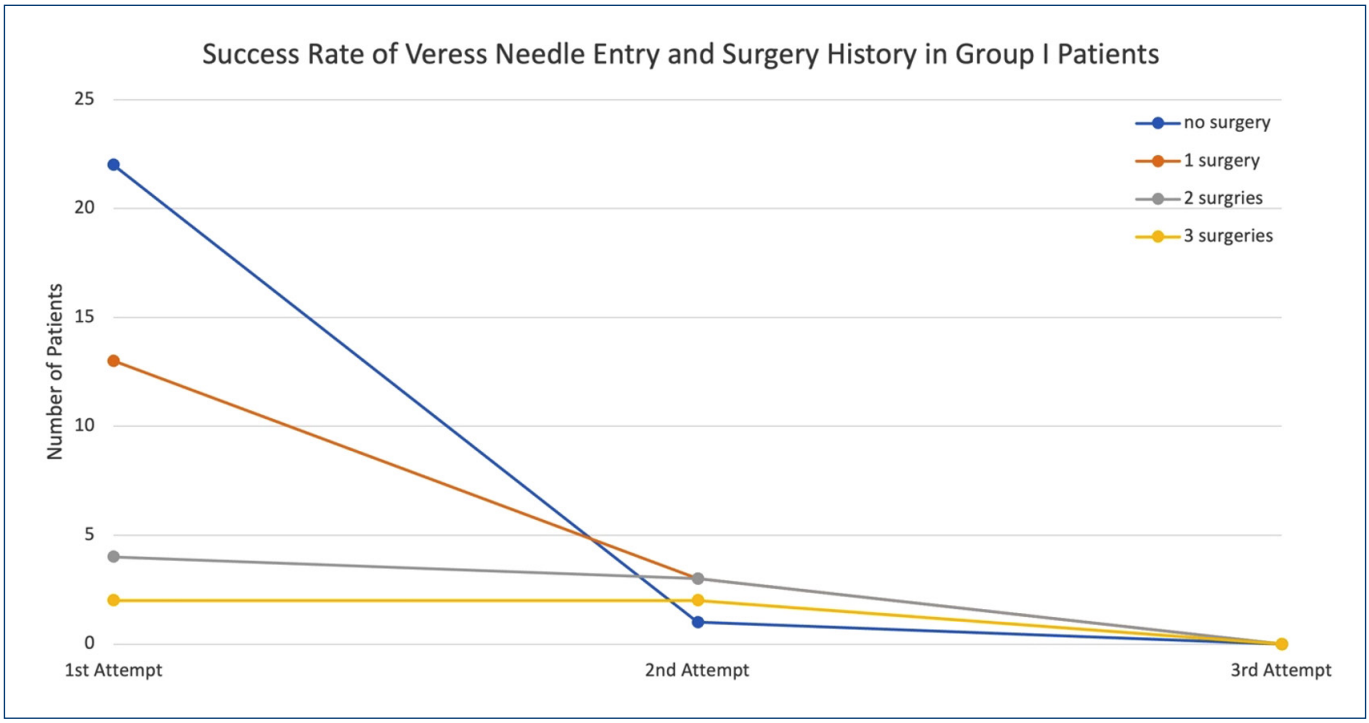

Figure 1. Success Rate of Veress Needle Entry and Surgery History in Group I Patients

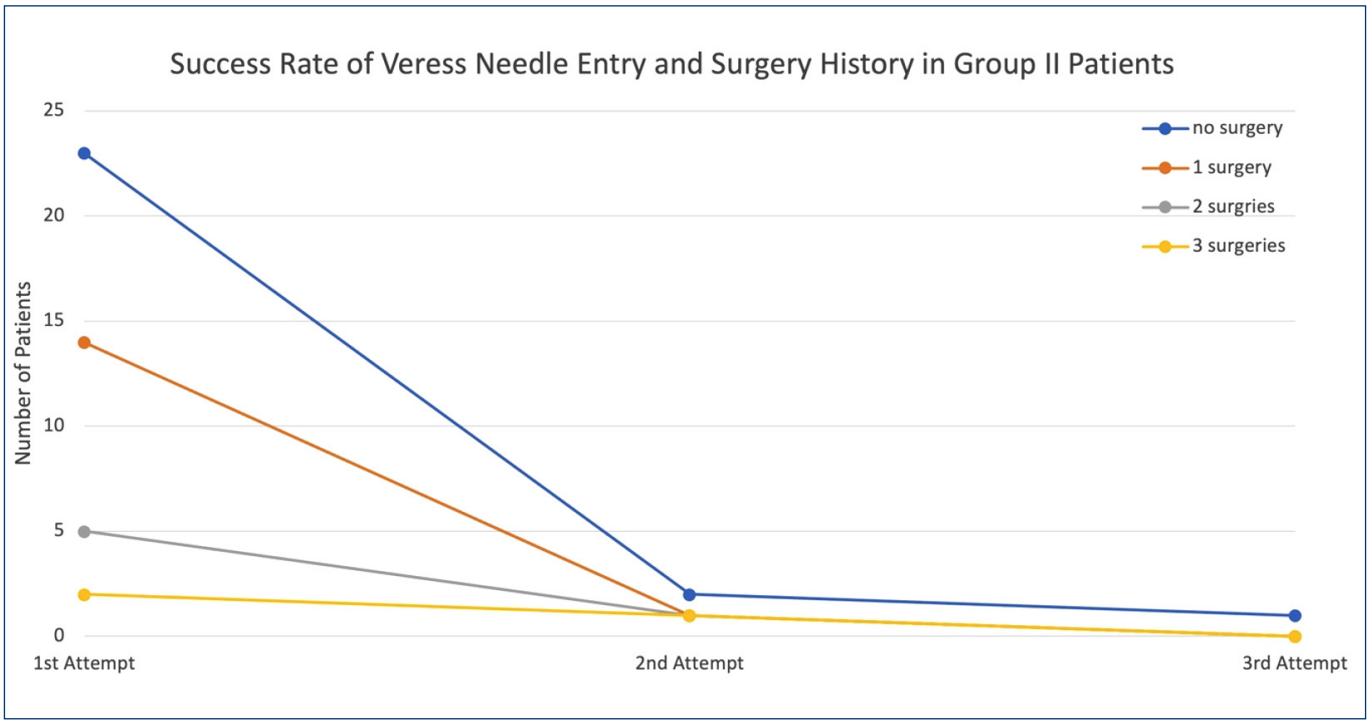

Figure 2. Success Rate of Veress Needle Entry and Surgery History in Group II Patients

DISCUSSION

The goal of this study was to determine whether ultrasound guidance can help to avoid complications while performing laparoscopic access with Veress needle. Laparoscopic surgical procedures become more complex depending on how abdominal access is achieved as this is the most sensitive and hazardous step of the surgery hence there is need for caution especially in the cases of patients on the high risk of complications. Ultrasound-guided Veress needle insertion helped shorten the insertion time without a statistically significant difference in the complication rate.

In laparoscopic surgery, the abdominal access phase is one of the most critical steps of the procedure. In the literature, although the Veress needle technique is the most commonly used method, it is reported to carry significant complication risks. In a systematic review by Azevedo et al. 1,575 (0.23%) injuries were found in 696,502 laparoscopic procedures, of which 126 (8%) were recorded as large vessel or hollow organ injuries (10). Rosen et al. compared different pneumoperitoneum creation methods including Veress needle, direct trocar access and open technique and concluded that no technique was completely superior (11). McKernan and Champion reported that the open technique was safer than the Veress needle in laparoscopic cholecystectomy (12). Günenç et al. showed that direct trocar access with elevation of the rectus sheath had a lower complication rate than the Veress needle technique (3.3% vs. 15.7%) (13). These literature findings suggest that laparoscopic access techniques are still controversial and more research is needed to determine the optimum method.

The technique of ultrasound-guided Veress needle insertion is an understudied topic in the literature. Several studies have shown the benefits of ultrasound guidance in surgery, but Veress needle research is scarce. For example, although Orlando et al. reported a low complication rate in Veress needle insertions, the role of ultrasound guidance in reducing these complications was not discussed in detail (14). The veterinary study by Fiorbianco et al. demonstrated the efficacy of ultrasound guidance in creating pneumoperitoneum and reducing complications in the use of Veress needle (15). Furthermore, in a retrospective evaluation, Zaraca and colleagues found that blind access with Veress needle increased complications and that open laparoscopy may be safer (16). In a study conducted by Santala and Järvelä on obese patients, it was shown that ultrasound-guided transfundal access was safer than Veress needle in transabdominal approach (17). These studies suggest that ultrasound-guided Veress needle access may be offer potential benefits in difficult anatomical situations, but more research is needed.

The Veress needle insertion success rates obtained in this study show some similarities and differences when compared with other studies in the literature. In a study by Inan et al. on laparoscopic cholecystectomy, it was reported that the access success rate was

92% with the use of Veress needle, but this rate increased to 98% with the direct trocar access method (18). A systematic review by Cornette and Berrevoet reported that no access technique for creating a pneumoperitoneum is free of complications and that the Veress method may also be associated with complications and failed access (19). These findings suggest that ultrasound-guided Veress needle access may potentially provide a higher success rate than blind access.

The complication rates obtained in this study show some important differences and similarities when compared with the available data in the literature. In a systematic review by Azevedo et al. it was reported that the complication rate in laparoscopic access with Veress needle was 0.23% and 8% of these complications were large vessel or hollow organ injuries (10). Sigman et al. reported that blind Veress needle accesses carried a higher risk of complications compared to open accesses and especially intestinal and vascular injuries were more common in blind accesses (20). Zaraca and colleagues compared the routinely applied Hasson technique with blind Veress needle access and reported that the Hasson technique had lower complication rates (16). Cornette and Berrevoet reported that minor complications were more frequent with Veress needle access, but most of these complications were not serious (19).

The safety and efficacy of ultrasound-guided Veress needle placement can be demonstrated by the lack of a statistical increase in the complication rate. Limitations of the study include the limited sample size, the lack of a multicenter study, and the lack of additional statistical analyses to confirm the initial homogeneity of the groups. This should be considered a methodological limitation of this study. These limitations affect the scope of the study.

CONCLUSION

The results of this study suggest that ultrasound-guided Veress needle placement can be used as an alternative method for abdominal access without statistically increasing the risk of complications. Larger, multicenter studies are needed to support this hypothesis and to evaluate its rationale in larger populations. More studies are needed to understand the impact of the increased use of ultrasound assistance in different surgical scenarios and populations and the impact of the learning curve of this technique on surgical outcomes.

Ethics Committee Approval:
The approval of the Ethics Committee of Süleyman Demirel University Faculty of Medicine was received (Ethics Committee Approval Number: 16042019-140).

Conflict of Interest:
The authors declare that they have no conflict of interest to disclose.

Author Contributions:
MB: Concept, author, analysis and interpretation, design, statistical analysis, supervision, concept. SCI: Concept, author, data collection, analysis and interpretation. EE: Concept, statistical analysis and interpretation The final version was read and approved by all authors.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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The impact of the COVID-19 pandemic on the diagnosis and treatment of ectopic pregnancy: a retrospective comparison

COVID-19 pandemisinin ektopik gebelik tanı ve tedavi süreçlerine etkisi: Retrospektif bir karşılaştırma

Sıtkı ÖZBİLGEÇ[1], Fatih AKKUŞ[2], Sevcan SARIKAYA[1], Emin Erhan DÖNMEZ[3], Rahime Berfin DURMAZ[2], Ali ACAR[2]

[1]Konya Şehir Hastanesi, Kadın Hastalıkları ve Doğum Bölümü, Konya, Türkiye
[2]Necmettin Erbakan Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum/Perinatoloji, Türkiye
[3]İstanbul Eğitim ve Araştırma Hastanesi, Türkiye

ABSTRACT

Aim: To investigate the impact of the COVID-19 pandemic on the diagnosis and treatment processes of ectopic pregnancies (EP) at a tertiary hospital in Turkey.

Materials and Methods: This retrospective study compared 221 cases of tubal EP diagnosed after March 15, 2020, with 217 cases diagnosed before this date. Patient demographics, clinical characteristics, and treatment modalities were analyzed. Statistical analyses, including independent t-tests, Chi-square tests, and multinomial logistic regression, were conducted to assess differences between the COVID and pre-COVID periods.

Results: The study found no significant differences in maternal age, gravidity, parity, or gestational weeks between the COVID and pre-COVID periods. However, there was a notable increase in patients presenting with abdominal pain (52.5% vs. 37.8%) and intraperitoneal hemorrhage (26.7% vs. 7.4%) during the COVID period. Despite the higher frequency of abdominal pain, vaginal bleeding was less common during the pandemic. Treatment approaches also shifted, with a significant increase in medical management (41.2% vs. 29.0%) and a slight decrease in surgical interventions during the COVID period. Multinomial logistic regression revealed that parity, gestational week, presence of Douglas fluid, and the period of diagnosis (COVID vs. pre-COVID) were significant predictors of treatment modality.

Conclusion: The COVID-19 pandemic influenced the clinical presentation and management of ectopic pregnancies in our hospital. While there were no significant differences in key demographic or laboratory parameters, the increased presence of abdominal fluid and a shift towards medical management during the pandemic period suggest changes in patient presentation and treatment preferences. This study underscores the importance of maintaining vigilant diagnostic and therapeutic approaches for EP, even during global health crises.

Keywords: Ectopic pregnancy, COVID-19 pandemic, diagnosis, treatment modalities, maternal health

ÖZ

Amaç: Bu çalışmanın amacı, COVID-19 pandemisinin Türkiye'deki bir üçüncü basamak hastanede ektopik gebeliklerin (EG) tanı ve tedavi süreçleri üzerindeki etkisini araştırmaktır.

Gereçler ve Yöntem: Bu retrospektif çalışmada, 15 Mart 2020'den sonra tanı konulan 221 tübal ektopik gebelik olgusu, bu tarihten önce tanı konulan 217 olgu ile karşılaştırıldı. Hasta demografik bilgileri, klinik özellikler ve tedavi yöntemleri analiz edildi. Gruplar arasındaki farkları değerlendirmek için bağımsız t-testi, Ki-kare testi ve multinominal lojistik regresyon analizleri yapıldı.

Bulgular: COVID dönemi ile COVID öncesi dönem arasında anne yaşı, gravida, parite veya gebelik haftası açısından anlamlı bir fark bulunmadı. Bununla birlikte, COVID döneminde karın ağrısı (COVID öncesi %37,8'e karşılık %52,5) ve intraperitoneal kanama (COVID öncesi %7,4'e karşılık %26,7) ile başvuran hasta sayısında artış gözlendi. Karın ağrısı daha sık görülmesine rağmen, pandemi sırasında vajinal kanama daha az yaygındı. Tedavi yaklaşımlarında da değişiklikler oldu; COVID döneminde medikal tedavi oranında (COVID öncesi %29,0'a karşılık %41,2) anlamlı bir artış ve cerrahi müdahalelerde hafif bir azalma görüldü. Multinominal lojistik regresyon analizine göre; parite, gebelik haftası, Douglas sıvısı varlığı ve tanı dönemi (COVID vs. COVID öncesi) tedavi modalitesinin önemli belirleyicileri olarak bulundu.

Sonuç: COVID-19 pandemisi, hastanemizde ektopik gebeliklerin klinik prezentasyonu ve yönetimini etkilemiştir. Önemli demografik veya laboratuvar parametrelerinde anlamlı farklılıklar bulunmamakla birlikte, karın içi sıvı varlığında artış ve pandemi döneminde medikal tedaviye kayma, hasta başvurularında ve tedavi tercihlerinde değişiklikler olduğunu göstermektedir. Bu çalışma, küresel sağlık krizleri sırasında bile ektopik gebeliklerde dikkatli tanı ve tedavi yaklaşımlarının sürdürülmesinin önemini vurgulamaktadır.

Anahtar Kelimeler: Ektopik gebelik, COVID-19 pandemisi, tanı, tedavi yöntemleri, anne sağlığı

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Sorumlu Yazar/Corresponding Author: Sıtkı ÖZBİLGEÇ, Konya Şehir Hastanesi, Kadın Hastalıkları ve Doğum Bölümü, Konya, Türkiye
E-mail: sozbilgec@yahoo.com

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INTRODUCTION

In an EP, implantation takes place outside of the uterus, most frequently in the fallopian tubes in roughly 95% of cases (1). While they may develop later, especially if the pregnancy is at an extrauterine location other than the fallopian tube, clinical signs of ectopic pregnancy normally present six to eight weeks following the last regular menstrual period. There are occasionally common pregnancy discomforts like nausea, frequent urination, and tender breasts. Since progesterone, estradiol, and human chorionic gonadotropin levels may be lower than during a typical pregnancy, early pregnancy symptoms may be less prevalent in ectopic pregnancy patients (2-4). In a retrospective research, 376 (18%) of 2026 pregnant women who had first-trimester vaginal bleeding and/or abdominal discomfort and went to the emergency room were found to have an ectopic pregnancy (5). The frequency of rupture was 18% in a population-based registry of ectopic pregnancies from France (6).

Early detection of tubal pregnancy, made possible by β-hCG, high-resolution ultrasonography, and more frequent use of laparoscopy, has significantly decreased maternal mortality and the need for major surgery. Furthermore, a conservative approach to medical therapy is possible when the problem is diagnosed before serious symptoms appear, particularly when methotrexate is used or when anticipated management is used. The advantages of medication therapy and avoiding surgery are numerous and obvious (7). Medical intervention is most effective in early pregnancy. The incidence of severe bleeding, difficulty in surgery, need for transfusion, and maternal death increases as EP continues (8).

The World Health Organization (WHO) proclaimed the COVID-19 sickness a pandemic affecting the Globe on March 11, 2020, and the Turkish Ministry of Health took swift action regarding health services.

In this study, we investigated the effects of COVID-19 disease on the diagnosis and treatment processes of ectopic pregnancies.

MATERIALS AND METHODS

Study Design

This study is a retrospective cohort analysis conducted at a tertiary hospital in Turkey. The objective was to compare the clinical presentation, diagnostic methods, and treatment modalities of ectopic pregnancy (EP) cases during the COVID-19 pandemic with those diagnosed in the pre-pandemic period. By focusing on tubal ectopic pregnancies, the study aimed to evaluate how healthcare constraints during the pandemic influenced clinical outcomes and decision-making processes.

Participants

The study included women diagnosed with tubal EP between January 1, 2018, and May 1, 2024. Cases after March 15, 2020, were categorized as the "COVID period," while cases before this date constituted the "pre-COVID period."

Inclusion criteria

- Patients with a confirmed diagnosis of ectopic pregnancy based on transvaginal or transabdominal ultrasonography and elevated β-hCG levels.
- Cases where detailed demographic, clinical, and laboratory data were available in the hospital records.

Exclusion criteria

- Cases with incomplete or missing records, including absent ultrasound or laboratory data.
- Non-tubal ectopic pregnancies, including interstitial or cervical ectopic pregnancies, due to differing diagnostic and management approaches.
- Cases where diagnosis remained uncertain or where treatment was initiated elsewhere and lacked detailed documentation.

Data Collection

All data were collected retrospectively from the hospital's electronic medical records and archived patient files. Information on demographic characteristics (e.g., maternal age, parity, gravidity), risk factors for ectopic pregnancy (e.g., history of cesarean section, prior ectopic pregnancy, intrauterine device use, or tubal surgery), and gestational age at presentation was extracted. Clinical presentations at hospital admission, including abdominal pain, vaginal bleeding, or both, were recorded. Laboratory findings, such as serum β-hCG levels and hemoglobin levels at admission and after 24 hours, were analyzed.

Sonographic data, particularly the presence of Douglas fluid (abdominal free fluid) and signs of intraperitoneal hemorrhage, were thoroughly reviewed. Abdominal fluid was identified through transabdominal or transvaginal ultrasonography and categorized based on its volume and echogenicity. In cases where surgical intervention was performed, findings were corroborated intraoperatively to enhance diagnostic accuracy.

Clinical Assessment

Patients with hemodynamic instability, sonographic evidence of ruptured EP (e.g., substantial Douglas fluid or evidence of hemoperitoneum), or a β-hCG level exceeding 5000 IU/

mL were prioritized for immediate surgical intervention. Surgical procedures included salpingectomy or salpingostomy, depending on the patient's condition and surgeon's discretion. For patients who were hemodynamically stable and had β-hCG levels below 5000 IU/mL, medical management with methotrexate was considered based on established clinical protocols. Expectant management was employed for select cases with declining β-hCG levels and no clinical symptoms, following patient consent and close monitoring.

Impact of the Pandemic

During the COVID-19 pandemic, outpatient and emergency services faced significant constraints due to reduced staff availability and resource reallocation. The hospital implemented a shift-based system, reducing the number of healthcare personnel by approximately 30%. To minimize exposure to the virus, patient consultations were limited to one physician and one nurse per session. These measures resulted in a 40% reduction in monthly outpatient admissions, dropping from an average of 1,500 visits pre-pandemic to 900 during the pandemic. During the initial pandemic wave (March to June 2020), weekly outpatient admissions dropped further to approximately 200, reflecting widespread patient hesitancy to seek care. Partial normalization in healthcare utilization was observed in subsequent months as pandemic restrictions eased and public awareness improved.

Statistical Analysis

The data in this study was analysed using IBM SPSS Statistics version 26.0 software (IBM Corp., Armonk, NY, USA). The data's normality distribution was determined using Kolmogorov-Smirnov and histograms. The two groups were compared using an independent t-test, and the values are presented as the mean ± standard deviation (SD). The categorical data were compared using the Chi-square test, and the values were presented as percentages (%). In order to assess the parameters that influence the treatment modalities for ectopic pregnancy, multinominal logistic regression analysis was implemented. Treatment modalities (surgical, medical, waiting) were employed as dependent variables in this analysis. The independent variables were the presence of fluid in the Douglas cavity, β-hCG levels, age, parity, gestational week, and the distinction between the Covid and pre-Covid periods. The odds ratio (OR) and 95% confidence interval (CI) were used to quantify the impact of each independent variable on treatment modalities. We accepted a statistical significance level of $p < 0.05$.

Ethical Considerations

This study was conducted in compliance with the Declaration of Helsinki. Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Necmettin Erbakan University, Faculty of Medicine (Approval No: 2022/3874). Written informed consent was waived due to the retrospective nature of the study. Patient confidentiality was maintained throughout, with data anonymized before analysis.

RESULTS

The research group consisted of 221 different instances of EP that were managed by our division after 15 March 2020. The control comprised 217 EP cases admitted to our department before 15 March 2020.

The research group consisted of 221 different instances of EP that were managed by our division after 15 March 2020. The control comprised 217 EP cases admitted to our department before 15 March 2020.

There was no statistically significant difference between the two periods in terms of maternal age, gravidity, parity and gestational weeks. When the risk factors for ectopic pregnancy were analysed, the proportion of patients without risk factors was 162 (73.3%) in the Covid period and 136 (62.7%) in the pre-Covid period. The rate of patients with a history of previous ectopic pregnancy was found to be 2.7% in the Covid period and 7.4% in the pre-Covid period. In addition, the proportion of patients with a history of previous caesarean section was 20.4% in the Covid period and 29.0% in the pre-Covid period. The number of patients with a history of tubal reanastomosis surgery or intrauterine device use was very low in both periods (Table 1).

Significant differences in clinical characteristics were observed between the COVID and pre-COVID periods (p=0.001). Abdominal pain was seen in 52.5% (116/221) patients in the Covid period and 37.8% (82/217) patients in the pre-Covid period. Vaginal bleeding was detected in 23.1% (51/221) patients in the Covid period and 40.1% (87/217) patients in the pre-COVID period. Both abdominal pain and vaginal bleeding were present in 2.7% (6/221) patients in the Covid period and 0.5% (1/217) in the pre-COVID period. Menstrual delay was not seen in the covid period, but was seen in one patient in the pre-covid period. In terms of laboratory findings, there was no statistically significant difference between β-hCG level, haemoglobin level at admission, haemoglobin level after 24 hours and endometrial thickness. However, intraperitoneal haemorrhage was observed in 26.7% (59/221) patients in Covid period and 7.4% (16/217) patients in pre-COVID period (p=0.001). Fetal heartbeat positivity was observed at a low rate in both periods (4.1% & 3.2%, p=0.637). There was no statistically significant difference in terms of ectopic pregnancy localisation (p=0.805).

Table 1. Comparison of Ectopic Pregnancies between Covid and Pre-Covid Periods in terms of Sociodemographic Characteristics

Variables		Ectopic pregnancies in the Covid period (n =221)	Ectopic pregnancies in the pre-Covid period (n=217)	p-value
Maternal age (years)		32.06 ± 6.58	33.09 ± 6.10	0.091
Gravidity		2 (0- 8)	1 (0- 13)	0.058
Parity		1 (0 - 7)	0 (0 - 6)	0.205
Gestational week		6.06 ± 1.48	6.03 ± 1.45	0.850
Ectopic pregnancy risk factors	None	162 (73.3%)[a]	136 (62.7%)[b]	**0.001**
	History of ectopic pregnancy	6 (2.7%)[a]	16 (7.4%)[b]	
	History of C/S	45 (20.4%)[a]	63 (29.0%)[b]	
	Tubal reanastomosis surgery	0 (0.0%)[a]	2 (0.9%)[a]	
	Intrauterine device	5 (2.3%)[a]	0 (0.0%)[b]	
	Others	3 (1.4%)[a]	0 (0.0%)[a]	

Table 2. Comparison of Clinical Characteristics and Outcomes in Ectopic Pregnancies Between Covid and Pre-Covid Periods

Variables		Ectopic pregnancies in the Covid period (n =221)	Ectopic pregnancies in the pre-Covid period (n=217)	p-value
Clinical characteristics	None	48 (21.7%)[a]	46 (21.2%)[a]	**0.001**
	Abdominal pain	116 (52.5%)[a]	82 (37.8%)[b]	
	Vaginal bleeding	51 (23.1%)[a]	87 (40.1%)[b]	
	Abdominal pain & Vaginal bleeding	6 (2.7 %)[a]	1 (0.5%)[a]	
	Menstrual delay	0 (0.0 %)[a]	1 (0.5%)[a]	
β-hCG level (mIU/mL)		3426.0 ± 1153.0	5080.9 ± 1452.9	0.085
Hgb level on admission (gr/dL)		12.49 ± 1.46	12.36 ± 1.25	0.334
Hgb level after 24 hours (gr/dL)		11.39 ± 1.48	11.20 ± 1.29	0.199
Endometrial thickness (mm)		9.80 ± 4.40	10.47 ± 4.45	0.115
Intraperitoneal haemorrhage		59 (26.7%)	16 (7.4%)	**0.001**
Fetal Heartbeat positivity		9 (4.1%)	7 (3.2%)	0.637
Blood tranfusion rate		17 (7.7%)	18 (8.3%)	0.816
Localization of ectopic pregnancy	Location unknown	108 (48.9%)	113 (52.6%)	0.805
	Right tuba uterina	63 (28.5%)	55 (25.6%)	
	Left tuba uterina	44 (19.9%)	43 (10.0%)	
	Scar pregnancy	6 (2.7%)	4 (1.9%)	
Treatment modalities	Expectant management	63 (28.5%)[a]	77 (35.5%)[a]	**0.028**
	Medical treatment	91 (41.2%)[a]	63 (29.0%)[b]	
	Surgical treatment	67 (30.3%)[a]	77 (35.5%)[a]	

When the Covid-19 period was compared with the pre-Covid-19 period, although there was no statistically significant difference in terms of expectation management and surgical treatment, differences in rates were observed (expectation management: 28.5% vs. 35.5%; surgical treatment: 30.3% vs. 35.5%). On the other hand, medical treatment was administered at a significantly higher rate during the Covid-19 period compared to the pre-Covid-19 period (41.2% vs. 29.0%) (Table 2).

The results of multinomial logistic regression analysis for the parameters affecting the treatment methods in ectopic pregnancy are as follows (Table 3).

Parity, gestational week, Douglas fluid presence, and the Covid period were all significant predictors in the comparison between surgical and expectant management. Parity was associated with an increased likelihood of selecting surgery over expectant management (OR: 1.147, 95% CI: 1.035–1.270, p=0.009). In the same vein, the probability of surgical intervention was significantly elevated by a later gestational week (OR: 1.212, 95% CI: 1.060–1.387, p=0.005). The presence of Douglas fluid significantly predicted a preference for surgery (OR: 4.202, 95% CI: 4.187–4.217, p=0.001). Furthermore, the odds of surgery were lower during the Covid-19 phase than during the pre-Covid-19 phase (OR: 0.783, 95% CI: 0.777–0.789, p=0.001).

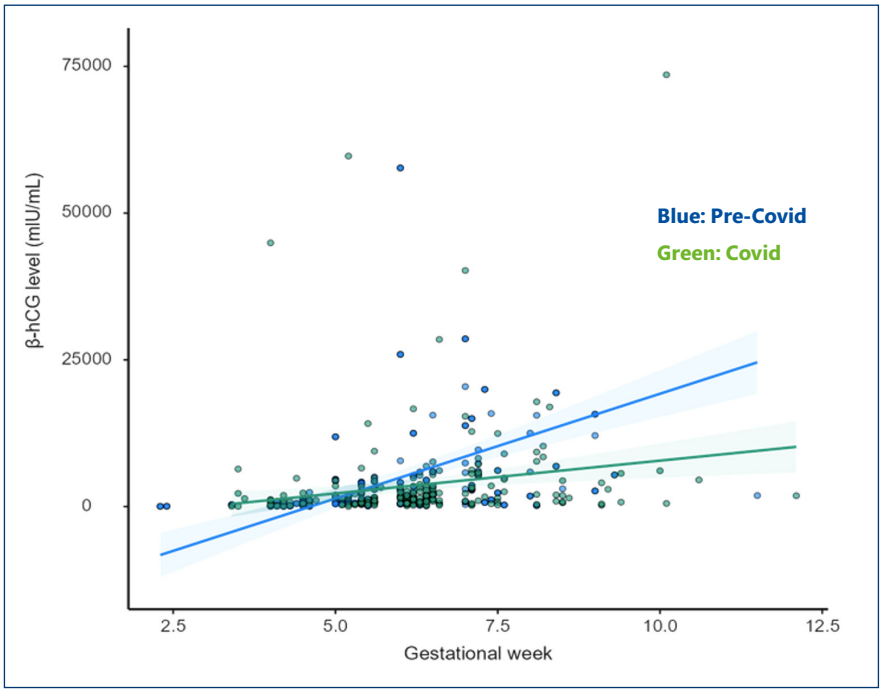

Figure 1. Relationship of β-hCG Levels with Gestational Week in Pre-Covid and Covid Periods

Table 3. Results of Multinomial Logistic Regression Analysis of Parameters Affecting Treatment Modalities in Ectopic Pregnancy

Surgery-Expectant / Predictors	β	SE	p-value	Odds Ratio	(95 % CI)
Parity	0.137	0.052	**0.009**	1.147	(1.035 - 1.270)
Age	-0.002	0.013	0.902	0.998	(0.973 - 1.024)
β-hCG Level (mIU/mL)	1.140	1.340	0.392	1.022	(0.996 - 1.036)
Gestational Week	0.193	0.069	**0.005**	1.212	(1.060 - 1.387)
Douglas Fluid	1.435	0.002	**0.001**	4.202	(4.187 - 4.217)
Covid Period - Pre-Covid Period	-0.244	0.004	**0.001**	0.783	(0.777 - 0.789)
Medical-Expectant / Predictors	**β**	**SE**	**p-value**	**Odds Ratio**	**(95 % CI)**
Parity	0.016	0.052	0.757	1.016	(0.918 - 1.126)
Age	0.029	0.012	**0.020**	1.029	(1.005 - 1.054)
β-hCG Level (mIU/mL)	1.460	4.190	0.226	1.013	(0.994 - 1.028)
Gestational Week	0.096	0.070	0.170	1.100	(0.960 - 1.261)
Douglas Fluid	0.410	0.001	**0.001**	1.507	(1.503 - 1.511)
Covid Period - Pre-Covid Period	0.443	0.006	**0.001**	1.558	(1.539 - 1.576)
Medical- Surgery / Predictors	**β**	**SE**	**p-value**	**Odds Ratio**	**(95 % CI)**
Parity	-0.121	0.055	**0.027**	0.886	(0.796 - 0.987)
Age	0.030	0.013	**0.015**	1.031	(1.006 - 1.056)
β-hCG Level (mIU/mL)	-1.570	4.180	**0.001**	0.983	(0.966 – 0.998)
Gestational Week	-0.097	0.068	0.156	0.907	(0.794 - 1.038)
Douglas Fluid	-1.025	0.001	**0.001**	0.359	(0.358 - 0.360)
Covid Period - Pre-Covid Period	0.687	0.006	**0.001**	1.988	(1.966 - 2.011)

Age, the presence of Douglas fluid, and the Covid period were significant predictors of medical versus expectant management. A higher likelihood of medical management was associated with older age (OR: 1.029, 95% CI: 1.005–1.054, p=0.020). The presence of Douglas fluid was also a significant factor, increasing the likelihood of medical management (OR: 1.507, 95% CI: 1.503–1.511, p=0.001). Additionally, the odds of medical management were significantly elevated when contrasted with the pre-Covid period (OR: 1.558, 95% CI: 1.539–1.576, p=0.001).

Parity, age, β-hCG levels, Douglas fluid presence, and the Covid period were all significant predictors in the comparison between medical and surgical management. A preference for medical management over surgery was associated with lower parity (OR: 0.886, 95% CI: 0.796–0.987, p=0.027). Medical management was once again significantly predicted by older age (OR: 1.031, 95% CI: 1.006–1.056, p=0.015). Medical management was preferred over surgery when β-hCG levels were lower (OR: 0.983, 95% CI: 0.966–0.998, p=0.001). The presence of Douglas fluid was significantly associated with a lower likelihood of selecting medical management over surgery (OR: 0.359, 95% CI: 0.358–0.360, p=0.001). Furthermore, the odds of medical management surpassing surgery were substantially elevated during the Covid-19 pandemic (OR: 1.988, 95% CI: 1.966–2.011, p=0.001).

DISCUSSION

This study aimed to evaluate the impact of the COVID-19 pandemic on the diagnosis and treatment of ectopic pregnancies (EP) in our clinic. Our findings reveal several noteworthy trends when comparing the pandemic period to the pre-pandemic period.

One of the most significant observations was the increase in intraperitoneal hemorrhage detected in EP patients during the COVID-19 period. Specifically, 26.7% of patients presented with intraperitoneal hemorrhage during the pandemic, compared to only 7.4% before the pandemic (p=0.001). This finding suggests a possible delay in the presentation of patients during the pandemic, leading to more advanced stages of EP at the time of diagnosis. This delay could be attributed to patients' fear of contracting the virus in healthcare settings, leading to postponement of hospital visits despite experiencing symptoms.

Interestingly, despite the increased rate of intraperitoneal hemorrhage, there was no significant difference in gestational age at the time of presentation between the two periods. This finding contradicts the hypothesis that delays in seeking care would result in more advanced gestational ages at presentation. However, it aligns with the study conducted in Israel, which also reported increased fluid in the Douglas space without a corresponding increase in gestational age at presentation (9).

Moreover, our study observed a higher rate of abdominal pain as a presenting symptom during the COVID-19 period (52.5% vs. 37.8%, p=0.001), while the incidence of vaginal bleeding was significantly lower (23.1% vs. 40.1%, p=0.001). The shift in clinical presentation could be due to variations in the stage at which EP was diagnosed, potentially driven by delayed healthcare access during the pandemic. The lower incidence of vaginal bleeding might indicate that patients were presenting at a later stage of the disease, when the bleeding had subsided, or that abdominal pain had become the predominant concern prompting medical attention.

Regarding treatment modalities, our study found that medical management with methotrexate was utilized more frequently during the COVID-19 period compared to the pre-pandemic period (41.2% vs. 29.0%, p=0.028). This could be explained by a shift towards more conservative management strategies during the pandemic to minimize surgical risks and reduce hospital stays. However, surgical treatment rates were slightly lower during the pandemic (30.3% vs. 35.5%, p=0.028), which may reflect a cautious approach to avoid potential COVID-19 exposure in surgical settings.

The results of our multinomial logistic regression analysis revealed that the presence of fluid in the Douglas cavity and the COVID-19 period were significant predictors of the treatment modality. Specifically, the odds of opting for surgery were lower during the pandemic, whereas medical management was more likely. These findings suggest that the pandemic influenced clinical decision-making, likely prioritizing less invasive treatments to reduce the burden on healthcare resources and limit patient exposure to the virus.

Our study's findings align with the results of studies conducted in Israel and USA, which reported similar trends in the clinical presentation and management of EP during the pandemic (9-11). However, unlike studies that reported an increase in tubal rupture cases due to delayed access to healthcare, our study did not find a significant increase in tubal rupture rates during the pandemic. This may indicate that despite delays in presentation, the management strategies employed were effective in preventing severe outcomes.

The strength of our study lies in its large sample size and the comprehensive analysis of a significant clinical issue during an unprecedented global health crisis. However, the retrospective nature of the study is a limitation, as it relies on existing records and may be subject to biases inherent in such analyses. Additionally, the

study is limited to a single center, which may limit the generalizability of the findings to other settings.

The limitation of our study is that it was conducted retrospectively. However, the difficulty of conducting a prospective study during a process such as the COVID-19 pandemic, which has deeply shaken the whole world and adversely affected health systems in many countries, is very clear.

CONCLUSION

In conclusion, our study indicates that the COVID-19 pandemic had a substantial impact on the presentation and management of ectopic pregnancies. The increased incidence of intraperitoneal hemorrhage and the shift towards medical management highlight the need for ongoing vigilance and adaptation of clinical practices during global health crises. Despite the challenges posed by the pandemic, our findings suggest that the adjustments made in patient management were effective in maintaining patient safety and outcomes.

Conflict of Interest
The authors declared that they have no conflict of interest.

Author Contributions
S.Ö.: Conceptualization, data interpretation, manuscript writing and supervision.

F.A.: Statistical analysis and interpretation of data.

E.E.D, R.B.D., S.S.: Data collection and review of clinical records.

A.A.: Supervision and critical revision as mentor.

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Data Availability Statement
Upon a reasonable request, the corresponding author will provide access to the data supporting the conclusions of this research.

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Evaluation of postoperative pain after abdominal, vaginal and laparoscopic hysterectomy for benign gynecological causes: a retrospective observational study

Benign jinekolojik nedenlerle yapılan abdominal, vajinal ve laparoskopik histerektomi sonrası postoperatif ağrının değerlendirilmesi: retrospektif gözlemsel çalışma

Emre Erdem TAS[1], Mohammad Ibrahim HALILZADE[2], Inci HALILZADE[2]

[1]Ankara Yıldırım Beyazıt Üniversitesi Kadın Hastalıkları ve Doğum ABD, Ankara Bilkent Şehir Hastanesi Kadın Doğum Kulesi, Türkiye
[2]Ankara Bilkent Şehir Hastanesi Kadın Doğum Kulesi, Türkiye

ABSTRACT

Aim: This retrospective observational study aimed to evaluate postoperative pain after abdominal hysterectomy (AH), vaginal hysterectomy (VH), and total laparoscopic hysterectomy (TLH) for benign gynecological causes.

Materials and Method: This retrospective clinical study investigated 90 patients who underwent AH, VH, and TLH at a tertiary hospital between January 2023 and December 2024. The groups compared in terms of demographics, clinical characteristics, and visual analog scale (VAS) pain scores at 1, 8, and 24 hours postoperatively.

Results: The mean age and ratio of postmenopausal women were significantly higher in the VH group compared to the AH and TLH groups (P<0.01). The rate of bilateral salpingo-oophorectomy performed simultaneously with hysterectomy was significantly lower in the VH group (P=0.01). The mean operation time was significantly shorter in the AH group compared to the VH and TLH groups (P=0.01). No significant difference was found between the groups in terms of postoperative 1-hour VAS scores (P=0.38). However, the VAS scores at 8 and 24 hours postoperatively were significantly higher in the AH group compared to the VH and TLH groups (P=0.01 and P<0.01, respectively).

Conclusion: These findings suggest that minimally invasive techniques like VH and TLH may offer advantages in postoperative pain management compared to AH. However, the choice of surgical approach should be individualized based on patient characteristics, surgical indications, and surgeon expertise.

Keywords: Hysterectomy, postoperative pain, visual analog scale, minimally invasive surgery

ÖZ

Amaç: Bu retrospektif gözlemsel çalışma, benign jinekolojik nedenlerle yapılan abdominal histerektomi (AH), vajinal histerektomi (VH) ve total laparoskopik histerektomi (TLH) sonrası postoperatif ağrıyı değerlendirmeyi amaçlamıştır.

Gereçler ve Yöntem: Bu retrospektif klinik çalışma, Ocak 2023 ile Aralık 2024 arasında üçüncü basamak bir hastanede AH, VH ve TLH operasyonu geçiren 90 hastayı incelemiştir. Gruplar demografik özellikler, klinik özellikler ve postoperatif 1, 8 ve 24. saatlerdeki görsel analog skala (VAS) ağrı skorları açısından karşılaştırılmıştır.

Bulgular: Postmenopozal kadınların ortalama yaşı ve oranı, VH grubunda AH ve TLH gruplarına kıyasla anlamlı derecede daha yüksekti (P<0,01). Histerektomi ile eş zamanlı olarak yapılan bilateral salpingo-ooferektomi oranı, VH grubunda anlamlı derecede daha düşüktü (P=0,01). Ortalama operasyon süresi AH grubunda VH ve TLH gruplarına kıyasla anlamlı derecede daha kısaydı (P=0,01). Gruplar arasında postoperatif 1 saatlik VAS skorları açısından anlamlı bir fark bulunmadı (P=0,38). Ancak, AH grubunda postoperatif 8 ve 24. saatlerdeki VAS skorları VH ve TLH gruplarına kıyasla anlamlı derecede daha yüksekti (sırasıyla P=0,01 ve P<0,01).

Sonuç: Bu bulgular, VH ve TLH gibi minimal invaziv tekniklerin AH'ye kıyasla postoperatif ağrı yönetiminde avantajlar sağlayabileceğini düşündürmektedir. Ancak, cerrahi yaklaşım seçimi hasta özelliklerine, cerrahi endikasyonlara ve cerrahın uzmanlığına göre kişiselleştirilmelidir.

Anahtar Kelimeler: Histerektomi, postoperatif ağrı, görsel analog skala, minimal invaziv cerrahi

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Sorumlu Yazar/Corresponding Author: Emre Erdem TAS, Mehmet Akif Eroy Mahallesi Yesilay Caddesi 5A/121 Yenimahalle-Ankara, Türkiye
E-mail: doctortas83@gmail.com

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INTRODUCTION

The surgical removal of the uterus, known as hysterectomy, is among the most frequently conducted gynecological operations for a range of non-cancerous and cancerous conditions affecting the female reproductive system (1). Several methods can be employed to perform a hysterectomy, with the most prevalent being abdominal hysterectomy (AH), vaginal hysterectomy (VH), and total laparoscopic hysterectomy (TLH) (2). Each of these approaches offers distinct benefits and drawbacks for both patients and surgeons (2). Nevertheless, comprehensive research on how these different techniques impact post-surgery pain levels is still lacking (3).

Postoperative pain is a significant concern following hysterectomy regardless of the surgical approach (4). The severity and duration of pain can vary depending on factors such as surgical technique, patient characteristics, and pain management strategies employed (5). Effectively managing pain after surgery has been shown to enhance patient satisfaction, promote earlier mobility, reduce hospital stay, and lower overall costs (6). Given these benefits, minimizing postoperative discomfort should be considered a top priority in routine surgical practice. However, studies on postoperative pain after different hysterectomy types have revealed varying outcomes and patterns (7-9). Therefore, further studies on the management of postoperative pain after hysterectomy are needed.

Surgical procedures invariably cause postoperative pain. However, the role of different hysterectomy techniques in postoperative pain has not been fully elucidated. This study aimed to investigate the effects of different hysterectomy techniques on postoperative pain 48 hours after surgery.

MATERIAL AND METHODS

This was a retrospective clinical study. The study was approved by the Ankara City Hospital Clinical Research and Ethics Committee (TABED.2-24-972) and was conducted between January 2023 and December 2024 at the Department of Gynecology of the Ankara City Hospital, Ministry of Health, where abdominal, vaginal, or total laparoscopic hysterectomies were performed in patients with benign gynecological reasons. Using G*Power Ver.3.0 Software® (Germany), the study determined a total sample size of 90 cases, with 30 women in each group. This calculation was based on a one-way ANOVA with a power of 92% (alpha level = 0.05, effect size = 0.40). Before the study commenced, explicit permission was obtained from all individuals who willingly agreed to participate in the research by signing a "Consent Form for Informed Voluntary Participation." This study was conducted in accordance with the 1964 Declaration of Helsinki and its subsequent amendments.

Patients who were pregnant or lactating, smoking, had a history of any additional medical illnesses or currently undergoing medical treatment, had a history of chemotherapy, radiotherapy, endometriosis, used hormonal contraceptives or intrauterine devices, had a >4-cm uterine myoma or ≥ Pelvic Organ Prolapse-Quantification (POP-Q) Grade 3 descensus uteri, acute inflammatory disease, or a premalignant/malignant lesion detected by Pap smear or endometrial sampling were excluded from the study. None of the volunteers had undergone any surgical operations concurrent with bilateral salpingo-oophorectomy (BSO) and hysterectomy or experienced any intraoperative or postoperative complications.

We recorded the patients' demographic data, including age, gravidity, body mass index (BMI) (kg/m^2), menopausal status, and personal and family medical histories. The clinical characteristics of the patients, including results from preoperative and postoperative laboratory testing, imaging, and histopathological examinations, were assessed using the hospital's computer automation system. Surgical methods and operative times (min) were obtained from medical records. Pain was evaluated using a 10-cm visual analog scale (VAS), where 0 indicated no pain and 10 indicated unbearable pain at 1, 8, and 24 h after the procedure.

Postoperative pain management involved administering 50 mg of intravenous pethidine hydrochloride every four hours for the initial 12 hours. Subsequently, 75 mg of diclofenac sodium was administered intramuscularly or intravenously, or 100 mg oral tablets were administered based on patient requirements. Fluid intake was allowed six hours post-surgery, with solid food permitted after the first bowel movement. Bladder catheters were removed once adequate mobilization was achieved. When necessary, vaginal packing was applied during the operation and removed after 24 h.

Statistical Analysis

Statistical analyses were performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to assess data normality. Descriptive parameters were expressed as mean ± standard deviation for normally distributed continuous variables and as median (interquartile range) for non-normally distributed continuous variables. Categorical parameters were expressed as numbers and percentages. One-way ANOVA and Kruskal–Wallis tests were used for intergroup comparisons. When a significant difference was observed in the Kruskal-Walli's test,

the Mann-Whitney U test was used for post-hoc analysis between the groups. The chi-squared test was used to compare categorical data. Statistical tests were considered significant at P-value <0.05, while post-hoc correction tests were considered significant at a P-value <0.017 (.05/3).

RESULTS

The mean age of all patients was 54.5±8.3 years, and the median gravida and parity values were 3(3) and 3(1), respectively. While 49 (54.4%) patients were menopausal, 41 (45.6%) were of reproductive age. The most common indications for surgery were abnormal uterine bleeding (AUB) (n=38, 42.2%), POP (n=29, 32.2%), myoma uteri (n=15, 16.7%), and endometrial hyperplasia (n=8, 8.9%). Hysterectomy with BSO was performed in 67 patients (74.4%); the remaining 23 patients (25.6%) underwent hysterectomy alone. The mean operation time was 103.6±35.3 minutes. The preoperative and postoperative 24th h hemoglobin (Hb) values were 12.3±1.6 g/dL and 11.3±1.5 g/dL, respectively. The median postoperative 1st, 8th and 24th h VAS values were 9(2), 6(2), and 2(1), respectively.

The clinical characteristics of the AH, VH, and TLH groups are presented in Table 1. The groups differed significantly in terms of age and menopausal status (P < 0.01). The mean age and ratio of postmenopausal women were significantly higher in the VH group than in the AH and TLH groups (P <0.01). However, the groups did not differ in terms of median gravida and parity values (P values were 0.05 and 0.08, respectively).

There was a significant difference between the AH, VH, and TLH groups in terms of the BSO rates performed simultaneously with hysterectomy (P=0.02), and significantly less BSO was performed in the VH group than in the AH and TLH groups (P=0.01). However, the groups did not differ in terms of preoperative and postoperative 24th h Hb levels (P values were 0.35 and 0.22, respectively). On the other hand, there was a significant difference between the groups in terms of operation time (P=0.04). The mean operation time was significantly shorter in the AH group than in the VH and TLH groups (P=0.01) (Table 1).

There was no significant difference between the groups in terms of the postoperative 1st h VAS scores (P=0.38). However, the groups differed significantly in terms of the VAS scores at 8th and 24th hours (P<0.01). In both postoperative 8th and 24th hours, VAS scores were significantly higher in the AH group than in the VH and TLH groups (P values were 0.01 and <0.01, respectively) (Table 1).

Table 1. Clinical characteristics of the abdominal, vaginal, and total laparoscopic hysterectomy groups.

Characteristics	Abdominal hysterectomy (n = 30)	Vaginal hysterectomy (n = 30)	Total laparoscopic hysterectomy (n = 30)	P*
Age (years)	52.7±8.5	58.3±8.7	52.6±6.2	**<0.01**
Gravida	2(2)	3(2)	3(3)	0.05
Parity	2(2)	3(2)	3(2)	0.08
Menopausal status **No** **Yes**	 21 (23.3) 9 (10.0)	 4 (4.4) 26 (28.9)	 16 (17.8) 14 (15.6)	**<0.01**
Concomitant BSO **No** **Yes**	 5 (5.6) 25 (27.8)	 13 (14.4) 17 (18.9)	 5 (5.6) 25 (27.8)	**0.02**
Preoperative Hb level (gr/dL)	12.0±1.8	12.6±1.4	12.2±1.6	0.35
Postoperative 24th hour Hb level (gr/dL)	11.6±1.4	11.5±1.5	10.9±1.5	0.22
Operation time (min)	91.2±21.4	107.7±45.1	112.6±32.9	**0.04**
VAS 1st hour	9(1)	9(1)	9(2)	0.38
VAS 8th hour	7(1)	6(1)	5(2)	**<0.01**
VAS 24th hour	4(1)	2(1)	2(1)	**<0.01**

Data are presented as the mean±standard deviation, median (interquartile range), or n (%).

*One-way ANOVA, Kruskal–Wallis test, and Pearson chi-square test were used for intergroup comparisons.

BSO, bilateral salpingo-oophorectomy; Hb, hemoglobin; VAS, visual analog score.

DISCUSSION

This study compared different hysterectomy techniques in terms of patient demographics, operative procedures, and laboratory parameters. We also aimed to determine the effects of different hysterectomy techniques on postoperative pain. We found that the mean age and menopausal status of patients who underwent VH were higher than those in the AH and TLH groups. In contrast, the rate of BSO performed simultaneously with hysterectomy was lower in the patients who underwent VH. The mean operative time was lower in the AH group. When VAS pain scores were evaluated, no difference was observed between the groups at postoperative 1st h, while VAS scores at postoperative 8th and 24th h were significantly higher in the AH group than in the VH and TLH groups.

The surgical technique of VH is generally used in patients with uterine descent (10). Uterine descent occurs as a result of weakening of the ligaments of the uterus and levator ani muscle, which provides pelvic support (11). Causes include advanced age, history of difficult delivery, increased parity, chronic cough, and constipation (12). A decrease in tissue collagen, especially with increasing age, is also an important factor. In addition, the decrease in estrogen due to menopause contributes to weakening of the pelvic floor connective tissue (13). Therefore, the average age and incidence of menopause are higher in patients with VH. Inal et al. found the average age of VH patients to be significantly higher than AH and TLH patients in their study (14). Similarly, the fact that patients with VH were older and had a higher incidence of menopause than those with AH and TLH in our study is consistent with the literature.

Several factors affect the performance of BSO simultaneously with hysterectomy. However, the American College of Obstetricians and Gynecologists suggests that BSO choice should not affect the surgical route (15). In contrast, previous studies found that VH was less likely to be associated with BSO than TLH or AH, and concomitant BSO during VH was performed in only 65–78% of patients (16–18). This may be because these studies included younger patients, allowing the ovary to continue its estrogen-secreting function. However, Greene et al. found that in older patients with prolapse, the likelihood of concomitant BSO was still significantly lower when hysterectomies were performed vaginally than when performed abdominally or laparoscopically (19). They suggested that this is because BSO during VH is more difficult, may require longer anesthesia, and may lead to complications in older patients (19). Geron et al. reported adnexal pathology findings in 35 patients who underwent BSO during VH as 77.2% normal or 22.8% benign (20). The authors stated that the risk of unexpected adnexal malignancy was low in patients who underwent hysterectomy for uterine prolapse and had no preoperative adnexal pathology (20). Similarly, we found that the rate of simultaneous BSO was lower in patients who underwent VH than in those who underwent AH or TLH. In elderly patients undergoing VH for prolapse without adnexal pathology, we believe that simultaneous BSO is not preferred because of the low risk of unexpected adnexal malignancy, difficulty in performing the BSO procedure, prolonged anesthesia, and increased risk of complications.

Numerous investigations have documented the operative time for hysterectomy procedures. The prevailing belief is that VH typically requires a shorter operative time. A previous study revealed that VH procedures are quicker than TLH and AH (14). Schindlbeck et al. determined that VH operations have the shortest durations (21). A meta-analysis by Azadi et al. comparing VH to TLH concluded that VH was associated with the shortest operative time (22). However, our findings indicate that AH procedures are faster than VH and TLH procedures. We attributed this to factors such as surgeon expertise and concurrent BSO. However, varying outcomes have been reported for intraoperative blood loss using different hysterectomy techniques. Some studies noted reduced blood loss with TLH compared with other techniques, whereas others found that VH resulted in less blood loss than TLH (14, 21, 22). In our study, we observed no significant differences in blood loss among different hysterectomy techniques.

Patients undergoing hysterectomy experienced significantly higher postoperative pain (23). This pain can negatively impact recovery, health outcomes, patient experience, and hospital stay (24). Therefore, it is important to determine whether there is a difference in the pain experienced by different types of hysterectomies. However, there is still debate regarding this issue. In a prospective study comparing the three groups' postoperative pain VAS scores in patients undergoing hysterectomy for uncomplicated benign causes, the AH group showed the highest pain perception (25). However, the TLH and VH groups were similar in terms of the perceived pain (25). Another prospective study comparing VH, TLH, and VH patients showed that patients with VH had the lowest VAS score on postoperative day 1 (26). However, Ghezzi et al. compared postoperative pain after TLH and VH for benign gynecologic diseases and found higher VAS scores in the VH group (3). Researchers have suggested that variations in surgical methods may explain this outcome. They proposed that pain levels were influenced by several factors: the different patient positions required for vaginal and laparoscopic procedures (with TLH allowing a more natural posture), forceful downward traction applied to the uterus during vaginal surgery (which was thought to increase discomfort), and the use of electrosurgical instruments for tissue coagulation and dissection in TLH (believed to reduce pain compared with traditional scissors and sutures) (3). In contrast, a large systematic

meta-analysis compared patients undergoing VH and TLH for benign gynecologic indications using the postoperative VAS pain score and reported lower VAS scores at postoperative 24th h in patients undergoing VH (7). The researchers suggested that increased postoperative discomfort in TLH was due to factors such as creation of pneumoperitoneum, pain resulting from uterine manipulation, and presence of abdominal incisions (7). In this study, we found that the AH, VH, and TLH groups' postoperative 1st h VAS scores were high, but the groups did not differ in terms of VAS scores. Nevertheless, the postoperative 8th and 24th h VAS scores were significantly higher in the AH group than in the VH and TLH groups. This may be related to the fact that a large abdominal incision was made during the laparotomic surgery. In contrast, small or no abdominal incision in laparoscopic and vaginal surgeries seems to be associated with a rapid decrease in patients' postoperative pain complaints. Interestingly, this study showed that VH and TLH, which are considered minimally invasive surgeries, had similar superiority in terms of postoperative pain. In a previous study, Holzer et al. compared laparoscopic and laparotomic myomectomy patients in terms of postoperative pain and found that laparoscopic surgery was associated with less postoperative pain, supporting our results (27). In another study, patients undergoing laparoscopic and laparotomic appendectomy were compared in terms of postoperative pain, but no significant difference was found between the groups (28). This indicates that postoperative pain is increased especially in laparotomic surgeries with wide incisions, as in AH.

In conclusion, this study provides valuable insights into the postoperative pain experiences associated with different hysterectomy techniques. While no significant differences were observed in pain levels immediately after surgery, abdominal hysterectomy was associated with higher pain scores at 8 and 24 hours postoperatively compared to vaginal and laparoscopic approaches. These findings suggest that minimally invasive techniques like vaginal and laparoscopic hysterectomy may offer advantages in terms of postoperative pain management. However, the choice of surgical approach should be individualized based on patient characteristics, surgical indications, and surgeon expertise. Further research is warranted to optimize pain management strategies and improve patient outcomes across all hysterectomy techniques.

Author Contributions:
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Conflict of Interest:
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Konizasyon sonrası endoservikal küretajın rolü: Ne kadar faydalıdır?

The role of post-conization endocervical curettage: How useful is it?

Selin ŞAHİN[1], Mustafa ŞAHİN[2], Hakan Raşit YALÇIN[2]

[1]Kadın Hastalıkarı ve Doğum Kliniği, Erciş Şehit Rıdvan Çevik Devlet Hastanesi, Van, Türkiye
[2]Jinekolojik Onkoloji Cerrahisi Kliniği, Ankara Şehir Hastanesi, Ankara,Türkiye

ÖZ

Amaç: Serviks kanseri dünya genelinde sık görülen jinekolojik malignitelerden biridir. Serviks kanserinin tarama, tanı ve tedavi stratejisini belirlemede prekanseröz lezyonların erken tanısı büyük önem taşımaktadır. Bu çalışmada servikal konizasyon (soğuk konizasyon) ve Loop Elektrocerrahi Eksizyon Prosedürü (LEEP) sonrasında yapılan endoservikal küretajın rezidü yüksek dereceli lezyonları ve servikal kanseri saptamada yeri olup olmadığını değerlendirmeyi amaçlıyoruz.

Gereçler ve Yöntem: 01.09.2019 ile 01.12.2022 tarihleri arasında Ankara Bilkent Şehir Hastanesi, Jinekolojik Onkoloji Cerrahisi kliniğinde servikal eksizyonel işlemleri ve endoservikal küretaj işlemi yapılan 620 hastanın verileri retrospektif olarak, elektronik veri tabanı sisteminden, hasta dosyalarından, patoloji raporlarından ve ameliyat notlarından elde edildi. Endoservikal küretaj ve kolposkopi sonuçlarına ulaşılamayan, hastanemizde eksizyonel işlem yapılmamış hastalar ve eksizyonel işlem sonrası endoservikal küretaj(ECC) yapılmayan hastalar çalışmaya dahil edilmedi.

Bulgular: Konizasyon sonrası ECC'de servikal intraepitelyal neoplazi 2 (CIN2) ve üzeri sonuç gelen 43 hastanın 40'ında (%93) konizasyon sonucunda da CIN2 ve üzeri sonuç saptandı. Konizasyon sonrası ECC'nin doğru pozitif sayısı 43, yanlış pozitif sayısı 0, yanlış negatif sayısı 367 ve doğru negatif sayısı 210 olarak bulunmuştur. Buna göre konizasyon sonrası ECC'nin sensitivitesi %10,5, spesifitesi %100, pozitif prediktif değeri %100, negatif prediktif değeri %36,4 ve doğruluk oranı ise %40,8 olarak bulunmuştur.

Sonuç: Düşük sensitiviteye rağmen, yüksek spesitite ve pozitif prediktif değerlere sahip olması nedeniyle ve yalnızca üç hastada olsa bile sedece ECC' de ileri lezyon tespit etmesi nedeni ile konizasyon sonrası ECC yapılmasını öneriyoruz. ECC sonuçlarının hastanın sonraki aşamadaki takip ve tedavisi açısından önemli olduğunu düşünmekteyiz. Ancak konizasyon sonrası ECC'nin yeri konusunda haha kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Endoservikal küretaj, konizasyon, servikal preinvaziv lezyon

ABSTRACT

Aim: Cervical cancer is one of the most common gynecological malignancies worldwide. Early diagnosis of precancerous lesions is of great importance in determining the screening, diagnosis and treatment strategy of cervical cancer. In this study, we aim to evaluate whether endocervical curettage performed after cervical conization (cold conization) and Loop Electrosurgical Excision Procedure (LEEP) has a place in detecting residual high-grade lesions and cervical cancer.

Materials and Methods: The data of 620 patients who underwent cervical excisional procedures and endocervical curettage procedures at Ankara Bilkent City Hospital, Gynecological Oncology Surgery clinic between 01.09.2019 and 01.12.2022 were obtained retrospectively from the electronic database system, patient files, pathology reports and surgery notes. Patients whose endocervical curettage and colposcopy results could not be obtained, patients who did not undergo an excisional procedure in our hospital, and patients who did not undergo endocervical curettage (ECC) after the excisional procedure were not included in the study.

Results: In 40 of 43 patients (93%) whose ECC results were cervical intraepithelial neoplasia 2 (CIN2) and above after conization, CIN2 and above were also detected as a result of conization. After conization, the number of true positives of ECC was found to be 43, the number of false positives was 0, the number of false negatives was 367 and the number of true negatives was 210. Accordingly, the sensitivity of ECC after conization was found to be 10.5%, specificity 100%, positive predictive value 100%, negative predictive value 36.4% and accuracy rate 40.8%.

Conclusion: Despite its low sensitivity, we recommend performing ECC after conization because it has high specificity and positive predictive values, and because it detects advanced lesions only in ECC, even in only three patients. We believe that ECC results are important for the patient's follow-up and treatment in the next stage. However, there is a need for comprehensive studies on the location of ECC after conization.

Keywords: Endocervical curettage, conization, cervical preinvasive lesion

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Sorumlu Yazar/Corresponding Author: Mustafa ŞAHİN, Ankara Şehir Hastanesi, Jinekolojik Onkoloji Cerrahisi Kliniği, Çankaya-Ankara, Türkiye
E-mail: mustafasahin1163@gmail.com

Çevrimiçi Erişim/Available online at: https://dergipark.org.tr/tr/pub/jgon

GİRİŞ

Human papillomavirus (HPV) servikal kanserin primer sebebi olarak kabul edilir (1) Taramadaki gelişmeler ve HPV aşılarının popülaritesinin artması nedeniyle serviks kanseri insidansı azaltılabilir. Bununla birlikte, son yıllarda servikal intraepitelyal neoplazi (CIN) olarak bilinen premalign lezyonların insidansı artmıştır. Yüksek riskli CIN (CIN2 ve CIN3) için en sık kullanılan tedavi yöntemleri transformasyon bölgesinin Loop Elektrocerrahi Eksizyon Prosedürü (LEEP), soğuk bistüri konizasyonu veya lazer konizasyonu gibi eksizyonel işlemlerdir (2). Servikal eksizyonel işlem yüksek dereceli preinvaziv lezyonlarda önemli bir tanı ve tedavi yöntemidir.

Her ne kadar CIN yukarıda belirtilen yöntemlerle etkili bir şekilde tedavi edilebilse de, çıkarılan dokuların histolojik sınırı hala tedavi edilebilmektedir. Arbyn ve ark. (3) çalışmasında pozitif cerrahi sınır oranının genel olarak %23,1 olduğunu ve tedavi edilen lezyonun ciddiyetine göre arttığını belirtti.

Endoservikal küretaj (ECC), endoservikal kanalın bir küret ile çevresel olarak kazınmasını içeren prosedürdür. ECC genel olarak yetersiz kolposkopide, endoservikal kanala uzanım gösteren lezyon varlığında, sitoloji-kolposkopi uyumsuzluğunda önerilmektedir. Bazı kolposkopistler, ECC yapılmasının endoservikal kanaldaki prekanseröz lezyonların ve invaziv servikal kanserin kaçırılmasını önleyebileceğini düşünmektedir (4). Pretorius ve ark. (5) ECC'nin CIN 2+ lezyonların %2-6'sının tanınmasını sağlayarak kolposkopinin duyarlılığını artırdığını belirtmektedir. Ancak eksizyonel işlem esnasında kalan endoservikal kanalın küretajı genelde cerrahın takdirine kalmaktadır ve günümüzde ECC'nin hangi hastaya yapılması gerektiği konusunda tartışmalar devam etmektedir.

Bununla birlikte eksizyonel işlem esnasında kalan endoservikal kanal küretajının konizasyon sonrasında gözden kaçabilecek rezidü lezyonu veya servikal kanseri saptamak için rutin uygulamada yeri var mıdır? sorusunun cevabı henüz netleşmemiştir.Daha geniş kapsamlı çalışmalara ihtiyaç vardır.

GEREÇLER VE YÖNTEM

Ankara Bilkent Şehir Hastanesi Jinekolojik Onkoloji Cerrahisi Kliniği'ne 01.09.2019 ile 01.12.2022 tarihleri arasında başvuran, servikal eksizyonel işlem (konizasyon veya LEEP) ve beraberinde endoservikal küretaj işlemi yapılan 620 hastanın verileri retrospektif olarak değerlendirildi. Veriler elektronik veri tabanı sisteminden, hasta dosyalarından, patoloji raporlarından ve ameliyat notlarından elde edildi. Çalışma için Ankara Bilkent Şehir Hastanesi 2 Nolu Klinik Araştırmalar Etik Kurul Başkanlığından 28.09.2022 tarihli E2-22-2472 etik kurul kararı ile onayı alındı.

18 yaş ve üzeri, daha önceden servikal eksizyonel işlem yapılmamış olan, hastanemizde eksizyonel işlem (LEEP, konizasyon) ve bereberinde ECC yapılan hastalar çalışmaya dahil edildi. Daha önceden eksizyonel işlem yapılmış hastalar, başka merkezde eksizyonel işlem yapılmış hastalar, ECC yapılmamış hastalar çalışmaya alınmadı. Eksizyonel işlem öncesinde her hastanın kolposkopik muayenesi yapıldı. Hastaların yaşı, fertilite beklentisi, medikal durumları ve lezyonun özelliğine servikal eksizyonel işlemde soğuk konizasyon veya LEEP tercih edildi. Eksizyonel işlemler ve ECC alanında uzman jineko-onkologlar tarafından yapıldı.

Statistical Analysis

Analizler SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) 22 paket programında değerlendirilmiştir. Çalışmada tanımlayıcı veriler kategorik verilerde n, % değerleri, sürekli verilerde ise ortalama±standart sapma (Ort ±SS) değerleri ile gösterilmiştir. Gruplar arası kategorik değişkenlerin karşılaştırılmasında Ki-kare analizi (Pearson Chi-kare) uygulanmıştır. Konizasyonun ECC'nin tanısal değeri için sensitivite ve spesifite hesaplamaları yapılmıştır ve bu hesaplamada altın standart yöntem konizasyon kabul edilmiştir. Analizlerde istatistiksel anlamlılık düzeyi $p<0.05$ olarak kabul edilmiştir.

BULGULAR

Çalışmaya dahil edilen hastaların ortalama yaşı 40,8±10,5 olup 20 ile 78 arasında değişmekteydi.Servikal sitoloji negatif olan 145 (%23,4), ASC-US olan 201 (%32,4), LSIL olan 137 (%22,1), HSIL olan 54 (%8,7), ASC-H olan 73 (%11,8), AGC olan 8 (%1,3) ve AIS olan 2 (%0.3) hasta vardı. HPV negatif olan 112 (%18,1), HPV pozitif olan 508 (%81,9) hasta vardı. HPV 16 pozitif olan 228 (36,7), HPV 18 pozitif olan 16 (%2,6), HPV 16 ve 18 pozitif olan 9 (%1,5), HPV 16 ve 18 dışı pozitif olan 162 (%26,1) ve diğer HPV tiplerinden pozitif olan 93 (%15) hasta vardı. Kolposkopik biopsi sonucunda kronik servisit olan 29 (%4,7), CIN1 olan 54 (%8.7), CIN2 olan 279 (%45) ve CIN3 olan 258 (%41,6) hasta vardı. ECC yapılmayan 26 (%4,2) hasta vardı.ECC sonucu yüzeyel epitel olan 226 (%36,5), mukoid olan 131 (%21,1), polip olan 6 (%1), servisit olan 57 (%9,2), CIN1 olan 49 (%7,9),CIN2 olan 52 (%8,4), CIN3 olan 67 (%10,8) ve insitu kanser olan 6 (%1) hasta vardı (Tablo 1).

Premenapozal ve postmenapozal hastalarda konizasyon sonrası ECC sonuçları açısından anlamlı farklılık görüldü ($p<0.015$).

Tablo 1. Hastaların kliniko-patolojik özellikleri ve konizasyon sonrası ECC ile olan ilişki durumları

	Sonuç	n	%	p
Menapozal durum	Premenapozal	426	67,8	**0,015**
	Postmenapozal	194	32,2	
Servikal sitoloji	Negatif	145	23,4	0,693
	ASC-US	201	32,4	
	LSIL	137	22,1	
	HSIL	54	8,7	
	ASC-H	73	11,8	
	AGC	8	1,3	
	AIS	2	0,3	
HPV	HPV Negatif	112	18,1	0,127
	Kolposkopi biyopsi patolojisi HPV 16	228	36,7	
	HPV 18	16	2,6	
	HPV 16 ve 18	9	1,5	
	HPV 16 ve 18 dışı	162	26,1	
	HPV diğer	93	15	
Serviks biopsi	Kronik servisit	29	4,7	
	CIN1	54	8,7	
	CIN2	279	45	
	CIN3	258	41,6	
Kolposkopi ECC	Yok	26	4,2	
	Yüzeyel epitel	226	36,5	
	Mukoid	131	21,1	
	Polip	6	1,0	
	Servisit	57	9,2	
	CIN1	49	7,9	
	CIN2	52	8,4	
	CIN3	67	10,8	
	Karsinoma in situ	6	1,0	
Glandüler tutulum	var	174	68,5	**0,006**
	yok	80	31,5	

*Kikare analizi uygulanmıştır.
n; hasta sayısı: p; anlamlılık düzeyi

Glandüler tutulum oranlarında konizasyon sonrası ECC sonuçları açısından anlamlı farklılık tespit edildi (p=0.006). Konizasyon sonrası ECC sonuçları açısından yüksek riskli HPV varlığı (p=0.127) ve servikal sitoloji sonuçları (p=0.693) açısından anlamlı farklılık yoktu (Tablo 1).

Konizasyon sonuçlarında kronik servisit olan 65 (%10.5), CIN1 olan 145 (%23.4), CIN2 olan 153 (%24.7), CIN3 olan 233 (%37.6), karsinoma in situ olan 9 (%1.5) ve kanser 15 (%2.4) hasta vardı. Konizasyon sonrası ECC' de yüzeyel epitel hücre olan 290 (%46.8), mukoid olan 163 (%26.3), polip olan 14 (%2.3), servisit olan 54 (%8.7), endometrial doku olan 40 (%6.5), CIN1 olan 16 (%2.6), CIN2 olan 11 (%1,8), CIN3 olan 25 (%4), karsinoma in situ olan 4 (%0,6) ve kanser olan 3 (%0,5) hasta vardı.

Konizasyon sonrası ECC yapılan olan 35 (%7,7) hastada, LEEP sonrası ECC yapılan 8 (%4.8) hastada CIN2+ lezyon saptandı. Konizasyon ve LEEP işlemleri arasında CIN2+ lezyonları saptamada anlamlı farklılık görülmedi (p=0.202).

Konizasyonda CIN2+ saptanan hasta sayısı 410 (%66,1), konizasyon sonrası ECC' de CIN2+ saptanan hasta sayısı 43 (%6,9) idi. Konizasyona ek ECC'de CIN2+ lezyon saptanan 43 hastanın 40'ında (%93) konizasyon spesmeninde de CIN2+ lezyon saptanmıştı.

Konizasyon patolojilerinde saptanamayan CIN2+ 3 (%7) hasta ise sadece ECC' saptandı.

Konizasyonda pozitif cerrahisi sınırı endoservikal olan 92 (22,4), endoservikal ve ektoservikal olan 13 (%3,1), ektoservikal olan 17 (4.1) hasta vardı. Toplamda 105 (%25,6) hastada endoservikal cerrahi sınır pozitifti (Tablo 2). Konizasyon sonrası ECC' de CIN2+ saptanan 43 (%6,9) hastanın 25'inde (%4) endoservikal cerrahi sınır negatif ve 18'inde (2,9) endoservikal cerrahi sınır pozitifti (Tablo 3).

Konizasyon ECC'nin sensitivitesi %10,5, spesifitesi %100, pozitif prediktif değeri %100, negatif prediktif değeri %36.4 bulunmuştur (Tablo 4).

Konizasyonda CIN1 saptanan 2 (%1,4), CIN2 saptanan 5 (%3,3), CIN3 saptanan 20 (%8,6), in situ kanser saptanan 2 (%22,2) ve kanser saptanan 3 (%20) hasta aynı zamanda ECC'de saptanmıştır (Tablo 5).

Tablo 2. Hastaların konizasyon ve ECC patoloji sonuçları

	Sonuç	n	%
Konizasyon	Kronik servisit	65	10,5
	CIN1	145	23,4
	CIN2	153	24,7
	CIN3	233	37,6
	Karsinoma in situ	9	1,5
	Kanser	15	2,4
Konizasyon ECC	Yüzeyel epitel hücre	290	46,8
	Mukoid	163	26,3
	Polip	14	2,3
	Servisit	54	8,7
	Endometrial doku	40	6,5
	CIN1	16	2,6
	CIN2	11	1,8
	CIN3	25	4
	Karsinoma in situ	4	0,6
	Kanser	3	0,5
Cerrahi sınır pozitifliği	Endoservikal	92	14,8
	Ektoservikal	17	2,7
	Endoservikal ve Ektoservikal	13	2,1

Tablo 3. Konizasyon ve ECC'de CIN2+ lezyon gelenlerde cerrahi sınır durumu

	n (%)	Endoservikal cerrahi sınır pozitifliği n (%)	
Konizasyonda CIN2+ lezyon	410 (%66,1)	105 (%25,6)	
Konizasyon ECC' de CIN2+ lezyon	43 (%6,9)	18 (2,9)	
Konizasyon ve ECC'de CIN2+ lezyon	40 (%93)	40 (%100)	
Sadece konizasyon ECC' de CIN2+ lezyon	3 (%7)	0	

Tablo 4. Konizasyon ve ECC' de CIN2+ lezyon saptanma oranları

		ECC'de CIN2+ lezyon				p
		Var		Yok		
		n	%	n	%	
Konizasyonda CIN2+ lezyon	Var	43	100	0	0	<0,001
	Yok	367	63,6	210	36,4	

*Kikare analizi uygulanmıştır

Tablo 5. Konizasyon ve ECC sonuçlarının karşılaştırılması

		ECC patolojisi											
		Yetersiz		CIN1		CIN2		CIN3		İnsitu ca		Kanser	
		n	%	n	%	n	%	n	%	n	%	n	%
Konizasyon patolojisi	Yetersiz	65	100	0	0	0	0	0	0	0	0	0	0
	CIN1	143	98,6	2	1,4	0	0	0	0	0	0	0	0
	CIN 2	139	90,8	7	4,6	5	3,3	1	0,7	1	0,7	0	0
	CIN 3	201	86,3	7	3,0	5	2,1	20	8,6	0	0	0	0
	İnsitu ca	6	66,7	0	0	0	0	1	11,1	2	22,2	0	0
	Kanser	7	46,7	0	0	1	6,7	3	20,0	1	6,7	3	20

TARTIŞMA

Serviks kanseri tarama programları ve aşılama ile önlenebilir bir kanser olsa ülkemizde de ilk on kanser türü içinde yer alarak önemini korumaktadır.

Menapoz sonrasında skuamokolumnar bileşke sıklıkla endoservikal kanalda yer aldığından CIN2+ lezyonlar daha çok endoservikal kanalda görülür ve CIN2+ lezyonlar içeren konizasyon sonrası ECC, rezidüel hastalığın bir göstergesidir (6). Kobak ve ark. (6) çalışmasında konizasyon sonrası ECC' si pozitif olan hastaların invaziv kanser açısından daha yüksek risk taşıdığı buldu. Özellikle 50 yaş ve üzerinde konizasyon spesmeninde pozitif endoservikal cerrahi sınır ve konizasyon sonrası ECC'de CIN2+ lezyon oranının arttığını saptadı. Servikal konizasyon yapılan bütün hastalara konizasyonun hemen ardından ECC yapılmasını önerdi. Çalışmamızda da premenapozal ve postmenapozal hastalarda konizasyon sonrası ECC sonuçları açısından anlamlı farklılık görüldü ($p<0.015$). Bu sonuçlara göre hastanın yaşı, konizasyonda ECC yapılıp yapılması açısından unutulmaması gereken bir paremetre gibi durmaktadır.

Demirkıran ve ark. (7) çalışmada ASCUS, LSIL, ASC-H ve HSIL sitoloji sonucu olan hastalarda CIN 2 ve üzeri lezyon oranları sırasıyla %32, %37, %65 ve %82 idi. Çalışmada pozitif cerrahi sınır oranının ve ECC' deki CIN2+ lezyonların servikal sitolojideki anormallik derecesi ile giderek arttığı gösterildi. HSIL sitolojisi olanlarda ECC pozitifliğinin yüksek oranda olması nedeniyle, HSIL sitolojisi olan her hastaya LEEP sırasında ECC de yapılması önerildi. Ancak bizim çalışmamızda servikal sitoloji sonuçları ile ECC' deki CIN2+ lezyonlar arasında anlamlı farklılık yoktu ($p=0.693$).

Suzuki ve ark. (4) çalışmasında ECC ile hiçbir hastaya konizasyonda yakalanandan daha ileri bir lezyon tanısı konulmamıştı. ECC'nin rezidü endoservikal lezyonları belirlemede sensitivitesi %42,9 , spesifitesi %83,9 ve pozitif prediktif değeri %54,5 idi. Düşük sensitivite ve pozitif prediktif değerlere rağmen konizasyon sonrasında ECC yapılmasının endoservikal lezyonları değerlendirmede yararı olduğu belirtilmişti. Bizim çalışmamızda Suzuki ve arkadaşlarının çalışmasından farklı olarak ECC'nin ileri lezyon yakaladığı 3 hasta mevcuttu. Hastaların üçünde konizasyon sonucu CIN 1 iken, konizasyon ECC sonuçları CIN2, CIN 3 ve in situ karsinomdu. Konizasyon sonrası ECC'nin sensitivitesi %10,5, spesifitesi %100, pozitif prediktif değeri %100, negatif prediktif değeri %36,4 ve doğruluk oranı ise %40,8 olarak bulunmuştu. Çalışmamızda Suzuki ve arkadaşlarının çalışmasına kıyasla sensitivite değerinin daha düşük olmasına rağmen spesifite ve pozitif prediktif değerinin daha yüksek olduğu bulundu.

Schneider ve ark.(8) konizasyon sonrası ECC'nin, CIN veya kanser açısından rezidü lezyonları belirlemedeki değeri araştırdı. Çalışmada ECC' nin sensitivitesi %38, spesifitesi %85, pozitif prediktif değeri (PPV) %56 olarak bulunurken, 50 yaş ve üzeri hastalarda bu değerler sırasıyla %44, %94, %88 olarak bulundu. Konizasyon sonrası ECC'nin genel olarak rezidüel lezyonları tespit etmeyi geliştirmediği ancak 50 yaş ve üzeri alt çalışma gruplarında faydalı olduğu savunuldu. Bizim çalışmamızda da konizasyon sonrası ECC'nin premenapozal ve postmenapozal kadınlarda sırası ile CIN 2 yakalama oranları %16'ya %2,4, CIN 3 yakalama oranları %3'e %7,9 , in situ kanser yakalama oranları %0,4'e %1,6 ve kanser yakalama oranları %0.,2'ye %1,6 idi. Artan yaş ile ECC'nin CIN2+ rezidü lezyonları belirlemedeki yakalama oranının arttığı saptandı.

Vierhaut ve ark.(9) çalışmasında konizasyon ve ECC arasında zayif korelasyon bulundu. Çalışmada ECC sensitivitesi %50, spesifitesi %95 iken konizasyon için bu değerler sensitivite %80, spesifite %88 olarak bulunmuş. Sonuç olarak ECC'nin persiste hastalığı belirlemede küçük bir ek katkısı olduğu kanısına varılmış. Çalışmamızda kappa analizi ile konizasyon ve ECC uyumuna bakıldı ve kappa katsayısı 0,074 olarak hesaplanarak uyumlu kategorisinde yer aldı.

Lea ve ark.(10) konizasyon sonrasında ECC'nin fertilitesini korumak isteyen hastalarda rezidüel adenokasinoma in situ (AIS) için yaralı bir tanı aracı olup olmadığı araştırdı. Konizasyon sırasında gerçekleştirilen ECC'nin, fertilizasyonunu korumak isteyen kadınlarda AIS' yi tahmin etmek için yararlı bir araç olduğu sonucuna varıldı.

Cuello ve ark.(2) LEEP sonrası ECC'den elde edilen pozitif bulguların, cerrahi sınır pozitifliğine kıyasla nükseden hastalık için daha iyi bir öngörücü olduğunu gösterdi. CIN2+ nedeniyle yapılan LEEP sonrasında mutlaka ECC yapılmasını önerdi.

Çalışmamızdaki konizasyon sonrası ECC'de CIN 2 %1,8, CIN 3 %4, karsinoma in situ %0,6 ve kanser %0.5 olarak bulundu. Konizasyon sonucu CIN 2 gelenlerin %3,3'ü, CIN 3 gelenlerin %8,6'sı, in situ kanser gelenlerin %22,2'si ve kanserlerin %20'si konizasyon sonrası ECC de yakalanmıştı. ECC'nin CIN2+ lezyonlardaki hastaları yüksek oranda yakalayabilmesi ve konizasyonda atlanan CIN2+ lezyonları saptayabilmesi, bizlere konizasyon sonrası ECC yapılmasının gerekli olduğu düşündürmektedir.

Konizasyonda CIN2+ lezyon saptanan 410 hastanın dışında ,ECC' de 3 hastada istatistiksel olarak anlamlı olmasa da klinik olarak yaklaşımızı değiştiren, konizasyon patoloji sonucundan daha ileri patoloji saptandı. Çalışmamızın geneline baktığımızda; literatürdeki çalışmalarla benzer özellikleri olmasına rağmen, diğer çalışmalardan daha fazla hasta sayısı içermesi ve daha çok parametre analizi yapılmasıyla çalışmamız kendine özgü bir yapıya kavuşmuştur. Çalışmada elde ettiğimiz veriler doğrultusunda servikal konizasyon sonrası yapılacak ECC'nin faydalı olacağı kanaatindeyiz. ECC ile CIN 2+ lezyonlar ve servikal kanserin saptama oranı düşük olmasına rağmen, hastaya sonraki takip ve tedavilerine karar vermemiz açısından yol gösterici olabilir.

Hastaların sitoloji örneklemelerinin, kolposkopik muayenelerinin, konizasyon operasyonlarının jinekolog onkologlar tarafından uygulanması, hasta sayısının fazla olması çalışmanın güçlü yanlarıdır. Çalışmanın retrospektif olması, bazı dermografik kayıtlara ulaşılamamasını ve konizasyon sonrası ECC sonuçlarının büyük ölçüde yetersiz olarak sonuçlanmasını dejavantaj olarak değerlendiriyoruz.

SONUÇ

Çalışmamızın literatürdeki çalışmalarla benzer özellikleri olmasına rağmen, daha fazla hasta sayısı içermesi ve daha çok parametre analizi yapılmasıyla kendine özgü bir yapısı vardır. Çalışmamızda konizasyon sonrası yapılan ECC düşük sensitivite değerine rağmen yüksek spesifite ve pozitif prediktif değerlerine sahiptir. Çalışmada elde ettiğimiz veriler doğrultusunda servikal konizasyon sonrası yapılacak ECC'nin fayda sağlayacağını düşünmekteyiz. Daha fazla merkezin katıldığı kapsamlı çalışmalar yapılarak konizasyon sonrası ECC'nin yapılıp yapılmayacağı konusundaki belirsizliğin giderilebileceğini düşünmekteyiz.

Yazar Katkıları:
Yazarların çalışmadaki katkı oranları eşittir.

Çıkar Çatışması Beyanı:
Çalışma kapsamında herhangi bir kurum veya kişi ile çıkar çatışması bulunmamaktadır.

Destek Beyanı:
Çalışma herhangi bir destek almamıştır.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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The impact of COVID-19 (SARS-CoV-2) vaccines on high-risk human papillomavirus clearance and cervical cytology in patients undergoing cervical excisional procedures

COVID-19 (SARS-CoV-2) aşılarının servikal eksizyonel işlem yapılan hastalarda yüksek riskli human papilloma virüsü temizliği ve servikal sitoloji üzerindeki etkisi

Mustafa ŞAHİN[1], Tufan ARSLANCA[2]

[1]Gynecological Oncology Surgery Clinic, Konya City Hospital, Konya, Türkiye
[2]Gynecological Oncology Surgery Clinic, Ankara Bilkent City Hospital, Ankara, Türkiye

ABSTRACT

Aim: This study aims to investigate the effects of COVID-19 (SARS-CoV-2) vaccines on high-risk Human Papillomavirus (hr-HPV) clearance and cervical cytology results in patients undergoing cervical excisional procedures.

Materials and Methods: A total of 686 patients were analyzed in the Gynecological Oncology Surgery Clinic between October 2020 and July 2022. Among these, 350 patients had not received the COVID-19 vaccine, and 336 had received it. Cervical cytology and hr-HPV DNA analysis were performed on the patients 6 months after the cervical excisional procedure. Clinical data, including patients' vaccination status, were obtained from the national electronic medical record database, patient files, and face-to-face inquiries.

Results: There was no significant difference between the vaccinated and unvaccinated groups in terms of age, parity, smoking, oral contraceptive use, cervical cytology, hr-HPV DNA status, cervical biopsy, endocervical curettage, type of excisional procedure, results of excisional procedure and endocervical curettage, and surgical margin status (p>0.05 for all comparisons). No significant difference was observed in the cervical cytology results 6 months post-procedure between the vaccinated and unvaccinated groups (p=0.566, 95% CI=1.130-1.549). Similarly, no significant difference was found in hr-HPV DNA clearance between the two groups 6 months post-procedure (p=0.217, 95% CI=1.412-1.750).

Conclusion: The systemic effects of COVID-19 vaccines are not fully understood. Our study is among the few that investigate the impact of COVID-19 vaccines on hr-HPV DNA clearance and cervical cytology results. Current literature, similar to our findings, does not demonstrate a significant effect of COVID-19 vaccination on hr-HPV clearance and cervical cytology results. Given the strong immunogenic response elicited by COVID-19 vaccination, the potential impact of this non-specific systemic inflammatory response on hr-HPV DNA clearance warrants further investigation. This study found no difference in cervical cytology and hr-HPV DNA persistence between vaccinated and unvaccinated patients 6 months post-cervical excisional procedure. However, comprehensive studies are needed for better interpretation and acceptance of these findings.

Keywords: COVID-19 (SARS-CoV-2) vaccines, cervical excisional procedure, high-risk human papillomavirus clearance, cervical cytology

ÖZ

Amaç: Bu çalışmada servikal eksizyonel işlem uygulanan hastalarda Covid 19 (SARS-CoV-2) aşılarının yüksek riskli Human Papilloma Virüs klerensine ve servikal sitoloji sonuçlarına etkilerini araştırmayı amaçlıyoruz.

Gereçler ve Yöntem: Ekim 2020 ile Temmuz 2022 tarihleri arasında Jinekolojik onkoloji cerrahisi kliniğinde Covid 19 aşısı olmamış 350 hasta veCovid 19 aşısı olmuş 336 hasta olmak üzere toplam 686 hasta analiz edildi. Hastaların servikal eksizyonel işlemden 6 ay sonraki servikal sitoloji ve hr-HPV DNA analizi yapıldı. Hastaların aşı durumu da dahil olmak üzere klinik veriler, ulusal elektronik tıbbi kayıt veri tabanından, hasta dosyalarından ve hastanın kendisinden yüz yüze sorularak elde edildi.

Bulgular: İki grup arasında yaş, parite, sigara, oral kontraseptif kullanımı, servikal sitoloji, hr-HPV DNA durumu, servikal biopsi ve endoservikal küretaj, eksizyonel işlem tipi, eksizyonel işlem ve endoservikal küretaj sonucu, cerrahi sınır durumu, açısından fark yoktu (sırasıyla p=0,588, p=0,464, p=0,319, p=0,315, p=0,428, p=0,655, p=0,302, p=0,610, p=0,734, p=0,237, p=0,198, p= 0,594). Aşılanmayan ve aşılanan gruplarda 6 ay sonrasi servikal sitoloji sonuçlarında anlamlı fark yoktu (p=0,566, %95 CI=1,130-1,549). Aşılanmayan ve aşılanan gruplarda 6 ay sonrasi hr-HPV DNA açısından anlamlı fark yoktu (p=0,217, %95 CI=1,412-1,750).

Tartışma: Covid 19 aşılarının neden olduğu sistemik etkileri günümüzde tam olarak aydınlatılamamıştır. Çalışmamız Covid 19 aşılarının hr-HPV DNA klerensine ve servikal sitoloji sonuçlarına olan etkisini araştıran literatürdeki yapılmış sayılı çalışmadan biridir. Yapılmış güncel çalışmalarda çalışmamızda elde ettiğimiz sonuçlara benzer şekilde Covid 19 aşılamasının hr-HPV klerensinde ve servikal sitoloji sonuçları üzerinde etkisi gösterilemedi. Covid 19 aşılamasının güçlü bir immünojenik reaksiyon ortaya çıkardığı göz önüne alındığında, bu spesifik olmayan sistemik inflamatuar yanıtın, hr-HPV DNA klerensine olası etkisi merak konusudur.

Sonuç: Çalışmamızda Covid 19 için aşılanmayan ve aşılanan hastaların servikal eksizyonel işlemden 6 ay sonrasındaki servikal sitoloji ve hr-HPV DNA persistans sonuçları arasında fark saptanmadı. Ancak elde edilen sonuçların daha iyi yorumlanıp kabul görmesi için kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Covid 19 (SARS-CoV-2) aşıları, servikal eksizyonel işlem, yüksek riskli human papilloma virüs klerensi, servikal sitoloji

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Sorumlu Yazar/Corresponding Author: Mustafa ŞAHİN, Akabe Mahallesi, Adana Çevre Yolu Caddesi. No:135/1, 42020 Karatay-Konya, Türkiye
E-mail: mustafasahin1163@gmail.com

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INTRODUCTION

Human papilloma virus (HPV) is an oncogenic DNA virus with a central role in the development of cervical cancer. The presence of HPV alone is not sufficient for the development of a pre-invasive cervical lesion and HPV persistence plays a critical role (1). Persistent infection with Human Papilloma Virus (HPV) is the primary cause of nearly all preinvasive cervical lesions and cervical cancer. There are over 200 different types of HPV, including high-risk (hr) HPV subtypes. Few HPV subtypes have carcinogenic potential. The high-risk HPV types (HR-HPV) are 18, 31, 33, 35, 39, 45, 51, 56, 58, 59, 68, 73 and 82, especially 16 (2). Of these, HPV 16 and HPV 18 are the types most associated with invasive cancers and cause 65-75% of cases (3). While most HPV infections are typically cleared by the immune system within an average of 6-18 months, approximately 10% of cases persist in women, leading to cervical intraepithelial neoplasia (CIN) in 20-30% of cases and cervical cancer in 1-2% of cases (1).

CIN is a preinvasive condition that precedes cervical cancer and is equivalent to the term cervical dysplasia. Cervical lesions with mitoses and immature cells limited to the lower third of the epithelium are typically referred to as CIN 1, and involvement of the middle and upper thirds are referred to as CIN 2 and CIN 3, respectively. In contrast, for patients with CIN 2 and 3 lesions, the recommended strategy is excision, intended to stop progress toward carcinoma, followed by intensified surveillance. The main treatment methods for preinvasive cervical lesions include excisional procedures such as Loop Electrosurgical Excision Procedure (LEEP) or conization. Studies have shown a residual disease rate of 5-20% following excisional procedures (2).

COVID-19, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), is an infectious disease affecting the respiratory tract. Lymphocytopenia observed during infection potentially involves CD4+ and some CD8+ T cells. This impairs the innate and acquired immune responses, delaying the clearance of the virus and causing an overactive neutrophil and macrophage response (3).

Various vaccines are available for COVID-19 in our country. The Pfizer/BioNTech mRNA vaccine induces an immune response by injecting the genetic code of the virus's Spike protein (S-protein) encapsulated in lipid nanoparticles into the human body. The CoronaVac (Sinovac) vaccine is an inactivated vaccine developed by growing and inactivating the live SARS-CoV-2 virus in the laboratory.

A study on the effectiveness of COVID-19 vaccines and the waning of immunity over time showed that 8 months after the administration of two doses of COVID-19 vaccine, immune function was lower in vaccinated individuals than in unvaccinated individuals (1).

The systemic effects caused by Covid 19 vaccines have not been fully elucidated to date. İnflammatory processes play an active role in the persistent development of HPV infections. Considering that Covid 19 vaccination elicits a strong immunogenic reaction, the possible effect of this nonspecific systemic inflammatory response on HPV persistence is a matter of curiosity.

The systemic effects caused by Covid 19 vaccines have not been fully elucidated to date. İnflammatory processes play an active role in the persistent development of HPV infections. Considering that Covid 19 vaccination elicits a strong immunogenic reaction, the possible effect of this nonspecific systemic inflammatory response on HPV persistence is a matter of curiosity. While studies have shown potential effects of COVID-19 vaccines on the immune system, their possible effects on hr-HPV DNA clearance remain uncertain.

In our study, we investigated the effects of COVID-19 vaccines on HR-HPV clearance and cervical cytology.

MATERIALS AND METHODS

Ethical approval for the study was obtained from the Ethics Committee of Necmettin Erbakan University (Decision No: 5439, dated 10.01.2025). All patients signed informed consent forms allowing the use of their clinical data. The study protocol complies with the ethical principles of the 1975 Declaration of Helsinki.

Between October 2020 and July 2022, 686 patients over 24 years of age with high-risk cervical preinvasive lesions and hr-HPV DNA positivity who underwent cervical excisional procedures at Konya City Hospital Gynecological Oncology Surgery Clinic were analyzed. Patients who received the COVID-19 vaccine 3 months before or after the excisional procedure, with no additional medical problems or medication history that could impair immune response, were included. Patients with malignant or carcinoma in situ pathology reports, those requiring reconization, unvaccinated patients with additional medical problems or medication history that could impair immune response, were excluded from the study.

Cervical excisional procedures were performed by a surgical team specialized in gynecological oncology. Cytology and surgical samples were evaluated by specialized pathologists. Pathology and HPV DNA test results were assessed following the 2019 ASCCP guidelines (4). Conization was performed using a scalpel (cold conization) or needle-tip cautery, depending on the surgeon's

preference. HPV DNA analysis was performed using the Hybrid Capture 2 HPV DNA test (hc2; Qiagen, Hilden, Germany). The 6-month post-procedure HPV DNA and cervical cytology results were compared with the pre-procedure results. Patients who received at least one dose of Pfizer/BioNTech mRNA vaccine or Sinovac Life Sciences (inactivated) vaccine were included. Clinical data, including vaccination status, were obtained from the national electronic medical record database, patient files, and face-to-face inquiries.

Statistical Analysis

Statistical analysis was performed using SPSS version 22 (IBM, Chicago, USA). Descriptive data were presented as n (%) for categorical variables and mean±standard deviation (Mean±SD) for continuous variables. Chi-square and Fisher's Exact tests were used to evaluate differences between groups. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 786 patients were evaluated for eligibility. Fifty-three individuals were excluded for not meeting the inclusion criteria, leaving 733 patients with hr-HPV DNA infection, 372 of whom were unvaccinated and 361 vaccinated. During follow-up, 22 and 25 patients in the unvaccinated and vaccinated groups, respectively, were lost to follow-up or discontinued treatment. Ultimately, 350 unvaccinated and 336 vaccinated patients were analyzed. The patient selection flowchart is shown in Figure 1.

The mean age of the unvaccinated group (n=350) was 35.22±6.92 years, and the vaccinated group (n=336) was 33.65±5.48 years. The mean parity was 2.12±1.30 in the unvaccinated group and 1.91±1.04 in the vaccinated group. Smoking prevalence was 67.4% in the unvaccinated group and 61.6% in the vaccinated group. Oral contraceptive use was reported in 42.9% of unvaccinated patients and 39.2% of vaccinated patients. There was no significant difference between the unvaccinated and vaccinated groups in terms of age, parity, smoking, oral contraceptive use, cervical cytology, hr-HPV DNA status, cervical biopsy, endocervical curettage, type of excisional procedure, results of excisional procedure and endocervical curettage, and surgical margin status (p>0.05 for all comparisons). Demographic and clinicopathological data of the patients are summarized in Table 1.

There was no significant difference in cervical cytology results between the unvaccinated and vaccinated groups 6 months post-procedure, with benign cytology rates of 50.3% vs. 47.9%, ASCUS, LSIL rates of 28% vs. 29%, ASC-H, AGC, HSIL rates of 12.6% vs. 14.7%, and unknown rates of 9.1% vs. 4.1%, respectively (p=0.566, 95% CI=1.130-1.549). Similarly, there was no significant difference in hr-HPV DNA clearance between the unvaccinated and vaccinated groups 6 months post-procedure, with negative rates of 85.1% vs. 75.5% and positive rates of 14.9% vs. 24.5%, respectively (p=0.217, 95% CI=1.412-1.750). The 6-month post-procedure cervical cytology and hr-HPV DNA status of the unvaccinated and vaccinated groups are summarized in Table 2.

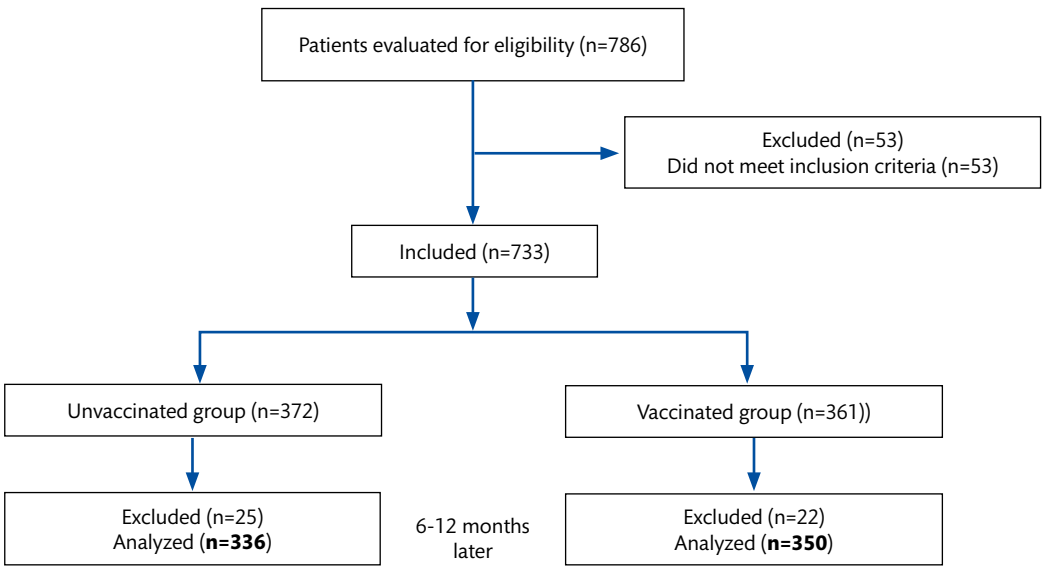

Figure 1. Patient Selection Flow Chart

Table 1. Demographic and clinicopathological data of the unvaccinated and vaccinated groups

		COVID-19 Vaccine		
		No (*n=350*)	Yes (*n=336*)	
Characteristics		**Mean ±SD**	**Mean ±SD**	**P value**
Age, (years, range)		35±6.92	33±5.48	0.588
Parity, (range)		2.12±1.30	1.91±1.04	0.464
		n (%)	**n (%)**	
Smoking		236 (67.4)	207 (61.6)	0.319
Oral contraceptive use		150 (42.9)	132 (39.2)	0.315
Menopause		62 (17.7)	69 (20.5)	0.398
STDs		88 (25.1)	101 (30.3)	0.417
Low socio-economics status		133 (38)	120 (35.7)	0.510
Cervical cytology	Benign	44 (12.6)	56 (31.3)	0.428
	AS-CUS/LSIL	154 (44)	142 (58.8)	
	ASC-H/AGC/HSIL	114 (32.6)	99 (5.8)	
	Unknown	38 (10.8)	39 (11.6)	
HPV	16	98 (28)	84 (25)	0.655
	18	32 (9.1)	30 (8.9)	
	16 and 18	42 (12)	54 (16.1)	
	Non-16/18	136 (38.9)	140 (40)	
	Unknown type	42 (12)	26 (7.7)	
Cervical biopsy	Normal	17 (4.8)	15 (4.5)	0.302
	CIN 1	33 (9.4)	30 (8.9)	
	CIN 2	169 (48.4)	189 (56.3)	
	CIN 3	131 (37.4)	102 (36.3)	
Endocervical curettage[1] (colposcopy)	Normal	141 (40)	156 (46.4)	0.610
	CIN 1	24 (6.8)	29 (8.6)	
	CIN 2	18 (5.1)	21 (6.3)	
	CIN 3	16 (4.6)	13 (3.9)	
	Insufficient sample	140 (40.3)	117 (34.8)	
Type of excisional procedure	LEEP	79 (22.6)	56 (16.6)	0.734
	Conization	271 (77.4)	280 (83.6)	
Excisional procedure result	Normal	41 (11.7)	54 (16.1)	0.237
	CIN 1	124 (35.4)	105 (31.3)	
	CIN 2	147 (42)	114 (33.9)	
	CIN 3	68 (19.4)	63 (18.7)	
Endocervical curettage[2] (excision)	Normal	128 (36.6)	164 (48.9)	0.198
	CIN 1	31 (8.8)	35 (10.4)	
	CIN 2	17 (4.8)	29 (8.6)	
	CIN 3	12 (3.5)	10 (2.9)	
	Insufficient sample	162 (46.3)	127 (37.8)	
Surgical margin	Negative	318 (90.8)	297 (88.4)	0.594
	Positive	32 (9.2)	39 (11.6)	

[1]Endocervical curettage at colposcopy
[2]Endocervical curettage during excisional procedure
Chi-square test; p: Significance value; p<0.05; n: Number of patients; Mean: Average; SD: Standard Deviation
STDs: Sexually Transmitted Diseases; AS-CUS: Atypical Squamous Cells of Undetermined Significance; LSIL: Low-grade Squamous Intraepithelial Lesion; HSIL: High-grade Squamous Intraepithelial Lesion; AGC: Atypical Glandular Cells; ASC-H: Atypical Squamous Cells, cannot exclude HSIL; CIN: Cervical Intraepithelial Neoplasia; hr-HPV: High-risk Human Papilloma Virus

Table 2. Cervical Cytology and hr-HPV Results Post-Excisional Procedure

Characteristics		COVID-19 Vaccine			
		No (n, %)	Yes (n, %)	95% CI	P value
Cervical Cytology	Benign	176 (50.3)	161 (47.9)	1.130-1.549	0.566
	AS-CUS/LSIL	98 (28)	106 (29)		
	ASC-H/AGC/HSIL	44 (12.6)	54 (14.7)		
	Unknown	32 (9.1)	15 (4.1)		
hr-HPV	Negative	298 (85.1)	277 (75.5)	1.412-1.750	0.217
	Positive	52 (14.9)	69 (24.5)		
	16	18 (5.2)	17 (5.1)		
	18	8 (2.3)	10 (3)		
	16 and 18	4 (1.1)	7 (2.1)		
	Non-16/18	22 (6.3)	35 (10.4)		

Chi-square test; p: Significance value; p < 0.05; CI: Confidence Interval
AS-CUS: Atypical Squamous Cells of Undetermined Significance; LSIL: Low-grade Squamous Intraepithelial Lesion; HSIL: High-grade Squamous Intraepithelial Lesion; AGC: Atypical Glandular Cells; ASC-H: Atypical Squamous Cells, cannot exclude HSIL; hr-HPV: High-risk Human Papilloma Virus

DISCUSSION

Our study found no significant difference between the cervical cytology and hr-HPV DNA persistence results of unvaccinated and vaccinated patients 6 months post-cervical excisional procedure. The persistence rate of hr-HPV DNA after excision ranges from 2% to 69.3%, varying due to differences in cervical biopsy pathology, patient age, follow-up duration, and hr-HPV DNA type (5),(6).

Costa et al. reported an hr-HPV persistence rate of 36.5% in a 2.4-39.2 month follow-up after excision (7). Bodner et al. reported an hr-HPV DNA rate of 27% at 3 months post-conization (8). Kreimer et al. showed a persistence rate of 75-105% for hr-HPV DNA in patients with CIN1-3 biopsy results following excisional procedures (9). Livasy et al. demonstrated an increasing persistence of hr-HPV DNA infection with extended follow-up duration (22% at 6 months, 31% at 12 months, and 32% at 24 months) (10). In our study, the hr-HPV DNA persistence rate was 14.9% in unvaccinated and 14.6% in vaccinated patients 6 months post-excision. Our study is one of the few investigating the effect of COVID-19 vaccination on hr-HPV persistence post-cervical excisional procedure, finding no association between vaccination and hr-HPV persistence.

The value of HPV genotype as a risk factor for hr-HPV DNA persistence post-treatment is debated. Zang et al. and Bogani et al. reported reduced HPV clearance for HPV 16/18 positive cases compared to other HPV types (11),(12). In contrast, So et al. found no relationship between HPV type and post-excision HPV persistence (13). Similarly, our study did not find an association between hr-HPV DNA type and post-excision HPV persistence. Ayhan et al. also reported no effect of COVID-19 vaccination, history of SARS-CoV-2 infection, or medication for SARS-CoV-2 on HPV persistence and cytology results (14).

The study's strengths include its single-center design allowing standardization, sufficient sample size, excisional procedures performed by a gynecological oncology team, and pathology results evaluated by experienced pathologists. The main limitation is its retrospective design.

CONCLUSION

This study found no significant difference in cervical cytology and hr-HPV DNA persistence results between vaccinated and unvaccinated patients for COVID-19 6 months post-cervical excisional procedure. Our study is among the few on this topic, and comprehensive studies are needed for better interpretation and acceptance of these findings.

Conflict of interest
The authors declare that they have no conflict of interest.

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TA contributed to the design of the article, collection of data, MS contributed to the analysis and interpretation of the article, and wrote the main text.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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The importance of atypical squamous cells in cervical PAP smear in patients aged 65 years and older and their association with HPV

65 yaş ve üzeri hastalarda servikal PAP smearde atipik skuamöz hücrelerin önemi ve HPV ile ilişkisi

Ayşegül AKSOY ALTINBOĞA[1,2], Tuba Dilay KÖKENEK ÜNAL[1,2], Nuran SÜNGÜ[1,2], Kübra KATİPOĞLU[2], Özge BAŞARAN AYDOĞDU[2], Merve Meryem KIRAN[2], Merve Nur ÇELİK[2], Esra ŞENGÜL[2], Zeynep Ruken HAKKOYMAZ[2], Şafak BULUT[2], Düriye ÖZER TÜRKAY[2], Fazlı ERDOĞAN[1,2], Orhan ALTINBOĞA[3]

[1]Department of Pathology, Ankara Yıldırım Beyazıt University, Ankara, Türkiye
[2]Department of Pathology, Ankara Bilkent City Hospital, Ankara, Türkiye
[3]Division of Perinatology, Department of Obstetrics and Gynecology, Ankara Bilkent City Hospital, Ankara, Türkiye

ABSTRACT

Aim: This study aims to determine the significance of atypical squamous cells (ASC) in women 65 years of age and older, and the high-risk HPV (hrHPV) status of patients diagnosed with ASCs.

Materials and Methods: Data base of the Department of Pathology between February 2019 and December 2020 were screened and patients over the age of 65 who had 'ASC of undetermined significance' (ASC-US) and 'ASC-cannot exclude high-grade squamous intraepithelial lesion' (ASC-H) diagnosis on cervical PAP smear (CPS) were identified. hrHPV positive and negative patients were also examined.

Results: 164 patients (151 (92.1%) ASCUS and 13 (7.9%) ASC-H were included in the study. Follow-up information of 95 cases showed 16.8% low grade squamous intraepithelial lesion (LSIL), 5.3% high grade squamous intraepithelial lesion (HSIL), 1.1% endocervical adenocarcinoma following ASC diagnosis. 19.6% patients were hrHPV positive. In the follow-up of HrHPV positive patients, 38.9% LSIL, 22.2% HSIL, 5.6% cervical adenocarcinoma developed. Intraepithelial lesions (LSIL + HSIL) and high-grade cervical lesions (HSIL + invasive cervical carcinoma) were more common in hrHPV positive ASC-US cases compared to hrHPV negative ASC-US cases. Patients with ASC-H were more likely to have LSIL and intraepithelial lesions at follow-up compared to patients with ASC-US.

Conclusion : In patients aged 65 years and older, hrHPV positive ASC cases carry a high risk for LSIL, HSIL and high grade cervical lesions. Further studies on absolute referral to hrHPV test screening in these patients would significantly contribute to the management of these patients.

Keywords: Atypical squamous cells, cervical cancer, PAP smear, HPV, age over 65

ÖZ

Amaç: Bu çalışmanın amacı 65 yaş ve üzeri kadınlarda atipik skuamöz hücrelerin (ASH) önemini ve ASH tanısı alan hastaların yüksek riskli HPV (hrHPV) durumunu belirlemektir.

Gereçler ve Yöntem: Şubat 2019 ve Aralık 2020 tarihleri arasında Patoloji Anabilim Dalı veri tabanı taranmış ve servikal PAP smear (CPS) incelemesinde 'önemi belirsiz ASH' (ASCUS) ve 'yüksek dereceli skuamöz intraepitelyal lezyonu dışlayamayan ASH' (ASC-H) tanısı olan 65 yaş üstü hastalar belirlenmiştir. hrHPV pozitif ve negatif hastalar da incelenmiştir.

Bulgular: 164 hasta (151 (%92,1) ASCUS ve 13 (%7,9) ASC-H çalışmaya dahil edilmiştir. Takip bilgileri olan ASH tanılı 95 olguda %16,8 düşük dereceli skuamöz intraepitelyal lezyon (LSIL), %5,3 yüksek dereceli skuamöz intraepitelyal lezyon (HSIL), %1,1 endoservikal adenokarsinom saptandı. Hastaların %19,6'sında hrHPV pozitifti. HrHPV pozitif hastaların takibinde %38,9 LSIL, %22,2 HSIL, %5,6 servikal adenokarsinom gelişti. İntraepitelyal lezyonlar (LSIL + HSIL) ve yüksek dereceli servikal lezyonlar (HSIL + invaziv servikal karsinom) hrHPV pozitif ASC-US olgularında, hrHPV negatif ASC-US olgularına kıyasla daha yaygındı. ASC-H hastalarında takip sırasında LSIL ve intraepitelyal lezyonların görülme olasılığı ASC-US hastalarına kıyasla daha yüksekti.

Sonuç: Yaşları 65 ve üzeri olan hrHPV pozitif ASH vakaları LSIL, HSIL ve yüksek dereceli servikal lezyonlar için yüksek risk taşımaktadır. Bu hastalarda hrHPV testi taramasına mutlak yönlendirmeye ilişkin daha fazla çalışma yapılması, bu hastaların yönetimine önemli katkı sağlayacaktır.

Anahtar Kelimeler: Atipik skuamöz hücre, serviks kanseri, PAP smear, HPV, 65 yaş üstü

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Sorumlu Yazar/Corresponding Author: Ayşegül AKSOY ALTINBOĞA, Ankara Bilkent Şehir Hastanesi, Üniversiteler Mahallesi 1604. Cadde No: 9 Bilkent/Çankaya/Ankara, Türkiye
E-mail: aysegulaksoy@hotmail.com

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INTRODUCTION

Despite the invention of the cervical PAP smear (CPS) by George Papanicolaou in 1928, which resulted in a notable reduction in cervical intraepithelial neoplasms and malignancies, cervical cancer continues to pose a substantial health challenge today (1). The CPS is the most effective cancer screening test ever developed to identify cervical precancerous lesions, with a well-established reporting system called the Bethesda system (2).

In the Bethesda system, "Epithelial cell abnormality: Squamous" encompasses the squamous intraepithelial lesion (SIL) category, which includes a range of squamous cell lesions starting from the precancerous lesions of low-grade SIL (LSIL) to high-grade SIL (HSIL), and ultimately invasive squamous cell carcinoma (1).

Nonetheless, due to the qualitative and quantitative constraints of the specimen, certain ambiguous morphological characteristics indicative of squamous cell abnormalities may be classified as "Atypical Squamous Cells" (ASCs), which are further divided into two categories: "Atypical Squamous Cells of Undetermined Significance" (ASC-US) and "Atypical Squamous Cells, HSIL cannot be excluded"(ASC-H), based on the suspected underlying lesion of LSIL versus HSIL, respectively (2).

The United States Preventive Services Task Force (USPSTF) and the American Cancer Society (ASC) advise women over 65 who have not had a CIN2 or more advanced lesion within the previous 25 years and have been properly screened in the past to stop screening for cervical cancer (3,4). The ASC considers three consecutive negative cytologies during the last 10 years, with the last screening conducted within the last 5 years, or the presence of two negative cotests or primary HPV tests as sufficient screening criteria. However, in the United States, 20% of cervical cancer cases are discovered in people over 65 (5). In cancers diagnosed at an older age, the prognosis is worse and mortality rates increase (6). Despite this, since 2012, screening for cervical cancer in women 65 and older has been ceased (7).

Numerous studies have evaluated the role of CPS in recognizing cervical intraepithelial lesions in the young population (1). However, studies on the importance of CPS in patients over 65 years of age are limited due to the cessation of screening under appropriate conditions (5,6). Today, women are living longer, and patients 65 and older are expected to have a longer life. As it is well known, the mortality rate decreases when cervical cancer is detected early.

In this study, in order to determine the significance of ASCs in women 65 years of age and older, we aimed to investigate the clinical and histopathologic follow-up of patients diagnosed with ASCs in CPS. We also aimed to determine the high-risk HPV (hrHPV) status of patients diagnosed with ASCs.

MATERIALS AND METHODS

The study was approved by the Ethics Committee of Ankara Bilkent City Hospital on date 26.03.25 and TABED1-25-1190 numbered board. In this study, data base of the Department of Pathology of Ankara Bilkent City Hospital between February 2019 and December 2020 were screened and patients over the age of 65 who had CPS were identified. Among the CPS samples, patients diagnosed with ASC-US and ASC-H were identified and included in the study.

The presence of hrHPV examination was also investigated, and hrHPV positive and negative patients were identified in the study group. The follow-up information of the patients with biopsy and/or CPS within 3 years after the initial CPS was analyzed. In cases with follow-up information, the results were categorized as follows:

- LSIL
- HSIL
- high-grade cervical lesion (HSIL + invasive cervical carcinoma)
- invasive cervical carcinoma (squamous cell carcinoma and/or endocervical adenocarcinoma)
- invasive gynecologic malignancy (including cervical and/or endometrial and/or ovarian carcinomas)
- benign (cases with benign histopathologic diagnosis and/or CPS diagnosis of 'negative for malignancy and intraepithelial lesions' (NMIL) within 3 years)

Statistical Analysis

The SPSS 22.0 for Windows software (SPSS, Inc.; Chicago, IL. USA) was conducted to analyse the obtained data. The normal distribution of data was assessed using histogram, q-q plot, and Shapiro-Wilk's test. Descriptive statistics were reported as number (n), percentage (%), mean ± standard deviation, and median [min-max] values. The Fisher's exact test and Pearson chi-square were employed to evaluate the categorical variables. A value of $p<0.05$ was considered statistically significant.

RESULTS

A total of 7653 were examined in the study period and among these 164 (2.1%) cases with diagnosis of ASC-US and ASC-H were

included in the study. The mean age of the patients was 70.9 (65-94).

Of the 164 patients, 151 (92.1%) were diagnosed with ASCUS and 13 (7.9%) with ASC-H (Table 1). The distribution of these diagnoses in total CPS samples in patients aged 65 years and older was as follows: ASC-US 1.97% and ASC-H 0.17%.

Table 1. General characteristics of the patients

		n (%)
CPS diagnosis		
	ASC-US	151 (92.1)
	ASC-H	13 (7.9)
hrHPV*		
	Positive	21 (19.6)
	Negative	86 (80.4)
Follow-up		
	Present	95 (57.9)
	NA	69 (42.1)
Total		164 (100)

CPS: cervical PAP smear, ASC-US: Atypical Squamous Cells of Undetermined Significance, ASC-H: Atypical Squamous Cells - HSIL cannot be excluded, NA: not-available
*hrHPV was not available in 57 patients.

Histopathologic follow-up and hrHPV status of all CPSs diagnosed as atypical:

Follow-up information was available for 95 of 164 patients. 63 (66.3%) were benign, 16 (16.8%) LSIL, 5 (5.3%) HSIL, 1 (1.1%) endocervical adenocarcinoma, 8 (8.4%) endometrial adenocarcinoma, 2 (2.1%) ovarian serous carcinoma. Follow-up data for each diagnostic group and total patient population are detailed in Table 2.

In 107 patients, hrHPV was evaluated, 21 of them were found to be hrHPV positive (19.6%), while 86 were found to be hrHPV negative (80.4%) (Table 3).

Of the 21 hrHPV-positive patients, 18 had follow-up and diagnosed as benign in 6 (33.3%), LSIL in 7 (38.9%), HSIL in 4 (22.2%), and cervical adenocarcinoma in 1 (5.6%) (total 11 intraepithelial lesions, 5 high-grade cervical lesions, 1 invasive cervix) (Table 3).

Of the 86 hrHPV-negative patients, 49 had follow-up and 40 (81.6%) were benign, 4 (8.2%) LSIL, 1 (2%) HSIL, and 4 (8.2%) endometrial carcinoma (total 5 intraepithelial lesions, 1 high-grade cervical lesion, 0 invasive cervical carcinoma, and 4 invasive gynecologic carcinoma) (Table 3)

hrHPV positive patients had a higher rate of intraepithelial lesions and high-grade cervical lesions at follow-up compared to hrHPV negative patients ($p<0.001$) (Table 3).

Follow-up information and hrHPV status of ASC-US cases:

86 of 151 ASC-US cases had follow-up, of which 60 (69.8%) were benign, 12 (13.9%) LSIL, 4 (4.7%) HSIL, 8 (9.3%) endometrial adenocarcinoma, 2 (2. 3%) were diagnosed as ovarian serous carcinoma (total 16 intraepithelial lesions, 4 high-grade cervical lesions, 0 invasive cervical carcinoma and 10 invasive gynecologic carcinomas) (Table 2).

Table 2. Follow-up results for patients with ASC in each group and in total

FOLLOW-UP	ASC-US n (%)	ASC-H n (%)	TOTAL n (%)	p values
Benign	60 (69.8)	3 (33)	63 (66.3)	
LSIL	12 (13.9)	4 (44.5)	16 (16.8)	0.028*
HSIL	4 (4.7)	1 (11.1)	5 (5.3)	0.402**
İnvasive cervical carcinoma	-	1 (11.1)	1 (10.1)	
Intraepithelial lesion (LSIL +HSIL)	16 (18.6)	5 (55.5)	21 (22.1)	0.021***
High grade cervical lesion (HSIL + invasive cervical cancer)	4 (4.7)	2 (22.2)	6 (6.3)	0.057****
Invasive gynecologic cancer (invasive cervical and/or endometrial and/or ovarian cancer)	10 (11.6)	1 (11.1)	11 (11.6)	1.000*****
Total	86/151 (57)	9/13 (69.2)	95/164	

P values according to follow-ups between ASC-US and ASC-H: Follow-ups: *Benign and LSIL, **Benign+LSIL and HSIL, ***Benign and LSIL+HSIL, ****Benign+LSIL and HSIL+invasive cervical carcinoma *****Benign and invasive gynecologic
Abbreviations: LSIL: low-grade squamous intraepithelial lesion, HSIL: high-grade squamous intraepithelial lesion, ASC-US: Atypical Squamous Cells of Undetermined Significance, ASC-H: Atypical Squamous Cells - HSIL cannot be excluded

Table 3. Follow-up information for patients with ASC in each group and in total according to hrHPV status

	hrHPV	ASC-US n/total (%)	ASC-H n/total (%)	TOTAL n/total (%)
	hrHPV positive	17 *	4 **	21/107 (19.6)
1	Benign	5 (35.7)	1 (25)	6/18 (33.3)
2	Intraepithelial lesion (LSIL +HSIL)	9 (64.3)	2 (50)	11/18 (61.1)
3	High grade cervical lesion (HSIL + invasive cervical cancer)	3 (21.4)	2 (50)	5/18 (27.8)
	hrHPV negative	**84*** **	**2**** **	**86/107 (80.4)**
1	Benign	39 (81.3)	1 (100)	40/49 (81.6)
2	Intraepithelial lesion (LSIL +HSIL)	5 (10.4)	-	5/49 (10.2)
3	High grade cervical lesion (HSIL + invasive cervical cancer)	1 (2.1)	-	1/49 (2)
	p^1	0.001	1.000	<0.001
	p^2	0.033	1.000	<0.001

*14 of 17 patients, **all the patients, ***48 of 84 patients, ****1 of 2 patients have follow-ups
p^1:comparisons of follow-ups as benign or intraepithelial lesion between hrHPV positive and hrHPV negative cases
p^2: p value for comparing the benign+LSIL and high grade cervical lesion follow-usps between hrHPV positive and hrHPV negative cases
Abbreviations: LSIL: low-grade squamous intraepithelial lesion, HSIL: high-grade squamous intraepithelial lesion, ASC-US: Atypical Squamous Cells of Undetermined Significance, ASC-H: Atypical Squamous Cells-HSIL cannot be excluded

HPV was examined in 101 (66.9%) of 151 ASCUS patients and hrHPV was found to be positive in 17 (16.8%) of these patients. 14 of the 17 hrHPV positive cases had follow-up information, of which 5 (35.7%) were diagnosed as benign, 6 (42.9%) as LSIL and 3 (21.4%) as HSIL (9 intraepithelial lesions, 3 high-grade cervical lesions, 0 invasive cervical carcinoma and 0 invasive gynecologic carcinoma). 3 cases had no follow-up information (Table 3).

Of 151 patients with ASCUS, 84 (83.2%) were found to be hrHPV negative. Of these, 48 had follow-up information, of which 39 (81.3%) were diagnosed as benign, 4 (8.3%) as LSIL, 1 (2.1%) as HSIL, and 4 (8.3%) as endometrial adenocarcinoma. (5 intraepithelial lesions, 1 high-grade cervical lesion, 0 invasive cervical carcinoma and 4 invasive gynecologic carcinoma) (Table 3). 36 patients had no follow-up information

In cases with ASC-US diagnosis, intraepithelial lesions (LSIL + HSIL) and high-grade cervical lesions (HSIL + invasive cervical carcinoma) were more common in hrHPV positive patients compared to hrHPV negative patients (p=0.001 for intraepithelial lesions and p=0.033 for high-grade cervical lesions).

Follow-up information and hrHPV status of ASC-H patients:

9 of 13 ASC-H patients had follow-up information, of which 3 (33.3%) were diagnosed as benign, 4 (44.5%) as LSIL, 1 (11.1%) as HSIL, and 1 (11.1%) as endocervical adenocarcinoma (5 intraepithelial lesions, 2 high-grade cervical lesions, 1 invasive cervical carcinoma and 1 invasive gynecologic carcinoma) (Table 2).

Of the patients diagnosed with ASC-H, 4 were hrHPV positive and 2 were hrHPV negative. In 7 cases, hrHPV was not evaluated.

Of the 4 hrHPV positive cases, 1 (25%) was diagnosed as benign, 1 (25%) as LSIL, 1 (25%) as HSIL, 1 (25%) as endocervical adenocarcinoma (2 intraepithelial lesions, 2 high-grade cervical lesions, 1 invasive cervical carcinoma and 1 invasive gynecologic carcinoma) (Table 3).

One of the 2 hrHPV-negative cases (50%) was diagnosed as benign, while no follow-up was observed in 1 case.

There was no statistically significant difference between hrHPV positive and hrHPV negative patients with intraepithelial lesions (LSIL + HSIL), high-grade cervical lesions (HSIL + invasive cervical carcinoma) in cases diagnosed with ASC-H (p>0.05).

Comparison of follow-up data of patients with ASC-US and ASC-H:

Patients with ASC-H were more likely to have LSIL and intraepithelial lesions at follow-up compared to patients with ASC-US (p=0.028 for LSIL and p=0.021 for intraepithelial lesions). However, there

Table 4. Previous diagnosis, current diagnosis, follow-up information and hrHPV status in patients with an abnormal previous smear

Previous CPS diagnosis	Current CPS diagnosis	Follow-up	hrHPV	Total number of the cases
ASC-US	ASC-US	2 BENİGN 2 LSIL 2 HSIL 4 NA	3 Positive 6 Negative 1 NA	10
ASC-H	ASC-US	1 LSIL 1 NA	1 Positive 1 Negative	2
AGC	ASC-US	2 BENİGN	2 Negative	2
LSIL	ASC-US	NA	Negative	1
HPV 16 Positive	ASC-H	BENİGN	Negative	1
				16

CPS: cervical PAP smear, NA: not-available, hrHPV: high risk-Human Papilloma Virus
ASC-US: atypical squamous cells of undermined significance, ASC-H: atypical squamous cells-HSIL cannot be exluded, AGC: atypical glandular cells LSIL: low grade squamous intraepitehlial lesion, HSIL: high grade squamous intraepithelial lesion

was no statistically significant difference between patients with ASC-US and ASC-H in terms of the detection of HSIL, high-grade cervical lesion or invasive gynecologic cancer during follow-up (p>0.05). (Table 2)

Previous CPS screening:

16 (9.5%) of 169 patients had a previous abnormal CPS diagnosis, while 153 (90.5%) did not have sufficient follow-up and negative smear results to decide to discontinue screening. Table 4 shows the previous abnormal smear diagnosis, hrHPV status and follow-up information in these patients.

DISCUSSION

The present study examined the role of ASCs in CPS test among the patients over their 65 years of age. In cases with follow-up information, 16.8% LSIL, 5.3% HSIL, 1.1% endocervical adenocarcinoma were detected following ASC diagnosis. 19.6% of 107 patients were hrHPV positive. It was observed that 38.9% LSIL, 22.2% HSIL, 5.6% cervical adenocarcinoma developed in the follow-up of hrHPV positive patients. hrHPV positive patients had a higher rate of intraepithelial lesions and high-grade cervical lesions at follow-up compared to hrHPV negative patients.

Cervical PAP testing is an effective and organized population-based screening program that has been used for decades and has significantly reduced the risk of cervical cancer (8). In our country, cervical cancer is observed as 4.7/100,000 according to the 2020 Turkey Unified Database and ranks 8th in women's cancers in Turkey (9). In the world, it ranks 4th in women according to the 2022 GLOBAN database (10).

The American Society for Colposcopy and Cervical Pathology (ASCCP) and the USPSTF advise starting cervical cancer screening at age 25 and recommends stopping screening in women over 65 years of age (11,12). There are publications showing the benefits of continuing screening beyond age 65, for women who have not been adequately screened between the ages 50-64 years (13,14). Therefore, in patients with abnormal screening results, and in whom adequate screening results cannot be documented, screening should be continued until the necessary conditions for discontinuation of screening are obtained (12). There are also results suggesting that it may be inadvisable to discontinue cervical cancer screening at 65 years of age and older, even if there are sufficient negative results (15,16). According to the United Kingdom National Health Service (NHS) cervical cancer screening data, 40% of cervical cancer cases diagnosed at the age of 65 years and older are patients in whom screening was stopped at age 65 years with adequate normal cytology results (17).

According to another UK study, women who have not been screened since the age of 50 had nearly six times the risk of developing cervical cancer at age 65 and beyond compared to those who have been adequately screened (14). As life expectancy rises and hysterectomy rates decline [5,6], it is possible that the incidence of cervical cancer in women aged 65 and older might be expected to rise even more than already seen (5). In our study, 9.8% of the patients were continued screening due to abnormal CPS results and 90.2% were continued screening due to insufficient negative screening before. There were no patients who continued screening despite adequate negative results.

ASC is used to describe cytologic alterations that are suggestive of SIL but that are not sufficiently qualitative or quantitative to be definitively interpreted as such (1). The differential diagnosis is

complicated by the fact that many nonneoplastic conditions can cause cytologic changes that warrant an ASC designation, such as inflammation, reactive/reparative or degenerative changes, air-drying with artifactual enlargerment, atrophy patterns, hormonal effects, and other artifacts. Even after a diagnostic workup, the process that led to the ASC interpretation is frequently still unclear (1). In order to use CPS as an effective screening test in laboratories, it is recommended to keep ASC rates low in the Bethesda classification and not to use this intermediate diagnostic category as a wastebasket. In this context, the diagnosis of ASC-US in a cytopathology laboratory should not be more than 5% of all CPSs and this is an important criterion for the quality control of a laboratory (18).

In different studies, the ASC accounts for about 4% of CPSs (2). In studies conducted in different centers in our country, these ratios vary between 0.8% to 3% (19-22). In our study, the total ASC rate among all CPSs was 2.1% (ASC-US 1.97%, ASC-H 0.17%). This rate is similar to both international and national studies and are consistent with the recommendations of the Bethesda system.

The last ten years have seen a shift in cervical cancer preventive strategies from primary cytology testing to HPV analysis due to the discovery that HPV is a precondition for cervical cancer (23). According to screening programs that are representative of the US population, between 40-50% of women with ASC had high-risk/oncogenic HPV infections (1). In the current study, hrHPV positivity rate was 19.6% in patients diagnosed with ASC.

Changes that are suggestive of LSIL but not sufficient for a conclusive determination as such are referred to as ASC-US. About 90% of ASC interpretations in the majority of laboratories are anticipated to be ASC-US (1,19-22). Consistent with this result, ASC-US cases constituted 92.1% of all ASC cases in our study. The qualifier “undetermined significance” is favored since roughly 10–20% of women with ASC-US turn out to have an underlying HSIL (CIN 2 or CIN 3), even though the majority of ASC-US interpretations are suggestive of LSIL (1). In studies conducted in Turkey, it was reported that 11-23% of ASC-US cases developed HSIL during follow-up (21,22,24). In our study, HSIL was detected in 4.7% of ASC-US cases, which is lower than other studies. However, this rate increases in hrHPV positive ASC-US cases and the rate of high-grade cervical lesion was found to be 21.4% in this population. High grade cervical lesion rate decreases to 2.1% in hrHPV negative ASC-US cases. The difference between these two groups is statistically significant. This finding proves the association of hrHPV-positive ASC-US cases with high-grade cervical lesions and suggests that the follow-up and treatment of hrHPV-positive ASC-US cases should be more closely.

The ASC-H category is designed for situations where cytologic alterations are indicative of HSIL but not sufficient for a conclusive diagnosis. ASC-H have a higher positive predictive value for identifying an underlying HSIL (CIN 2 or CIN 3) than ASC-US (1). Studies from Turkey reported that 8-67% of ASC-H cases developed HSIL during follow-up (21,22,24). In the current study, the rate of HSIL was 11.1% in ASC-H patients. The rate of HSIL detection in ASC-H cases was higher than in ASC-US cases, but no statistically significant difference was observed. It was thought that the lack of statistically significant difference may be due to the significantly lower number of ASC-H cases. On the other hand, in all ASC cases evaluated for hrHPV (ASC-US+ASC-H), there was a significant difference in the detection of intraepithelial lesions and high-grade cervical lesions between hrHPV positive and negative patients, with a higher rate in hrHPV positive patients. Since mimetic lesions including changes caused by atrophy are frequently observed in patients aged 65 years and older, interobserver agreement in both intermediate diagnostic categories may be low. Therefore, hrHPV evaluation after ASC diagnosis in this age group may contribute more to the detection of high-grade lesions and patient management than ASC-US or ASC-H differentiation.

Studies in the literature have reported that high-grade cervical lesions are less common in postmenopausal patients compared to premenopausal patients (25). Since our study included only patients aged 65 years and older, this comparison could not be made. Izadimood et al. found significant anomalies in 74.2% of patients over 50 years of age with ASC, when they considered ‘LSIL, HSIL, adenocarcinoma insitu, squamous cell carcinoma, adenocarcinoma, endometrial hyperplasia and endometrial adenocarcinoma’ as significant anomalies (26). In the current study, the rate of high-grade cervical lesions was 6.3% and the rate of ‘significant anomalies’ was 33.7%.

Women over 60 years of age are more likely to have uterine and ovarian cancers (27). Although the PAP smear is a screening test developed for detection of intraepithelial lesions and the early detection of cervical cancer, it can occasionally contribute to the early detection of endometrial pathologies and rarely even ovarian cancers due to the collection of shed cells. In our study, the rate of invasive gynecologic cancers, most of which were endometrial cancers, was 11.6% in the follow-up of ASC patients. The rate of endometrial cancer was higher than cervical cancer. This is due to the fact that the study population consisted of elderly patients.

The current study is a single-center study evaluating the importance of ASC diagnosis and its association with hrHPV in patients aged 65 years and older. This is a single-center study and that patients under 65 years of age were not included. These were the limiting factors in our study.

The level of knowledge and awareness of the impact of hrHPV infection on cervical cancer and the importance of CPS in screening for cervical cancer and precursor lesions is generally lower in older patients compared to younger patients. This is an important reason why these patients are not adequately screened until the age of 65. Also discomfort and pain during gynecological examination in this age group should be other common barriers toward cervical cancer secreening (28). In our study, most of the patients did not have sufficient screening that could lead to a decision to terminate screening. This suggests that in order to terminate screening in patients aged 65 years and older, there is a need for national plans to increase the participation of these patients in screening in earlier years.

CONCLUSION

Considering the efficacy of hrHPV test screening, further studies on absolute referral to hrHPV test screening in patients aged 65 years and older, would significantly contribute to the management of these patients. The planning of multicenter national studies including larger case series will help us to answer more clearly the questions of how to intervene when ASC is diagnosed in this age group, and whether to terminate or continue screening when appropriate conditions are met.

Author Contributions

AAA, TDKÖ, ŞB: methodology, data collection, analysis, writing, editing, KK, DÖT, MNÇ, EŞ, MMK, ÖBA, ZRH, OA: technical assistance, data collection, analysis, NS,FE: methodology, design, correction

Conflict of Interest

No conflict of interest was declared by the authors.

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Pregnancy outcomes in infertile patients who had hysterescopy

Histereskopi yapılan infertil hastalarda gebelik sonuçları

Hüseyin KAYAALP[1], Aydın ÖCAL[2], Fatih Mehmet FINDIK[3], Mehmet Sait İÇEN[3]

[1]Ankara Bilkent Şehir Hastanesi Kadın Hastalıkları ve Doğum Bölümü Perinatoloji Kliniği, Ankara, Türkiye
[2]Sağlık Bilimleri Üniversitesi, İstanbul Haseki Sağlık Uygulama ve Araştırma Merkezi, Cerrahi Tıp Bilimleri Bölümü, Kadın Hastalıkları ve Doğum Anabilim Dalı, İstanbul, Türkiye
[3]Dicle Üniversitesi Tıp Fakültesi, Cerrahi Tıp Bilimleri Bölümü, Kadın Hastalıkları ve Doğum Anabilim Dalı, Diyarbakır, Türkiye

ABSTRACT

Aim: To evaluate pregnancy outcomes following hysteroscopic correction in patients diagnosed with primary or secondary infertility and found to have congenital or acquired uterine pathology.

Materials and Methods: This study included 52 patients who underwent diagnostic hysteroscopy (H/S) and laparoscopy (L/S) due to primary or secondary infertility and were subsequently found to have intrauterine pathology requiring operative hysteroscopy at the Department of Obstetrics and Gynecology, Dicle University Medical Faculty, between January 2011 and December 2014. Patients were contacted via telephone numbers retrieved from hospital archives and provided verbal informed consent after receiving information about the clinical study. Data were collected regarding patients' age, gravidity, parity, number of living children, and other demographic characteristics before and after the procedure. The aim was to investigate the effects of operative hysteroscopy on pregnancy outcomes.

Results: Of the patients, 46% (n=24) were diagnosed with primary infertility (PI), and 54% (n=28) with secondary infertility (SI). No pregnancies were observed in the PI group prior to the operation, whereas 65 pregnancies were reported in the SI group. Of these, 69.23% (n=45) resulted in spontaneous abortion, 10.76% (n=7) in preterm birth, and 20% (n=13) in term delivery. The live birth rate per patient in the SI group before the operation was 53.5%. Following operative hysteroscopy, 17 pregnancies were detected in the PI group. The live birth rate per patient was 58.3%, with 11.7% (n=2) resulting in spontaneous abortion, 11.7% (n=2) in preterm birth, and 76.4% (n=13) in term birth. In the SI group, 31 pregnancies occurred postoperatively. The live birth rate per patient in this group increased to 67.8%, with 32% (n=10) resulting in spontaneous abortion, 12.9% (n=4) in preterm birth, and 54.8% (n=17) in term birth.

Conclusion: In infertile patients with congenital or acquired uterine cavity pathologies, operative hysteroscopy was associated with a decrease in spontaneous abortions and an increase in term and live births.

Keywords: Infertility, congenital uterine anomaly, hysteroscopy

ÖZ

Amaç: Primer, sekonder infertilite tanısı ile başvuran, konjenital veya edinsel uterin patoloji tespit edilen olgularda histeroskopik onarım sonrası gebelik sonuçlarının incelenmesidir.

Gereçler ve Yöntem: Bu çalışmada Ocak 2011-Aralık 2014 tarihleri arasında Dicle Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Kliniğine primer, sekonder infertilite nedeni ile diagnositik H/S ve L/S yapılıp intrauterin patoloji izlenen ve sonrasında ise operatif H/S yapılan 52 hasta değerlendirildi. Hastalara hastane arşiv kayıtlarından elde edilen telefon numaraları aranarak ulaşıldı, Yapılan klinik çalışmayla ilgili bilgi verilip sözlü onamları alındı. Hastaların operasyon öncesi ve sonrası yaş, gravide, parite, yaşayan çocuk ve diğer demografik yapılarıyla ilgili sorular soruldu. Bu çalışma ile op H/S' nin gebelik sonuçları üzerindeki etkilerini araştırmak amaçlandı.

Bulgular: Primer infertil (PI) %46'ı (n=24) idi. Sekonder infertil (SI) %54'ü (n=28) idi. PI'de gebelik izlenmedi. SI'de ise 65 gebelik izlendi. Bu gebeliklerin%69,23'ü (n=45) spontan abortustu,%10,76'sı (n=7) preterm, %20'si (n=13) term doğumdu. SI'de hasta başına düşen canlı doğum oranı %53,5'di. PI'de operasyon sonrası 17 gebelik tespit edildi. Operasyon sonrası PI'de hasta başına canlı doğum oranı %58,3'tü. Bu gebeliklerin %11,7'si (n=2) spontan abortus, %11,7'si (n=2) preterm doğum, %76,4'ü (n=13) term doğumdu. SI'de ise operasyon sonrası 31 gebelik tespit edildi. Operasyon sonrası SI'de hasta başına canlı doğum oranı %67,8'di. Bu gebeliklerin %32'si (n=10) spontan abortus, %12,9'u (n=4) preterm doğum, %54,8'i (n=17) term doğumdu.

Sonuç: Uterin kaviteye konjenital veya edinsel bir patoloji nedeni ile müdahale edilen infertil hastalarda operatif H/S sonrası hastaların spontan abortus sayıları azalırken term doğum ve canlı doğum sayısında artışlar izlendi.

Anahtar Kelimeler: İnfertilite, konjenital uterin anomali, histereskopi

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Sorumlu Yazar/Corresponding Author: Hüseyin KAYAALP, Talaytepe Mah, 4007. Sok., Kayapınar-Diyarbakır, Türkiye
E-mail: huseyinkayaalp.2121@gmail.com

Çevrimiçi Erişim/Available online at: https://dergipark.org.tr/tr/pub/jgon

INTRODUCTION

Infertility is the inability of couples to become pregnant despite full unprotected intercourse for 1 year. If the infertile woman has never been able to get pregnant before, it is called primary infertility (PI); If pregnancy occurs even once, it is called secondary infertility (SI) (1).When women who conceive spontaneously are examined, it is seen that most of them become pregnant within the first 3 years (2). As a result, infertility emerges as a health problem that affects approximately 10-15% of women (3). In the latest research conducted by the World Health Organization (WHO) in developed countries regarding these patients suffering from infertility problems, it was found that female factor was responsible for 37% of infertility, male factor was responsible for 8%, and female and male factors were responsible for 35% (4). If a woman has passed 2 years despite regular intercourse and still cannot get pregnant, the reason that prevents pregnancy should be investigated. The most prevalent causes of infertility in women are as follows: 1. Ovulatory dysfunction, 2. Endometriosis, 3. Pelvic adhesion, 4. Tubal and uterine causes (5). When we look at uterine pathologies, there are congenital uterine anomalies (septate, bicornuate, didelfus, arcuate, unicornuate) and acquired uterine anomalies (myoma, polyp, asherman, diethylstilbesterol), but congenital uterine anomalies are observed more frequently. It has been known for many years that uterine anomalies cause obstetric complications. Congenital or acquired pathologies of the uterus; It is associated with recurrent pregnancy losses, preterm birth, abnormal fetal position, dysmenorrhea and infertility (6). While the frequency of congenital anomalies, which constitute the majority of uterine anomalies, is unknown, many cases are discovered incidentally after examination, while some cannot be diagnosed because they do not cause symptoms (7). In the studies conducted so far, there are very different results regarding pregnancy outcomes after hysteroscopy in infertile patients with uterine anomalies. In this study, we investigated the effects of operative hysteroscopy on the pregnancy and live birth rates of couples in primary or secondary infertile patients with uterine pathology diagnosed in our clinic.

MATERIALS AND METHODS

In the study, patients who applied to our clinic due to primary or secondary infertility between January 2011 and December 2014, were diagnosed with uterine anomalies, and underwent operative hysteroscopy were retrospectively examined. Before starting this study, approval was obtained from our institution's human research ethics committee. The patients were informed about the clinical study and their verbal and written consent was obtained. The following variables were recorded: age, gravidity, parity, spontaneous abortion, preterm delivery, term delivery, number of living children, number of dead fetuses, comorbidities, history of surgery, intrauterine insemination (IUI)-in vitro fertilization (IVF), duration of infertility, mode of delivery, and the time elapsed between the operation and the conception of the pregnancy. The hospital electronic archive was consulted to obtain the following reports: hysterosalphngography (HSG), ultrasound, magnetic resonance imaging, laparoscopy, and hysteroscopy operation notes, as well as hormone profiles of the cases. Women with abnormal spermiograms of their husbands and those who smoked, consumed alcohol, were obese (body mass index >25), and had bilateral tubal obstruction on HSG were excluded from the study because they might have influenced the results.

All patients underwent diagnostic laparoscopy and hysteroscopy as the initial procedure. Subsequently, operative hysteroscopy was performed in patients with pathological findings. In the context of operative hysteroscopy, septum resection was performed in cases where a septum was present, polyp resection in cases where polyps were identified, and myoma resection in cases where fibroids were observed. These 52 patients were divided into 2 groups as PI and SI according to infertility status. Subsequently, the postoperative pregnancy outcomes were evaluated.

In the study, the SPSS 15 (Statistical Package for the Social Sciences) package program was used to analyze the data. The significance limit of all statistical tests used was set at 0.05. The Shapiro-Wilk test was utilized to assess normality. Parametric tests were used for data showing a normal distribution, and non-parametric tests were used for data that did not. Descriptive statistics were used for demographic descriptions.

RESULTS

The present study included 52 patients presenting at our clinic due to infertility who had undergone surgical intervention with hysteroscopy. The distribution of the patients according to infertility type was 46% (n=24) PI and 54% (n=28) SI. When all patients in our study were evaluated, the age range was 18-44, with an average age of 28.1. (p: 0.822), The preoperative follicular stimulating hormone (FSH) (p: 0.753), luteinizing hormone (LH) (p: 0.721), and estradiol (E2) (p: 0.690), levels of the patients were evaluated on the third day of the menstrual cycle. The age, duration of infertility, and hormonal values of the patients are presented in Table 1. Of the patients who underwent hysteroscopy, 73.1% were diagnosed with congenital and 26.9% with acquired uterine anomalies. A comparison of the average duration of pregnancy following surgery, stratified by type of infertility, revealed that the mean was 14.42±5.7 months for PI and 14±4.71 months for SI. There was no significant difference in the duration of pregnancy between the two groups (p = 0.987).

Table 1. Distribution of patients' ages, hormone profiles, and infertility periods

	Primary infertility Mean ± S.D. (Min – max)	Secondary infertility Mean ± S.D. (Min – max)	P value
Age	27,5 ± 6,31 (18-43)	28,78 ± 6,85 (20-44)	0.822
FSH (mIU/ml)	6,20 ± 1,84(4-9)	5,80 ± 1,98 (2-9)	0,753
LH (mIU/ml)	6,16 ± 1,78 (2-9)	5,78 ± 1,87 (2-10)	0.721
E2 (pg/ml)	45,70 ± 13 (25-82)	45,96 ± 16(19-80)	0.690
Infertility time (years)	3,81 ± 2,51 (1,5-10)	3,46 ± 1,88 (1-8)	0.987

Abbreviations: E2: estradiol, FSH: follicular stimulating hormone, LH: luteinizing hormone, Min-Max: minimum-maximum, S.D.: standart deviation

Upon examination of the pregnancy outcomes of patients who underwent operative hysteroscopy, it was observed that 14 of the patients in the PI group became pregnant, while 10 did not. In the PI group, 17 pregnancies were identified following the operation. A total of 11.7% (n=2) of the pregnancies were spontaneous abortions, 11.7% (n=2) were preterm births, and 76.4% (n=13) were term births. In a preterm patient, an intrauterine fetal demise was observed. Following the operation, live births occurred in 14 of the pregnancies. The live birth rate per patient in postoperative PI was 58.3%. Twenty-two of the patients with spontaneous intrauterine death became pregnant, while six did not. In total, 31 pregnancies were detected in patients with SI after the operation. Of these pregnancies, 32% (n=10) were spontaneous abortions, 12.9% (n=4) were preterm births, and 54.8% (n=17) were term births. Two patients exhibited intrauterine fetal demise. Live births were observed in 19 of these pregnancies. The live birth rate per patient in postoperative SI was 67.8%. Table 2 shows the number of pregnancies and live birth rates before and after the operation. Table 3 presents the pregnancy outcomes according to the uterine anomaly status of PI and SI following operative hysteroscopy. The comparison of the time between the operation and the occurrence of pregnancy in PI and SI patients is shown in figure 1.

In our study, 71% (n=37) of 52 patients exhibited a concordance between HSG and hysteroscopy, while 29% (n=15) exhibited a discordance. A frequency distribution of the patients' pregnancy

Table 2. Number of pregnancies before and after the operation, live birth rates

	Before Op H/S			After Op H/S		
	Primary İnfertility (PI) n:0 (percent)	Secondary İnfertility (SI) n:65 (percent)	Total (percent)	Primary İnfertility (PI) n:17 (percent)	Secondary İnfertility (SI) n:31 (percent)	Total (percent)
Spontaneous abortion	0	45 (%69.2)		2 (%11.7)	10 (%32.2)	
Preterm birth	0	7 (%10.8)		2 (%11.7)	4 (%12.9)	
Term birth	0	13 (%20)		13 (%76.4)	17 (%54.8)	
Live birth rate (per patient)		%53.5	%28.8	%58.3	%67.8	%63.4

Table 3. Evaluation of pregnancy outcomes according to the uterine anomaly status of PI and SI after operative hysteroscopy

	Primary İnfertility (PI)			Secondary İnfertility (SI)		
Uterine anomaly type	Spontaneous abortion	Preterm birth	Term birth	Spontaneous abortion	Preterm birth	Term birth
Septate Uterus	2	0	11	5	3	13
Bicornuate Uterus	0	0	0	1	0	3
Arcuate Uterus	0	0	0	0	1	1
Polyp	0	2	1	3	0	0
Myoma	0	0	1	1	1	0
Total	2 (%11,7)	2(%11,7)	13(%76,4)	10(%32)	5(%12,9)	17(%54,8)

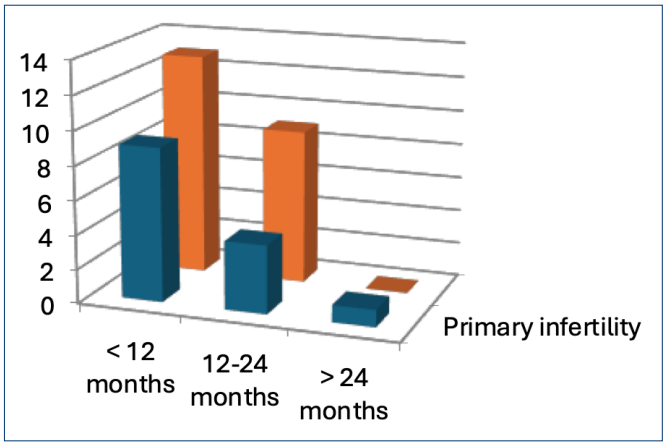

Figure 1. Frequency distribution of the time between surgery and pregnancy according to groups

times after the operation was conducted, revealing that 42% (n = 22) of the patients became pregnant in the first year, 25% (n = 13) in the second year, and 2% (n = 1) in the third year.

DISCUSSION

The objective of this study was to evaluate the cases diagnosed as PI or SI and who underwent operative hysteroscopy in our clinic. The available data in our study support the conclusion that operative hysteroscopy significantly affects pregnancy outcomes in a positive way. Our findings indicate that the occurrence of pregnancy and the course of pregnancies in the first two years after operative hysteroscopy were significantly higher in the primary and secondary infertile patient groups.

In the study conducted by Grimbizis GF et al., it was observed that the uterine septum was the most common uterine anomaly, accounting for 35% of all uterine malformations. Additionally, the bicornuate uterus and arcuate uterus were observed in 25% and 20% of cases, respectively (8). In a study conducted by Fox et al.,(9) in which 556 patients participated, the uterine anomaly rate was 17 (3.1%), with the following order of prevalence: septate, bicornuate, arcuate, unicornuate, and didelphys. In a study conducted in China, in which 21,961 pregnant women participated, the prevalence of uterine septum was 37%, followed by uterus didelphys (24%), bicornuate uterus (18%), arcuate uterus (13%), and unicornuate uterus (10%), respectively (10). In our study, the prevalence of uterine septum, bicornuate uterus, and arcuate uterus was 61.5%, 5.8%, and 5.8%, respectively. The septate uterus is the most prevalent type of uterine anomaly across studies, yet rates vary. Approximately 50% of women attempting to conceive during the reproductive age become pregnant within the first three months, 75% within the first six months, and more than 85% within the first year (2). In the study by Röyale et al., the mean interval between surgery and pregnancy was reported to be 10.8 ± 9.6 months across all groups (11). The results demonstrated that the mean duration of pregnancy in patients undergoing the procedure was 14.42 ± 5.7 months in the PI group and 14 ± 4.71 months in the SI group. Furthermore, 35 of the 36 patients who became pregnant after the operation became pregnant within the first two years. These findings indicate that, similar to fertile patients, the first two years of attempting to conceive are crucial for operated infertile patients.

A substantial body of research has been conducted to assess the impact of surgical intervention on pregnancy outcomes in women with uterine anomalies. The majority of these studies have demonstrated a positive effect of surgery on pregnancy outcomes. A review of the relevant literature revealed a significant reduction in the spontaneous abortion rate, from 86-92% preoperatively to 44.3% - 9.4% postoperatively (7, 12-14). Concurrently, the term birth rate increased from 3% - 14% to 33% - 79% (8, 12-14).

Once more, the live birth rate, which was between 3% and 4% before the operation, increased between 50% and 85.7% after the operation (8, 15, 16). In our study, the incidence of postoperative spontaneous abortion was found to decrease from 69.2% to 25%, while the term birth rate increased from 20% to 62.5%. Once more, the live birth rate following the operation increased from 53.5% to 67.8%. Once more, our findings align with those of previous studies, which have demonstrated that intervention in patients with uterine anomalies can enhance pregnancy rates. This has led to the conclusion that if uterine anomaly is detected in patients for any reason and pregnancy cannot be achieved, operative hysteroscopy is a valuable procedure in such patients and should be performed.

In a study conducted by Selçuk et al., which included a total of 181 patients diagnosed with primary and secondary infertility, the spontaneous abortion rate in PI increased from 0% to 17%, while the term birth rate increased from 0% to 61%. In SI, the rate of spontaneous abortion decreased from 96.6% to 17.1%, while the rate of term birth increased from 1.1% to 70.7%. A proportion of patients in both groups were unable to become pregnant (17). In our study, the rate of spontaneous abortion in PI increased from 0% to 11.7%, while the rate of term birth increased from 0% to 76.4%. In the SI group, the rate of spontaneous abortion decreased from 69.2% to 32%, while the rate of term birth increased from 20% to 54.8%. Nevertheless, the discrepancy in efficacy between the two groups and the fact that there were patients who were unable to become pregnant suggest that uterine anomalies are not the primary cause of infertility, but rather other factors that impede pregnancy. This discrepancy indicates that the underlying causes are multifactorial, including uterine anomalies. Furthermore, the observed increase in pregnancy rates among PI patients post-operatively is likely

attributable to a lack of awareness among these patients and their families regarding the processes involved in pregnancy. This lack of awareness is likely to have been addressed by the information provided by the researchers following the operation. In the context of uterine malformations, the low pregnancy rates can be attributed to the narrowing of the environment and the increase in intrauterine pressure. A study concluded that premature births may be caused by increased intrauterine pressure combined with relative cervical insufficiency (18). In a separate study, 556 patients, all of whom were twin pregnancies, were examined. During the follow-up period, it was observed that the patients gave birth earlier, had lower birth weights, and had a higher number of preterm births compared to twin pregnancies with normal uterine cavities (9). In our study, the number of spontaneous abortions in patients with a septum decreased from 40 to 8, while the number of term births increased from 10 to 28. The increase in the number of term births and the decrease in the number of spontaneous abortions after the operation lends support to the hypothesis that the cavity expands and intrauterine pressure decreases after the operation. Furthermore, the rise in pregnancy rates after the operation in women with uterine pathology, particularly in those who have experienced early pregnancy losses, suggests that this may be due to implantation failure caused by decreased vascularization in the septum (19). In our study, the high number of spontaneous abortions before the operation lends support to this hypothesis.

The retrospective nature of the study and the relatively small number of cases were the limitations of our study. The strength of our study is that all cases were performed by the same experienced surgical team at our hospital, which is a tertiary center, and subsequent pregnancy follow-up of the patients was performed at our clinic.

CONCLUSION

The study revealed that the number of live pregnancies increased during the follow-up period in the patients who were followed up after the operation. In light of the data obtained at the conclusion of the study, it was concluded that it is beneficial to evaluate the uterine cavity with hysteroscopy in infertile patients, even in the absence of an abnormal HSG result. Furthermore, it was determined that intervention in the uterine cavity, for any reason, positively affects pregnancy outcomes. Finally, the first two years following the operation were identified as the optimal period for couples to conceive.

Ethics Committee Approval
The study was approved by the Dicle University Faculty of Medicine Ethics Committee (date: 13.07.2016 and approval number: 2016/262).

Conflict of Interest
Authors declared no conflict of interest.

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Author Contributions
Idea/Concept: HK, FMF; Design: HK, AÖ; Supervision: FMF; Data Collection/Processing: HK, AÖ; Analysis/Interpretation: FMF, MSİ; Literature Review: FMF, MSİ; Drafting/Writing: HK, AÖ, FMF.

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ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

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Basal LH/FSH ratio and basal estradiol level in relation to oocyte and embryo quality in cases with polycystic ovary syndrome

Polikistik over sendromlu olgularda bazal LH/FSH oranı ve bazal estradiol seviyesinin oosit ve embriyo kalitesiyle ilişkisi

Aslı AKDÖNER[1], Onur YAVUZ[1], Kadir Alper MANKAN[1], Umay BALCI[1], Müge KOVALI SEZER[1], Sultan Seda DOĞAN[1], Recep Emre OKYAY[1], Erkan ÇAĞLIYAN[1], Ömer Erbil DOĞAN[1], Murat CELİLOĞLU[1], Mehmet GÜNEY[1]

[1]Dokuz Eylül Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, İzmir, Türkiye

ABSTRACT

Aim: Our aim is to investigate the effect of the basal luteinizing hormone/follicle stimulating hormone ratio and basal estradiol levels on in vitro fertilization outcomes in patients with polycystic ovary syndrome.

Materials and Methods: Cases with polycystic ovary syndrome between the ages of 18-35 were involved in the study. The characteristic features of the cases, laboratory values, total stimulation duration and dose, endometrium thickness and dominant follicle number on the ovulation trigger day, maturity and number of oocytes, quality and number of embryos, number of transferred embryos, implantation rate and clinical pregnancy rates were recorded from the hospital registry system and files. SPSS version 26.0 is used for analyzing the data.

Results: The average number of oocytes obtained from all cases was 15, MII oocyte rate was 85%, embryo number was 8 and high quality embryo rate was 66%. Oocyte and embryo number were higher in group 2 (p=0,04 ve p<0,01). No notable correlation was detected between basal estradiol levels and MII oocyte rates (r=-0.1, p=0.06). No notable correlation was detected between basal estradiol levels and good quality embryo rate (r=0.03, p=0.6).

Conclusion: In conclusion, the number of oocytes and embryos was higher in polycystic ovary syndrome cases with a basal luteinizing hormone/follicle stimulating hormone ratio ≥ 1.5. However, basal luteinizing hormone /follicle stimulating hormone ratio and basal estradiol level were not related to oocyte and embryo quality.

Keywords: Oocyte maturation, embryo quality, in vitro fertilization

ÖZ

Amaç: Amacımız, polikistik over sendromlu olgularda, bazal lüteinize edici hormon/folikül stimüle edici hormon oranı ve bazal estradiol düzeyinin, in vitro fertilizasyon sonuçları üzerine etkisinin araştırılmasıdır.

Gereçler ve Yöntem: 18-35 yaş arası, polikistik over sendromlu olgular çalışmaya dahil edilmiştir. Olguların karakteristik özellikleri, laboratuvar değerleri, total stimülasyon süresi ve dozu, ovulasyon tetikleme günü endometrium kalınlığı ve dominant folikül sayısı, elde edilen oosit maturite ve sayısı, embriyo kalite ve sayısı, transfer edilen embriyo sayısı, implantasyon oranı ve klinik gebelik oranları hastane kayıt sistemi ve dosyalarından elde edilerek kaydedilmiştir. Elde edilen veriler SPSS 26.0 versiyonu ile analiz edilmiştir.

Bulgular: Tüm olgulardan elde edilen ortalama oosit sayısı 15, MII oosit oranı %85, embriyo sayısı 8 ve iyi kalite embriyo oranı %66 olarak saptanmıştır. Oosit ve embriyo sayısının grup 2'de daha yüksek olduğu saptanmıştır (p=0,04 ve p<0,01). Bazal estradiol düzeyleri ve MII oosit oranları arasında anlamlı korelasyon saptanmamıştır (r=-0,1, p=0,06). Bazal estradiol düzeyleri ve iyi kalite embriyo oranı arasında anlamlı korelasyon saptanmamıştır (r=0,03, p=0,6).

Sonuç: Bazal lüteinize edici hormon/folikül stimüle edici hormon oranı ≥ 1,5 olan polikistik over sendromlu olgularda, oosit ve embriyo sayısının daha yüksek olduğu saptanmıştır. Bazal lüteinize edici hormon/folikül stimüle edici hormon oranı ve bazal estradiol seviyesinin oosit ve embriyo kalitesi ile ilişkili olmadığı saptanmıştır.

Anahtar Kelimeler: Oosit matürasyonu, embriyo kalitesi, in vitro fertilizasyon

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Sorumlu Yazar/Corresponding Author: Aslı AKDÖNER, Dokuz Eylül Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, İzmir, Türkiye
E-mail: drasliakdoner@gmail.com

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INTRODUCTION

Polycystic ovary syndrome (PCOS), which is one of the most widespread hormonal conditions, affects 5-10% of reproductive age women (1). The serum luteinizing hormone (LH) level and the ratio of LH to follicle stimulating hormone (FSH) are higher in women with PCOS. The LH/FSH ratio may be increased in 35-90% of patients due to the raise in the frequency and amplitude of LH pulses (1-3). Some studies have indicated that an early-onset LH peak during antagonist cycles influences the quality of oocytes and embryos, as well as clinical pregnancy outcomes. On the other hand, it has been shown that the abnormal increase during the LH peak does not affect clinical results (4-7). Therefore, there are controversial results regarding the effect of basal LH level and LH/FSH ratio on fertility (8).

In a study evaluating factors related to ovarian hyperstimulation syndrome (OHSS), it was shown that basal estradiol (E2) levels are related to the severity of OHSS and that the number of oocytes obtained in these severe OHSS cases, is higher than in other cases, but the quality of oocytes is lower (9). In addition, there are conflicting results regarding whether basal E2 levels are negatively or not associated with oocyte number and maturation. Additionally, some studies have shown that low serum basal E2 levels are associated with low clinical pregnancy rates (10-13). Therefore, there is no clear data regarding the relationship of basal E2 level with in vitro fertilization (IVF) results.

As a result, there is no sufficient data regarding the effect of LH/FSH ratio and basal E2 level on IVF results in cases with polycystic ovary syndrome. Therefore, our aim is to investigate the relationship of basal LH/FSH ratio and basal E2 level with clinical pregnancy outcomes and the embryo and oocyte number and quality in patients with PCOS who received IVF/intracytoplasmic sperm injection (ICSI) treatment with an antagonist protocol.

MATERIALS AND METHODS

Our study was carried out at Dokuz Eylül University, Department of Gynecology and Obstetrics, In Vitro Fertilization Center, between March 2024 and July 2024, after obtaining ethics committee permission with decision number 2024/07-11. Our study followed the guidelines established by the 2008 Declaration of Helsinki. Cases between the ages of 18 and 35, who had infertility due to PCOS only or due to PCOS and tubal factor, and who received IVF/ICSI treatment with an antagonist protocol and whose treatment and follow-up were performed in our center, were involved in the study. And cases over 35 years of age and with additional causes of infertility were not involved in the study. Before any treatments were administered, we received informed consent forms from all patients treated in our clinic. Age, body mass index (BMI), Ferriman Gallwey score (FGS) cause of infertility, primary/secondary infertility, basal FSH, basal LH, basal E2, basal LH/FSH ratio, thyroid stimulating hormone (TSH), prolactin (PRL), IVF cycle protocol, total recombinant FSH (rFSH) dosage, total stimulation time (days), endometrium thickness on the ovulation trigger day, number of dominant follicles on the ovulation trigger day, number and maturity of oocytes (number and rate of mature oocytes, immature oocytes, germinal vesicle (GV) oocytes, degenerated oocytes), quality and number of embryos (quality I and II), number of transferred embryos, fertilization, cleavage, implantation, and clinical pregnancy rates were recorded from the hospital registry system and files.

The cases were first divided into two groups according to the LH/FSH ratio and these groups were compared in terms of oocyte maturity and number, embryo quality and number, and clinical pregnancy rates. The LH/FSH ratio threshold value was accepted as “1.5” based on previous studies (8,14,15). Then, the cases with fresh embryo transfer were divided into two groups according to whether there was a clinical pregnancy or not, and basal E2 levels were compared between the groups. Finally, correlation analysis was performed between the mature oocyte rate, high quality embryo rate and basal E2 level.

Human menopausal gonadotropin (HMG) and/or recombinant FSH was started on the 2nd-4th day of the cycle to the cases included in the study and who did not have any obstacle to start controlled ovarian stimulation (COS) and were planned to have a fresh or frozen cycle. Gonadotropin doses were administered in the range of 150-300 units with individualized protocols. The patients were called for intermittent check-ups and dose adjustments were made. When a follicle measuring 12-14 mm was formed in the TV-USG follow-ups, gonadotropin releasing hormone (GnRH) antagonist was given until ovulation was triggered in order to prevent the LH peak. GnRH agonist and/or recombinant human chorionic gonadotropin (rec-hCG) was used to trigger ovulation. Oocyte pick-up (OPU) was performed under TV-USG guidance 34-36 hours after ovulation triggering. The oocytes were examined mechanically and chemically and then evaluated morphologically with an inverted microscope (Olympus IX70, Olympus, Vienna, Austria). Oocytes were determined according to their nuclear maturation; mature, metaphase II (MII) oocytes, immature, metaphase I (MI) oocytes, germinal vesicle (GV) oocytes and degenerating oocytes. Then, IVF/ICSI procedure was applied to the oocytes with the sperm which obtained from the patients’ partners (16).

Fertilization was determined by observing two separate pronuclei under the microscope 16–18 hours after the IVF/ICSI procedure.

Cleavage was assessed 24 hours after fertilization. Embryo evaluation was performed approximately 48–72 hours after IVF/ICSI. Embryo quality; It was calculated using modified Veeck criteria based on morphological features, including cell number, symmetry, shape of blastomeres, size of cytoplasmic fragmentations in the perivitelline space, and cleavage rate (16). Grade 1 embryo (top quality embryo); blastomeres are round and equal in size, 0% fragmentation, grade 2 embryo; blastomeres are round and equal in size, 0–25% fragmentation, grade 3 embryo; blastomeres unequal in size and 25–50% fragmentation, grade 4 embryo; blastomeres were defined as equal or unequal size and >50% fragmentation rate (17-19).

Then, to the cases planned as fresh cycles, a maximum of two embryos were transferred on the 2nd, 3rd or 5th day, depending on the quality and number of embryos, and implantation and clinical pregnancy rates were evaluated. Cases found to be β-HCG positive after transfer were considered implantation positive. Cases in which a fetus with heartbeat was observed in intrauterin cavity during ultrasound control were evaluated as clinical pregnancy positive. In cases planned as frozen cycles, embryos were cryopreserved.

Data analysis was performed using SPSS version 26.0 (IBM Inc., Chicago, IL, USA). Mann-Whitney U test is used for analyzing the not normally distributed parameters. Categorical data were assessed using the Chi-square test and Fisher's exact test. Qualitative data are expressed as numbers and percentages (%). Quantitative data of all cases are stated as median (minimum-maximum). Spearman correlation analysis was performed for correlation analysis between variables. Kolmogorov-Smirnov test is used for evaluation of normal distribution of the data. Results were assessed using a 95% confidence interval (CI). $p<0.05$ was considered significant.

RESULTS

Among our cases, 90 cases (75%) with an LH/FSH ratio of <1.5 (Group 1) were detected, while 30 cases (25%) with an LH/FSH ratio of ≥1.5 (Group 2) were detected. While the median age of all our cases was 30 (20-35), the median age of group 1 was 30 and group 2 was 29. The age difference was significant ($p = 0.02$). While 119 (99.2%) of our cases were primary infertile, one (0.8%) was secondary infertile. In terms of BMI, FGS, basal FSH, basal, E2, TSH and PRL values, no notable difference was detected. However, there was a significant difference between the basal LH values and basal LH/FSH ratios ($p<0.0001$ and $p<0.0001$), (Table 1).

The average number of oocytes obtained from all cases was 15, the MII oocyte rate was 85%, the embryo number was 8 and the good quality embryo rate was 66%. When the groups were evaluated in relation to oocyte and embryo number, it was found that the oocyte and embryo number were significantly higher in group 2 cases than in group 1 cases (n=17 vs n=13, n=10.5 vs n=7) ($p=0.04$ and $p<0.01$). No notable difference was detected in relation to the embryo quality, MII oocyte rate, immature oocyte rate, GV oocyte rate, degenerated oocyte rate, fertilization and cleavage rates. While no notable difference was found in endometrial thickness and total FSH dosage, total stimulation duration (11 days vs 10 days) and total dominant follicle number (18 vs 13.5) were significantly higher in group 2 cases ($p=0.03$ and $p=0.01$), (Table 2).

Among our cases, there are 51 cases in which fresh embryo transfer was performed. These cases were splited into groups in accordance with LH/FSH ratios (Group 1-LH/FSH <1.5–Group 2-LH/FSH ≥1.5). The groups were compared in relation to oocyte and embryo number and quality, number of transferred embryos, implantation

Table 1. Characteristic Features of the Cases and Laboratory Findings

	All Cases (n=120, 100%) Median (Min.-Max.)	Group I (LH/FSH <1,5) (n=90, 75%)	Group II (LH/FSH ≥1,5) (n=30, 25%)	p
Age	30 (20-35)	30 (21-35)	29 (20-35)	0.02
BMI (Kg/m²)	26 (18-45)	25.7 (18-45)	26.6 (18-37)	0.3
FGS	7 (3-29)	7 (3-29)	8 (3-25)	0.8
Basal FSH	6.3 (2-12.2)	6.4 (3.1-12.2)	6.1 (2-8)	0.2
Basal LH	6.1 (1.7-53)	4,7 (1,7-17,4)	12.4 (3.9-53)	<0.0001
Basal E2	52 (20-628)	53 (20-628)	46.5 (20.7-102)	0.09
Basal LH/FSH Ratio	0.9 (0.2-7.4)	0.7 (0.2-1.4)	1.9 (1.5-7.4)	<0.0001
TSH	1.7 (0.1-5.7)	1.7 (0.1-5.7)	1.8 (0.6-5.2)	0.3
PRL	12.6 (2.5-141)	12.8 (2.5-35.3)	10.6 (3.7-141)	0.5

Table 2. Evaluation of All Cases in Terms of Oocyte Number and Maturation, Embryo Number and Quality, Fertilization Rate, Cleavage Rate, Total Recombinant FSH Dosage, Total Stimulation Duration, Endometrial Thickness, Total Dominant Follicle Number and Other Hormone Levels According to Basal LH/FSH Ratios

	All Cases (n=120, 100%) Median (Min.-Max.)	Group I (LH/FSH <1,5) (n=90, 75%)	Group II (LH/FSH ≥1,5) (n=30, 25%)	P
Oocyte number	15 (2-44)	13 (3-44)	17 (2-34)	0.04
MII Oocyte Rate	85% (33.3%-100%)	83.3% (33.3%-100%)	87.8% (64.2%-100%)	0.2
Immature Oocyte Rate	0% (0%-67%)	0% (0%-67%)	0% (0%-33%)	0.09
GV Oocyte Rate	5% (0%-43%)	5.5% (0%-43%)	4.5% (0%-36%)	0.5
Degenerate Oocyte Rate	0% (0%-30%)	0% (0%-30%)	0% (0%-22%)	0.9
Fertilization Rate	75% (10 %-100 %)	72.1% (10%-100%)	77% (41%-100%)	0.2
Cleavage Rate	100% (59 %-100 %)	100% (60%-100%)	100% (59%-100%)	0.5
Embryo number	8 (1-24)	7 (1-24)	10.5 (2-17)	<0.01
Good Quality Embryo Rate	66% (0 %-100 %)	66% (0%-100%)	66% (18%-100%)	0.4
Total recombinant FSH dosage (units)	1856.25 (300-5475)	1818.75 (600-5475)	1912.50 (300-4875)	0.7
Total stimulation duration (days)	11 (3-18)	10 (4-16)	11 (3-18)	0.03
Endometrial thickness (mm)	11 (4.9-16)	11 (4.9-16)	11.1 (7.2-14)	0.9
Total dominant follicle number	15 (4-35)	13.5 (4-34)	18 (4-35)	0.01

Table 3. Evaluation of Fresh Embryo Transfer Cases in Terms of Oocyte Number and Maturation, Embryo Number and Quality, Number of Transferred Embryos, Implantation Rates and Clinical Pregnancy Rates according to Basal LH/FSH Ratios

	All Cases (n=51, 100%)	Group I (LH/FSH <1,5) (n:41, 80.4%)	Group II (LH/FSH ≥1,5) (n=10, 19.6%)	p
Oocyte number	12 (3-23)	11 (3-23)	15.5 (3-19)	0.1
MII Oocyte Rate	87.5% (33.3%-100%)	83.3% (33.3%-100%)	92.3% (66.6%-100%)	0.08
Embryo number	7 (1-15)	6 (1-15)	9.5 (2-13)	0.02
Good Quality Embryo Rate	66% (0%-100%)	66% (0%-100%)	64.5% (31%-82%)	0.5
Transferred Embryo Number	1 (1-2)	1 (1-2)	1 (1-2)	0.4
Implantation Rate	23 (45.1%)	20 (48.8%)	3 (30%)	0.2
Clinical Pregnancy Rate	21 (41.2%)	18 (43.9%)	3 (30%)	0.4

and clinical pregnancy rate. While no notable difference was found in terms of oocyte number, MII oocyte rates and good quality embryo rates, the embryo number was significantly higher in group 2 (9.5 vs. 6, p = 0.02). No significant difference was found in relation to the number of embryos transferred, implantation rate and clinical pregnancy rate (Table 3).

The cases who underwent fresh embryo transfer were splited into two groups in accordance with clinical pregnancy status and compared in terms of basal FSH, LH, E2 and basal LH/FSH ratios. No significant difference was detected (Table 4).

Correlation analysis was performed to evaluate the relationship between MII oocyte rates and good quality embryo rates with basal hormone values (FSH, LH, E2), TSH, PRL, total rFSH dose, stimulation duration and dominant follicle numbers. No notable correlation was found between basal FSH, basal LH, basal E2, PRL, TSH values with MII oocyte rates and good quality embryo rates. When total rFSH dosage, total stimulation time, and good quality embryo and MII oocyte rates were evaluated, no significant correlation was detected. While there was no significant relationship between the total dominant follicle number and the MII oocyte rate, a significant negative correlation was found

Table 4. Comparison of Basal FSH, LH, E2 Levels and Basal LH/FSH Ratios in Cases with Fresh Embryo Transfer, According to Clinical Pregnancy Status

	All Cases (n=51, 100%)	Clinical Pregnancy + (n=21, 41.2%)	Clinical Pregnancy - (n=30, 58.8%)	p
Basal FSH	6.6 (2-12.2)	6.8 (3.6-12.2)	6.6 (2-12)	0.8
Basal LH	6.1 (1.7-53)	5.5 (2.3-53)	6.3 (1.7-25)	0.4
Basal E2	55 (20-628)	54 (25-628)	56 (20-154)	0.9
Basal LH/FSH Ratio	0.9 (0.2-7.4)	0.8 (0.3-7.4)	0.9 (0.2-3.6)	0.4

Table 5. Comparison of the Relationship Between Mature Oocyte Ratio and Embryo Quality and Basal Hormone Levels, Total FSH Dosage, Total Stimulation Duration and Total Dominant Follicle Number in All Cases

	MII Oocyte Rate (r-coefficient, p value)	Good Quality Embryo Rate (r-coefficient, p value)
Basal FSH	0.03, 0.7	0.03, 0.6
Basal LH	0.1, 0.05	0.1, 0.2
Basal E2	-0.1, 0.06	0.03, 0.6
TSH	-0.02, 0.7	-0.01, 0.8
PRL	0.04, 0.6	-0.01, 0.8
Total recombinant FSH dosage (units)	0.06, 0.5	0.03, 0.7
Total stimulation duration (days)	0.003, 0.9	0.004, 0.9
Total dominant follicle number	0.07, 0.3	-0.2, 0.01

between the total dominant follicle number and the good quality embryo rate (r =-0.2, p = 0.01), (Table 5).

DISCUSSION

According to the results of our study, when all cases were evaluated, the oocyte (p=0.04) and embryo number (p<0.01) were significantly higher in cases with basal LH/FSH ratio ≥1.5. However, when the groups were evaluated in terms of embryo quality, oocyte maturation, degenerated oocyte, immature oocyte and GV oocyte rate, fertilization rate, and cleavage rate, no significant difference was found. Furthermore, an evaluation of cases involving fresh embryo transfers revealed no significant differences in implantation and clinical prenancy rates. In line with the results, we can say that there is a positive relationship between high basal LH/FSH ratio and the oocyte and embryo number, but this relationship does not have a significant effect on IVF results. When the literature was evaluated, similar to our findings, Ganor-Paz et al. found in their study that a high basal LH/FSH ratio (>1.5) did not negatively affect pregnancy outcomes (15). In another study, it was found that high basal LH and high basal LH/FSH ratio did not have negative effects on embryological data, pregnancy outcomes and clinical characteristics (20). In the research of Singh et al., no notable relationship was observed between the basal LH/FSH ratio and the number of oocytes, embryo formation and clinical pregnancy rates (8). However, another study showed that high basal LH level was associated with lower success rates (21). As a difference, in our study, the oocyte and embryo number in the group with high basal LH/FSH ratio were significantly higher. However, no notable difference was detected in relation to oocyte maturation, high quality embryo rate and clinical pregnancy rates. While in Singh et al.'s research, fertilization rates were higher in groups with low basal LH/FSH ratio and low basal LH, we found no significant difference in relation to fertilization and cleavage rates (8). Considering that anti-mullerian hormone (AMH) is highly correlated with the basal LH/FSH ratio (22), it can be said that the reason why we obtained a higher number of oocytes in the group with a higher basal LH/FSH ratio is that the ovarian reserve in these cases is higher. The negative correlation between the total dominant follicle number and good quality embryo rates can be explained in a similar way. Although a higher number of follicles and oocytes are obtained in cases with high reserve, it can be thought that the rate of high quality embryos decreases due to the increase in the severity of PCOS. However,

there are contradictory data on this subject in the publications (8, 15, 20, 21). Similarly, it was thought that the fact that the cases in the second group consisted of younger women may be due to the fact that these women preferred to seek medical treatment earlier due to more severe symptoms. However, as a limitation of our study, this parameter could not be evaluated due to insufficient data in terms of AMH values of our cases. Also, in our study, unlike the literature, we found that the total stimulation duration is longer in group 2 cases (8, 20). This situation can similarly be explained by the fact that PCOS becomes more resistant to treatment as its severity increases (23).

During each menstrual cycle, the ratio changes between LH and FSH result in varying concentrations of androgens, estrogens and progesterone. The basal LH/FSH ratio shows that the maturation of the dominant follicle continues under the influence of FSH after the selection of the dominant follicle. On the other hand, in women with PCOS who are infertile, elevated amplitude and frequency of GnRH secretion result in heightened amplitude and frequency of LH secretion. Increased LH levels trigger raised androgen secretion from ovarian follicular theca cells. At the same time, FSH stimulates the conversion of excess androgen to estrogen in granulosa cells (24,25). Insufficient aromatization of androgens produced at increased levels by high LH causes low FSH levels and inadequate ovarian E2 levels in women with PCOS. Therefore, it can be said that high basal LH/FSH rates are associated with more deterioration in follicular development (8,26). It is hypothesized that this situation may be attributed as one of the reasons for the absence of a similar effect on quality of embryo and pregnancy outcomes despite the observed higher numbers of oocytes and embryos in the group characterized by a elevated basal LH/FSH ratio in our research. This suggests oocyte number alone is not sufficient for pregnancy success and pathologies at the follicular level are also effective in IVF success in PCOS cases.

In another study, an inverse relationship was found between LH levels on the day the antagonist was started and embryo quality, while no significant correlation was found in the correlation analysis between basal LH levels and LH levels on the day of the antagonist (27). In our study, consistent with this study, we did not detect a significant relation between basal LH levels and good quality embryo rates. It is thought that elevated basal LH levels may have a negative effect on the oocyte by causing a high androgenic environment (28). However, according to our study, no significant correlation was detected between basal LH levels and mature oocyte rates.

In a study evaluating the effect of estrogen on oocytes, it was shown that adding 17β estradiol to the medium in in vitro maturation (IVM) cycles increased fertilization and cleavage rates in oocytes. It can be said that estrogen affects the quality of mature oocytes, fertilization potential and early postfertilization development (29). As a difference, in our research, we found no correlation between basal E2 levels and mature oocyte rates. Upon literature review, alongside studies supporting our findings which asserting no significant relationship between basal E2 levels and oocyte maturation, there are also publications indicates a negative correlation between the oocyte number obtained in ART cycles and elevated basal E2 levels (10-12). Additionally, contrary to studies in the literature showing that elevated basal E2 negatively affects pregnancy rates, we found no notable difference in basal E2 levels between cases with and without clinical pregnancy (11,13). In order to clarify these contradictions regarding the relationship of basal E2 level with pregnancy outcomes and its effect on the oocyte, more specific studies on the effect of E2 at the follicular level need to be planned.

The strength of our study is that it aims to investigate the relationship between basal LH/FSH ratio and oocyte maturation and embryo quality in a specific patient group. There are not many studies in the literature evaluating the effect of the basal LH/FSH ratio on oocytes and embryos, and no definitive results have been obtained on this subject. In this respect, our study makes an important contribution to the literature. In addition, recently in our clinic, the number of fresh embryo transfer cases has decreased due to the preference of total cryopreservation in PCOS cases in order to decrease the risk of OHSS. Therefore, in our study, clinical pregnancy outcomes were evaluated with fewer cases. Studies with larger samples will be able to provide more precise data.

CONCLUSION

In conclusion, in our study, it was found that the oocyte and embryo number was higher in PCOS cases with a basal LH/FSH ratio ≥ 1.5. Yet, no significant effect was detected on oocyte maturation, embryo quality and clinical pregnancy outcomes. Similarly, there was no correlation between basal E2 level and mature oocyte rate and embryo quality. Based on these results, we can say that high basal LH/FSH ratio or high basal serum E2 level does not have a negative effect on IVF results. Nevertheless, it is believed that additional studies with larger sample sizes are still required.

Author Contributions

Conception and design: Aslı Akdöner; *Acquisition of data:* Kadir Alper Mankan, Umay Balci, Aslı Akdöner, Müge Kovalı Sezer, Sultan Seda Doğan; *Drafting the manuscript:* Aslı Akdöner, Onur Yavuz; *Statistical analysis:* Onur Yavuz, Aslı Akdöner; *Critical revision of the manuscript and supervision:* Murat Celiloğlu, Recep Emre Okyay, Mehmet Güney, Ömer Erbil Doğan, Erkan Çağlıyan

Conflict of Interest
The authors declare that there is no conflict of interest.

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