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"Mother & Suckling Child"-Pablo Picasso

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Bir çalışmamızda mezuniyet sonrası yapılandırılmış eğitim programlarına olan ihtiyaç dile getirilmiştir. Bir başka çalışmada ise Çin'in Hubei bölgesinin başkenti olan Vuhan'da ortaya çıkan, tüm dünyayı etkisi altına alan COVID-19 pandemisinin maternal ve neonatal etkileri literatür bilgileri eşliğinde derlenmiştir.

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INDEX
İÇİNDEKİLER

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Original Article

Improving the educational level of gynecologic oncology nurses via dedicated workshops

Özellikli çalıştaylar ile jinekolojik onkoloji hemşirelerinin öğrenim düzeyinin arttırılması

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Abstract

Aim: To evaluate the educational level of nurses through a pre and post-test after a gynecologic oncology workshop.

Material and method: During the 'Basic and Advanced Nursing Activities in Gynecologic Oncology' workshop, pre and post-test were applied to 33 nurses. The lessons consisted of patient care before and after basic surgical procedures in gynecologic oncology; pelvic and paraaortic lymphadenectomy, radical hysterectomy, radical vulvectomy with inguinofemoral lymphadenectomy, with the additional patient care managements for bowel operations, stoma formation, chemotherapy administration, radiotherapy and brachytherapy applications. Additionally, enhanced recovery after surgery and palliative care options were also discussed. Nurses scaled their pre and post-course knowledge ranging between 1-5 points. The post-course evaluation was held at the end of the first month after the workshop.

Results: Attending nurses were from all servicing parts of the hospital irrespective of their previous experience, education level or employment in gynecologic oncology. There was a statistically significant improvement of knowledge in all aspects of the course ($p<0.05$).

Conclusion: There is a need for a structured post-graduate educational program specific for nurses, and the dedicated workshops will achieve this.

Key words: Nurse; education; gynecologic oncology; workshop; surgery

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Öz

Amaç: Jinekolojik onkoloji çalıştayı sonrası hemşirelerin öğrenim seviyelerinin ön ve son-test ile değerlendirilmesi.

Gereç ve Yöntem: 'Jinekolojik Onkolojide Temel ve İleri Hemşirelik Uygulamaları' çalıştayı sonrası toplamda 33 hemşireye ön ve son-test uygulandı. Dersler; jinekolojik onkolojide pelvik ve paraaortik lenfadenektomi, radikal histerektomi, radikal vulvektomi ile inguinofemoral lenfadenektomi gibi temel cerrahi prosedürler öncesi ve sonrası hasta bakımı; ve barsak operasyonları, stoma oluşturulması, kemoterapi, radyoterapi ve brakiterapi uygulamaları sonrası hasta bakım yönetimini içermekteydi. Ek olarak, cerrahi sonrası hızlandırılmış iyileşme ve palyatif dönem bakım seçenekleri de tartışıldı. Hemşireler, kurs öncesi bilgi düzeyini ve kurs sonrası 1. ayda bilgi düzeyini 1-5 puan arasında değerlendirdiler.

Bulgular: Kursa katılan hemşireler daha önceki tecrübe, eğitim seviyesi ve jinekolojik onkolojide çalışma durumlarından bağımsız olarak hastanenin tüm çalışma alanlarından gelmişti. Kursa ait dersler için, yapılan ön ve son test arasında bilgi durumunda istatistiksel olarak anlamlı bir artış mevcuttu ($p<0.05$).

Sonuç: Hemşirelere özgü mezuniyet sonrası yapılandırılmış eğitim programlarına ihtiyaç vardır ve bu ihtiyaç odaklanmış çalıştaylar ile karşılanabilir.

Anahtar kelimeler: Hemşire; eğitim; jinekolojik onkoloji; çalıştay; cerrahi

1. Introduction

Gynecologic oncology is a structured discipline that aims to improve the well-being of women. Gynecologic oncology fellowship is a sub-speciality training after the residency of obstetrics and gynecology in which the surgical expertise covers the procedures of radical and reconstructive abdominal surgery, gastrointestinal, genitourinary and retroperitoneal surgery beyond the basic pelvic surgeries (1). Besides, during the clinical practice, administration of chemotherapy and management of side-effects are also included in the daily job of gynecological oncologists in many clinics.

Ovaries, fallopian tubes, uterus, cervix, vagina and vulva are the main potentially malignant sites that are practised in gynecologic oncology, however, due to the tumor burden, the area included inpatient care extends, like in patients with metastases to the abdominal structures, thorax or brain. The multi-disciplinary approach and collaboration of many disciplines (radiation oncology, medical oncology, surgery, radiology, pathology) let the nurses be an integral part of patient-based management in gynecologic oncology. Nurses assist each step of patient management during the daily hospital life from the diagnosis to the active management of illness (surgery, chemotherapy and radiotherapy) and follow-up; in that perspective, clinical nursing is the cornerstone of quality in patient care. Since the nurses prepare the patient to the procedures or provide primary care in the postoperative period, or frequently communicate with the patients; specialized nurses, educated in gynecologic oncology nursing may provide comprehensive care at the inpatient and outpatient clinics (2).

The literature changes in years, so far, the concept of nurse-led assistive management should be improved through the updated scientific workshops (3). This study evaluates the pre-, and post-course educational level of nurses concerning an educational workshop focused on gynecologic oncology nursing.

2. Material and Method

In April 2018, at University of Health Sciences, Zekai Tahir Burak Woman's Health Education and Research Hospital, the workshop of 'Basic and Advanced Nursing Activities in Gynecologic Oncology' was held to improve the knowledge of nurses in the field of gynecologic oncology practice. A total of 33 nurses attended the workshop and gave informed consent for their participation. The local committee approved the study. The one-day workshop was based on theoretical lessons, video demonstrations and patient management discussions (**Table 1**). The lessons consisted of patient care before and after basic surgical procedures in gynecologic oncology; pelvic and paraaortic lymphadenectomy, radical hysterectomy, radical vulvectomy with inguinofemoral lymphadenectomy, with the additional patient care managements after bowel operations, stoma formation, chemotherapy administration, radiotherapy and brachytherapy applications. Additionally, enhanced recovery after the surgery and palliative care options were also discussed. Video demonstration of the surgical procedures and interactive discussions on the proper patient care methods were the critical points of the workshop.

Table 1. Program of the 'Basic and Advanced Nursing Activities in Gynecologic Oncology' Workshop	
Pelvic and paraaortic lymphadenectomy procedure and patient care	15m
Radical hysterectomy procedure and patient care	15m
Vulvectomy and inguino-femoral lymphadenectomy procedure and patient care	15m
Stoma formation and bowel resection-anastomosis procedure and patient care	15m
Enhanced recovery after surgery in the perspective of nurses	15m
Chemotherapy administration and patient care	15m
Radiotherapy and brachytherapy applications and patient care	15m
Hospitalization and care of patients during the terminal period	15m
Palliative care and gynecologic oncology patients	15m
Proper nutrition choices for gynecologic oncology patients	15m
Psychological support for gynecologic oncology patients	15m
Menopause and symptom control for gynecologic oncology patients	15m
'm': minutes	

The prepared pre-course and post-course questionnaires aimed to evaluate the knowledge of nurses about the topics of demonstrated surgical procedures and patient care modalities. Nurses scaled their pre-course knowledge ranging between 1 (minimum)-5 (maximum) points and the post-course knowledge at the end of the first month. The participated nurses evaluated the contribution of the workshop to their knowledge.

Statistical analyses were performed with SPSS software version 21 for Mac (SPSS, IL, Chicago). Demographic values were identified with proper analytical tests, and the Wilcoxon test was used to compare the scores of pre and post-course test. A p-value <0.05 was set as the statistically significant result.

3. Results

A total of 33 nurses participated in the questionnaire. Attending nurses were from all servicing parts of the hospital irrespective of their previous experience, education level or employment in gynecologic oncology. Most of the nurses were working at the inpatient clinic (n=27, 81.8%), with a broad experience of more than 15 years (n=22, 66.7%) and an educational level of university degree (n=27, 81.8%) (**Table 2**).

Table 2. Demographic characteristics the nurses attended the workshop		
Demographic characteristics (n=33)		**Number (%)**
Range of age (years)	18-30	5 (15.1)
	31-40	7 (21.2)
	41-50	20 (60.6)
	51-65	1 (3.1)
Level of education	High-school	3 (9.1)
	University	27 (81.8)
	Post-graduate mastery	3 (9.1)
Years of experience (years)	<5 years	2 (6.1)
	5-10 years	2 (6.1)
	11-15 years	7 (21.2)
	>15 years	22 (66.7)
Active working service	Inpatient clinic	27 (81.8)
	Outpatient clinic	4 (12.1)
	Operating theatre	2 (6.1)
Previous attendance to a nurse education workshop	Yes	22 (66.6)
	No	11 (33.4)
Previous attendance to a nurse education workshop dedicated on gynecologic oncology	Yes	13 (39.4)
	No	20 (60.6)

The level of technical knowledge about the procedures and patient care methodologies for pelvic and paraaortic lymphadenectomy, radical hysterectomy, radical vulvectomy and inguinofemoral lymphadenectomy, bowel resection-anastomosis and stoma formation were evaluated with a pre and post-test. There was a statistically significant improvement of knowledge in all aspects of the course ($p<0.05$) (**Table 3**).

Table 3. Pre-course, post-course test results (n=33)

	Pre-course		Post-course		
	Mean ± SD	Median	Mean ± SD	Median	p values
Knowledge level of pelvic and paraaortic lymphadenectomy procedure	2.97 ± 1.28	3.0	4.36 ± 0.96	5.0	**<0.001***
Knowledge level of pelvic and paraaortic lymphadenectomy patient care	3.0 ± 1.14	3.0	4.52 ± 0.71	5.0	**<0.001***
Knowledge level of radical hysterectomy procedure	3.33 ± 1.19	3.0	4.45 ± 0.75	5.0	**<0.001***
Knowledge level of radical hysterectomy patient care	3.18 ± 1.10	3.0	4.55 ± 0.75	5.0	**<0.001***
Knowledge level of vulvectomy and inguino-femoral lymphadenectomy procedure	2.88 ± 1.21	3.0	4.30 ± 0.98	5.0	**<0.001***
Knowledge level of vulvectomy and inguino-femoral lymphadenectomy patient care	2.94 ± 1.17	3.0	4.45 ± 0.79	5.0	**<0.001***
Knowledge level of stoma formation and bowel anastomosis procedure	2.97 ± 1.13	3.0	4.45 ± 0.83	5.0	**<0.001***
Knowledge level of stoma formation and bowel anastomosis patient care	2.97 ± 1.04	3.0	4.45 ± 0.83	5.0	**<0.001***

*Statistically significant

4. Discussion

Nurses represent the most critical assisting medical staff for the patient care, and with the advancing improvements in the field of medical sciences, it is clear that continuing education programs should be developed for the patient care providers. This study revealed that a well-organized educational workshop would improve the level of technical knowledge of nurses both for surgical and medical interventions and also for the patient care activities.

The reader should notice that the limited number of participants as a heterogeneous group and subjective grading of the measured topics were the shortcomings of this study. Therefore, an objective-criteria to evaluate the long-term results of improved knowledge and patient care management is needed.

The educational degree of nurses influences their vision and attitudes during working hours. The study conducted by Aiken et al. (4) revealed that the educational level of nurses is directly related to patient survival outcomes. A bachelor's degree of nurses will provide a significant survival advantage for patients, and this will enable more comprehensive care for the patients, especially in whom with complications. Within this background, this study also showed that the experience of nurses was less important than the educational degree; because there was a lack of scientific knowledge that the median pre-course knowledge degree was not higher than '3' over '5' points, which was not correlated with the experience. On the other hand, another critical issue to be emphasized for patient care is the patient to nurse ratio; whenever the ratio gets higher, the survival period of patients decreases. Blegen et al. (5) found that the working period of nurses is also proportional to the adverse outcomes, and as the number of registered nurses increases, the rate of adverse outcomes decreases dramatically. Even though that the working climate is associated with adverse patient outcomes, maintaining highly educated nurses is one of the fundamentals of patient care (6). Nevertheless, this is not feasible all the time; in that condition, one of the government policies towards quality in patient care should be an integration of educational workshops into nurses' postgraduate curriculum.

Recently, cancer is one of the leading public health problems, and researches are focusing on not only curing the cancer but also on improving the quality of life. In this respect, providing high standards of care for the patients who are suffering from cancer will be achieved by dedicated educational programs and abandoning the gaps between the patients and care providers. Integration of cancer education programs to the nursing college curriculum had started from the early 1950s in the United States (3). Standard educational programs should be improved with continuous professional education to conquer the challenges those met while servicing. In this study, we found that 33.4% of nurses had never attended a post-graduate educational workshop. During this continuous professional education, the needs of the nurses should be well-observed before organizing a structured program. Because getting the right information about the courses, access to the courses, funding and support to adjust the working days while attending the course are the

main obstacles to overcome. Langton et al. (7) evaluated the deficiencies of oncology nurse education that the technical knowledge about cancer, palliative care nursing and the communication skills were the significant requests of nurses for post-graduate education. Within this context, a national framework program will ensure a core curriculum to maintain a competency level (8). In Turkey, a well-designed and structured palliative care nursing program exists; however, for the issues of surgery, chemotherapy and radiation therapy, there is a need for technical courses in the perspective of patient care methodologies. As far as our knowledge, this workshop was the first hospital-based course in Turkey that was held to improve the knowledge of nurses in the field of gynecologic oncology.

Those educational workshops maintain a high level of knowledge and improve the skills in the light of recent literature. Edwards et al. (9) evaluated the knowledge of nurse practitioners about the hereditary colorectal cancer with pre and post-course tests, and after the course, there was a significant improvement in the knowledge of nurses. By the way, the nurses got familiar with the syndrome and gained the skills to identify the patients who are at risk for hereditary colorectal cancers. Here, we also demonstrated similar results and obtained a significant improvement in the knowledge of nurses for gynecologic oncology. Furthermore, collaboration with nurses will also customize and facilitate patient management. After the implementation of an educational program on genetic cancer risk assessment, nurse practitioners successfully managed risk assessment, triage and coordination (10). The perspective of Enhanced Recovery After Surgery (ERAS) improves postoperative patient outcomes at inpatient clinics. However, this could be achieved by a team play, and the nurses are the complementary part of this approach. The study by Wickenbergh et al. (11) showed that educational programs for the nursing staff regarding the ERAS protocols improved adherence with the ERAS principles. It should be kept in mind that special courses should be designed for nurses to improve their communication skills, so to obtain the right level harmony with the patients.

In most of the countries, nurses get a comprehensive education both theoretically and practically. However, some issues need to be improved by particular tasks. Since nurses have close contact with patients and follow their situations, especially in the inpatient wards; specific courses in the field of oncology dedicated on pain management, psychosocial care and communication will achieve the collaboration in the triangle of patient, nurse and doctor (12). While considering those parameters, the balance between the workload of nurses and nurse per patient ratio must always be preserved (13).

In conclusion, a structured post-graduate educational program which will be achieved by dedicated workshops may improve the knowledge and skills of nurses, achieve the collaboration between the nurses, doctors and patients, and consequently facilitate the patient care.

Declaration of Interest

The authors report no conflicts of interest.

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Original Article

Hepatitis B, Hepatitis C and HIV seroprevalence in pregnant women: Six years of experience

Gebelerde Hepatit B, Hepatit C ve HIV Seroprevalansı: Altı yıllık deneyim

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Abstract

Aim: To determine the seroprevalence of hepatitis B (HBV), hepatitis C (HCV), and human immunodeficiency virus (HIV) in pregnant women who presented to the pregnancy outpatient clinic at Umraniye Training and Research Hospital between January 1, 2014, and December 31, 2019, and to reveal the distribution of cases by year.

Material and method: Hepatitis B surface antigen (HBsAg), hepatitis B surface antigen-antibody (Anti-HBs), hepatitis C virus antibody (Anti-HCV), and HIV antibody (Anti-HIV) results from blood samples taken from pregnant women admitted to our hospital's pregnancy outpatient clinic were retrospectively scanned. The results of the line immunoassay validation test performed on patients with Anti-HIV reactivity were obtained from hospital records.

Results: Anti-HBs values were examined in 11,263 pregnant women, and positive results were found in 3,898 (34.61%). HBsAg values were examined in 55,639 pregnant women, with positive results in 822 (1.48%). Anti-HCV values were examined in 47,990 pregnant women, and the results were positive in 159 (0.33%). Anti-HIV values were examined in 44,107 pregnant women, and the result was found to be reactive in 40 (0.09%). HIV infection was confirmed in 5 pregnant women (0.01%). The seropositivity rates by year between 2014 and 2019 were 26.16%, 28.94%, 32.20%, 34.82%, 39.66%, and 41.73% for Anti-HBs; 1.54%, 1.52%, 1.46%, 1.53%, 1.45%, and 1.36% for HBsAg; 0.25%, 0.40%, 0.32%, 0.39%, 0.29%, and 0.32% for Anti-HCV; and 0%, 0.07%, 0.13%, 0.07%, 0.15%, and 0.17% for Anti-HIV.

Conclusion: During the antenatal period, pregnant women should be screened for HBV, HCV and HIV. Early diagnosis and treatment of HCV and HIV in pregnancy is vital to prevent long-term complications of infections and to reduce the transmission from the mother to the infant.

Key words: Antenatal screening; pregnancy; Hepatitis B virus; Hepatitis C virus; Human immunodeficiency virus

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Öz

Amaç: 01 Ocak 2014 ile 31 Aralık 2019 tarihleri arasında Ümraniye Eğitim ve Araştırma Hastanesi'nin gebe polikliniğine başvuran gebelerdeki Hepatit B (HBV), Hepatit C (HCV) ve İnsan İmmun yetmezlik Virüsü (HIV) seroprevalansını belirlemek ve yıllara göre vakaların dağılımını ortaya çıkarmaktır.

Gereç ve Yöntem: Hastanemizin gebe polikliniğine başvuran gebelerden alınan kan örneklerinden çalışılan Hepatit B yüzey antijen (HBsAg), Hepatit B yüzey antijen antikoru (Anti-HBs), Hepatit C virüs antikoru (Anti-HCV) ve HIV antikoru (Anti-HIV) sonuçları hastane kayıtlarından retrospektif olarak tarandı. Anti-HIV reaktivitesi olan hastalara yapılan Line Immunassay doğrulama testi sonuçlarına hastane kayıtlarından ulaşıldı.

Bulgular: 11,263 gebede Anti-HBs bakılmış, 3898 gebede sonuç pozitif olarak gelmiştir (%34,61), 55,639 gebede HBsAg bakılmış, 822 gebede sonuç pozitif olarak gelmiştir (%1,48), 47,990 gebede Anti-HCV bakılmış, 159 gebede (%0,33) sonuç pozitif olarak gelmiştir. 44,107 gebede Anti-HIV bakılmış, 40 gebede sonuç reaktif olarak gelmiştir (%0,09). Anti-HIV reaktif gelen 40 gebede doğrulama line immunassay yöntemi ile yapılmıştır ve 5 gebede HIV enfeksiyonu kesin olarak doğrulanmıştır (%0,01). 2014 ile 2019 yılları arasında yıllara sırası ile göre seropozitiflik oranları Anti-HBs için %26,16, %28,94, %32,20, %34,82, %39,66, %41,73; HBsAg için %1,54, %1,52, %1,46, %1,53, %1,45, %1,36; Anti-HCV için %0,25, %0,40, %0,32, %0,39, %0,29, %0,32 ve Anti-HIV için %0, %0,07, %0,13, %0,07, %0,15, %0,17 olarak tespit edilmiştir.

Sonuç: Antenatal dönemde gebeler HBV, HCV ve HIV açısından taranmalıdır. HCV ve HIV için gebelikte erken tanı ve tedavi enfeksiyonların uzun dönem komplikasyonlarının önlenmesi ve anneden bebeğe olan geçişin azaltılması için önemlidir.

Anahtar kelimeler: Antenatal tarama; gebelik; Hepatit B Virüsü; Hepatit C Virüsü; İnsan İmmun Yetmezlik Virüsü

1. Introduction

Hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) are viral agents known to cause significant health problems around the world and in our country. HBV and HCV infections may progress from active hepatitis to chronic hepatitis, to liver cirrhosis and hepatocellular carcinoma. HIV may suppress an individual's immune system, giving way to various opportunistic infectious agents that may cause illness or death.

According to the World Health Organization (WHO) records, 257 million people were living with chronic HBV infection, and 71 million people were living with chronic HCV infection in 2015. In the same year, viral hepatitis, in general, resulted in 1.34 million deaths worldwide, with 720,000 caused by cirrhosis and 470,000 by hepatocellular carcinoma (1). Besides, in 2019, 38 million people were recorded as living with HIV or acquired immunodeficiency syndrome (AIDS), and 690,000 people died of HIV-related illnesses (2).

Countries are divided into three groups in terms of the prevalence of HBV infection: high (≥8%), moderate (2%–7%), and low (<2%) endemic countries. Our country is considered to be in the middle endemic group in terms of HBV carriers. According to current data, approximately 3.3 million individuals are reported to be infected with chronic HBV (3). In our country, a routine HBV vaccination program for newborn babies began in 1998. Previously, between 70% and 90% of babies born from an HBeAg-positive pregnant woman would have been infected with HBV, and 90% of the cases of babies with hepatitis would have resulted in chronic infection. Currently, infection in 85% to 95% of newborns can be prevented with HBV vaccines and immunoglobulins, which are administered to babies born of mothers who are HBV carriers (4).

HCV infection is a significant public health problem, but most people are unaware of the ongoing infection (5). According to 2016 data of the Ministry of Health, the HCV antibody (Anti-HCV) was found in 3.8% of hemodialysis patients, 1.7% of peritoneal dialysis patients, 1.96% of patients with kidney transplantation, and 7.6% of patients with liver transplantation. As of 2013, it was estimated that 514,000 individuals were infected with HCV (3).

In our country, HIV and AIDS are included in the list of reportable diseases, and surveillance has been carried out by the relevant departments of the Ministry of Health since the first case was reported in 1985. Between 1985 and June 30, 2019, there were 20,202 HIV-positive cases and 1,786 cases of AIDS, 89 of which were in the 0-age group, whose verification test was determined and reported. There were 676 HIV-positive cases in

our country in 2011, but this number increased more than five times in 2018, with 3,678 positive cases (6). HIV infection, which is increasingly seen among women in their reproductive years, is a siginificant risk factor for the proper course of pregnancy and newborn health.

The purpose of this study was to determine the seroprevalence of HBV, HCV, and HIV in pregnant women who presented to our hospital for their pregnancy follow-up between 2014 and 2019 and to reveal the distribution of cases by year during this period.

2. Material and Method

In this study, hepatitis B surface antigen (HBsAg), hepatitis B surface antigen-antibody (Anti-HBs), hepatitis C antibody (Anti-HCV), and HIV antibody (Anti-HIV) results, sampled from pregnant women who presented to the obstetric outpatient clinic at Umraniye Training and Research Hospital in their first or second trimester between January 1, 2014, and December 31, 2019, were obtained retrospectively from the hospital records. Blood samples taken from the patients were studied using the Abbott Architect i1000SR device using the chemiluminescence microparticle immunoassay method, according to the manufacturer's recommendations. The limit value for Anti-HBs was 9.99 mIU/mL, and values of 10.0 mIU/mL and greater were considered positive. The limit value for HBsAg, Anti-HCV, and Anti-HIV was 0.99 S/CO; values of 1.00 S/CO and greater were considered positive. For reaffirmation, results that showed reactive Anti-HIV were studied twice, as were blood samples obtained from patients whose results showed reactive Anti-HIV. The blood samples were rechecked with the line immunoassay method, and HIV positivity was confirmed.

This study was reviewed by the appropriate ethics committee and was performed in accordance with the ethical standards described in an appropriate version of the 1975 Declaration of Helsinki, as revised in 2000. Administrative approval for the usage of medical data was obtained from the Umraniye Training and Research Hospital Ethics Committee (No: B.10.1.TKH.4.34.H.GP.0.01/250).

Statistical Analysis

The data were analyzed using SPSS 25.0 (IBM Corp., Armonk, NY). While evaluating the study data, frequency values and percentage distributions of these values were calculated as the descriptive statistics.

3. Results

During these six years, Anti-HBs values were examined in a total of 11,263 pregnant women, and the results were positive in 3,898 patients (34.61%). Anti-HBs seropositivity rates by year from 2014 to 2019 were determined as 26.16%, 28.94%, 32.20%, 34.82%, 39.66%, and 41.73% (**Table 1)**. HBsAg was examined in 55,639 pregnant women, and the results were positive in 822 (1.48%). HBsAg seropositivity rates by year from 2014 to 2019 were determined as 1.54%, 1.52%, 1.46%, 1.53%, 1.45%, and 1.48% (**Table 2**). Anti-HCV was examined in 47,990 pregnant women, and the results were positive in 159 (0.33%). Anti-HCV seropositivity rates by year from 2014 to 2019 were determined as 0.25%, 0.40%, 0.32%, 0.39%, 0.29%, and 0.32% (**Table 3**). Anti-HIV was examined in 44,107 pregnant women, and the results were reactive in 40 (0.09%). Confirmation of Anti-HIV results which were found to be reactive in 40 pregnant women, was made using the line immunoassay method, and HIV infection was confirmed in 5 pregnant women (0.01%) (**Table 4**).

Table 1. Distribution of Anti-HBs results by years in pregnant women admitted to our hospital

	Anti-HBs Positive		Anti-HBs Negative		Total
Years	Number	Rate (%)	Number	Rate (%)	Number
2014	231	26.16	652	73.84	883
2015	531	28.94	1,304	71.06	1,835
2016	757	32.20	1,594	67.80	2,351
2017	788	34.82	1,475	65.18	2,263
2018	945	39.66	1,438	60.34	2,383
2019	646	41.73	902	58.27	1,548
Total	3,898	34.61	7,365	65.39	11,263

Table 2. Distribution of HBsAg results by years in pregnant women admitted to our hospital

	HBsAg Positive		HBsAg Negative		Total
Years	Number	Rate (%)	Number	Rate (%)	Number
2014	98	1.54	6,258	98.46	6,356
2015	131	1.52	8,498	98.48	8,629
2016	159	1.46	10,710	98.54	10,869
2017	173	1.53	11,117	98.47	11,290
2018	148	1.45	10,049	98.55	10,197
2019	113	1.36	8,185	98.64	8,298
Total	822	1.48	54,817	98.52	55,639

Table 3. Distribution of Anti-HCV results by years in pregnant women admitted to our hospital

	Anti-HCV Positive		Anti-HCV Negative		Total
Years	Number	Rate (%)	Number	Rate (%)	Number
2014	14	0.25	5,542	99.75	5,556
2015	31	0.40	7,708	99.60	7,739
2016	33	0.32	10,442	99.68	10,475
2017	34	0.39	8,663	99.61	8,697
2018	24	0.29	8,264	99.71	8,288
2019	23	0.32	7,212	99.68	7,235
Total	159	0.33	47,831	99.67	47,990

Table 4. Distribution of Anti-HIV results by years in pregnant women admitted to our hospital

	Anti HIV Reactive		Line Immunoassay Positive		Anti HIV Negative		Total
Years	Number	Rate (%)	Number	Rate (%)	Number	Rate (%)	Number
2014	0	0	0	0	8,274	100.00	8,274
2015	6	0.07	2	0.02	8,772	99.93	8,778
2016	8	0.13	0	0	6,276	99.87	6,284
2017	5	0.07	1	0.01	7,625	99.93	7,630
2018	11	0.15	2	0.03	7,146	99.85	7,157
2019	10	0.17	0	0	5,974	99.83	5,984
Total	40	0.09	5	0.01	44,067	99.91	44,107

4. Discussion

Both acute and chronic HBV infections in pregnancy are similar to those in the general adult population. HBV infection during pregnancy does not increase the maternal mortality rate and does not cause a teratogenic effect in the fetus (7). It is known that HBV can infect all types of cells in the placenta (decidual, trophoblastic, villous mesenchymal, and villous capillary endothelial cells). Maternal HBeAg-positive serological status, along with a high viral load, is the leading risk factor regarding the occurrence of HBV intrauterine infection (8).

Particularly in regions with high endemicity in terms of HBV, those with chronic infections acquire the infection during the perinatal or early childhood period (7). Our country has been reported as a moderately endemic country in terms of HBV; HBsAg seropositivity has been reported between 1.2% and 5.7% in studies among pregnant women (9, 10). Owing to the region where our hospital is located, our facility serves a population with low socioeconomic status, particularly refugees from Syria. In our study, we found that the HBsAg seropositivity among pregnant women was 1.54%, 1.52%, 1.46%, 1.53%, 1.45%, and 1.36% for the years from 2014 to 2019. During these six years, a total of 55,639 pregnant women were tested for HBsAg in the pregnancy outpatient clinic of our hospital. HbsAg positivity was found in 822 pregnant women, and HBsAg seropositivity was determined to be 1.48% overall.

The detection of women who are not immune to HBV before pregnancy and the administration of HBV vaccines is essential for preventive healthcare. Meanwhile, antenatal screening is vital in terms of detecting HBsAg-positive pregnant women, determining viral load, and determining antiviral treatments. Antiviral therapy with nucleoside reverse transcriptase inhibitors starting between 28 and 32 weeks of gestational age is recommended to reduce the risk of HBV perinatal transmission among HBsAg-positive pregnant women with an HBV deoxyribonucleic acid level of greater than 106 copies/mL (11). Besides, as soon as HBsAg-positive mothers are identified, their babies should receive passive and active immunoprophylaxis at birth to reduce vertical HBV transmission. The combination of hepatitis B immune globulin and HBV immunization, given within 12 hours of birth, has effectively reduced the rate of perinatal transmission from greater than 90% to less than 10%. Despite appropriate neonatal postexposure prophylaxis, however, perinatal transmission still occurs in approximately 2% of infants. Most of these cases occur in HBeAg-positive women with very high viral loads (12).

When invasive prenatal diagnostic testing is required for HBsAg-positive pregnant women, it is crucial to avoid a transplacental approach. The rate of neonatal HBV infection induced by amniocentesis may range up to 1.4% in newborns born of mothers positive for HBsAg, and 16% for hepatitis B e-antigen (13). In two meta-analysis studies that compared elective cesarean delivery with vaginal delivery in terms of the prevention of mother-to-child transmission (MTCT) at birth, it was determined that elective cesarean section significantly reduced the rate of maternal transmission of HBV (14, 15). In contrast, according to another meta-analysis published in 2019, vaginal delivery did not increase the MTCT incidence after immunoprophylaxis at six months or more, and the existing evidence does not support the conclusion that cesarean section can prevent MTCT in HBsAg-positive mothers after immunoprophylaxis (16). Cesarean delivery should not be performed only to prevent perinatal transmission, as the benefits have not been established in well-conducted controlled trials (12). Even though HBV DNA can be detected in breast milk, breastfeeding does not pose an additional risk of HBV infection. Mothers with chronic HBV infection who wish to breastfeed should be encouraged to do so (17). In our hospital, unless there is an obstetric indication, we do not encourage pregnant women who are HBV carriers to deliver by cesarean to avoid MTCT.

In studies conducted in various regions of our country, Anti-HBs seroprevalence has been reported between 3.7% and 45.8% in pregnant women (18-20). In this study, Anti-HBs was evaluated in a total of 11,263 pregnant women who presented to the pregnancy outpatient clinic of our hospital in a-six year period. Anti-Hbs was detected as seropositive in 3,898 of these pregnant women (34.61%). Between 2014 and 2019, we determined the

Anti-HBs seroprevalence by year to be 26.16%, 28.94%, 32.20%, 34.82%, 39.66%, and 41.73% (**Table 1**). The increase in Anti-HBs seroprevalence and the tendency of HBsAg seroprevalence to decrease over the years may indicate that the HBV vaccine is effective in preventing disease (**Figure 1**).

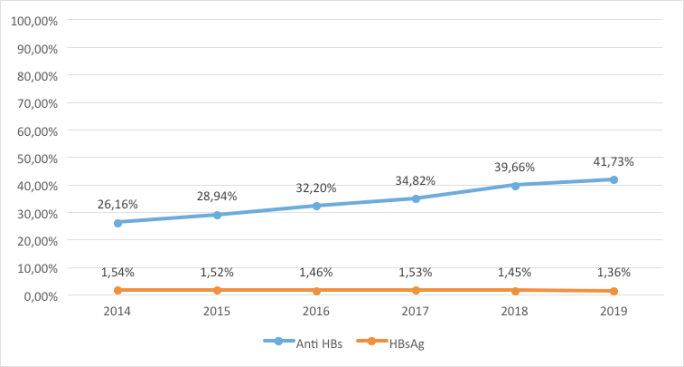

Figure 1. Distribution of Anti-Hbs and HBsAg seropositivity by years.

As many as 8% of pregnant women are known to be infected with HCV worldwide (21). Maternal well-being, MTCT, and the impact of maternal infection on pregnancy outcomes are the primary considerations regarding pregnancies with HCV infection. It has been reported that maternal HCV infection has been significantly associated with fetal growth restriction and low birthweight (22). The standard test used for HCV screening during pregnancy is Anti-HCV. Anti-HCV antibodies usually develop within 2 to 6 months after exposure. Therefore, even if the result in the first trimester is negative in pregnant women who are at risk for HCV, it is recommended that the test for Anti-HCV be conducted again in the later months of pregnancy (21). Anti-HCV was evaluated in 47,990 pregnant women in our outpatient clinic between 2014 and 2019, and the seropositivity was found in 159 patients (0.33%). The distribution of Anti-HCV seropositivity by years is shown in **Figure 2.** Other studies conducted in Turkey show Anti-HCV seropositivity rates ranging between 0.1% and 1.1% (10, 18-20, 23).

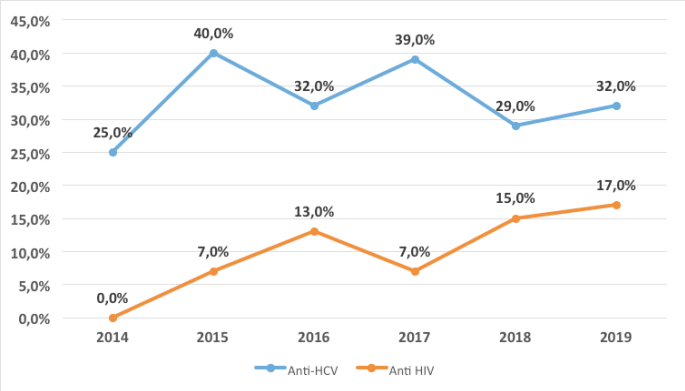

Figure 2. Distribution of Anti-HCV seropozitivity and Anti-HIV reactivity by years.

When an active HCV infection is confirmed in a pregnant woman, a quantitative HCV ribonucleic acid test should be performed to determine the baseline viral load. The risk of vertical transmission of HCV is 5.8% in women with chronic HCV infection who are HIV-negative, whereas the rate increases to 10.8% in HIV-positive women. The increased risk of vertical transmission in HIV-positive pregnant women may be the result of increased HCV viral load, issued by HIV-mediated immunosuppression (21). Should an invasive prenatal diagnostic testing be requested, amniocentesis is recommended rather than chorionic villus sampling. Amniocentesis does not appear to increase the risk of vertical transmission in Anti-HCV-positive pregnant women (13).

Studies have shown that there is no difference between vaginal birth and cesarean birth in terms of vertical transmission of HCV. It is recommended that obstetricians should avoid internal fetal monitoring, prolonged rupture of membranes, and episiotomy in managing labour in HCV-positive women. It has been stated that breastfeeding is safe in women with HCV infection. However, women should abstain from breastfeeding if there is preexisting nipple bleeding or cracked nipples (21). In our hospital, unless there is an obstetric indication, we do not encourage cesarean delivery for pregnant women who are HCV carriers only to avoid MTCT.

In our country, a total of 89 HIV-positive case reports were found in the 0-age group, whose validation test was determined between 1985 and 2019 (6). In most of these cases, HIV transmission occurred as MTCT. MTCT of HIV can occur during pregnancy, labour, delivery, or breastfeeding. A large prospective cohort study demonstrated that effective interventions such as performing antiretroviral therapies during pregnancy, planned pre-labor cesarean sections, and avoidance of breastfeeding would reduce the risk of MTCT of HIV from 20% to 1% (24). In light of such findings, it is feasible that antenatal screening for HIV is the proper course of action regarding the prevention of MTCT of HIV.

In a study conducted in Ankara, in 2007 by Madendağ et al. (4) to determine the Anti-HIV seropositivity in pregnant women, the authors detected Anti-HIV reactivity in 3 out of 60,562 pregnant women (0.004%). However, in 2017, a study conducted by Altuğlu et al (25), the authors detected Anti-HIV reactivity in 12 (0.1%) out of 8,803 pregnant women. In the current study, Anti-HIV was evaluated in 44,107 pregnant women between 2014 and 2019, with reactive Anti-HIV detected in 40 patients (0.09%). The distribution of Anti-HIV reactivity by year is shown in **Figure 2**. Forty patients with Anti-HIV reactivity were validated using the line immunoassay method, and only five patients had a positive result (0.01%). At our hospital, the Anti-HIV test is studied using the chemiluminescence microparticle immunoassay method. However, in Anti-HIV testing techniques,

some non-HIV-related proteins may be identified as HIV-specific antibodies, potentially leading to false-positive results. As a matter of fact, in our study, 35 of the 40 patients, whose Anti-HIV were found reactive, were also found to be false-positive. Particularly in societies where HIV prevalence is low, such as our country, false-positivities are one of the most common problems encountered concerning the identification of new HIV cases. It has been reported that pregnancy itself, or infections such as malaria, schistosomiasis, and human African trypanosomiasis, along with vaccines such as influenza, viral hepatitis, and rabies may be the cause of Anti-HIV false-positivity (26). Short confirmation of the newly detected Anti-HIV positivity in the near-term period may also prevent the newborn from receiving antiretroviral drug prophylaxis in vain.

If an invasive prenatal diagnostic testing is requested, amniocentesis in women infected with HIV under the antiretroviral therapy does not appear to significantly increase the risk of MTCT, mostly if the viral load is found to be undetectable. However, concerning women who are not taking antiretroviral therapy, the risk of MTCT has been found to increase with the performance of amniocentesis (13). In non-breastfeeding populations, the majority of MTCT of HIV occurs during late pregnancy and the intrapartum period. This issue indicates that appropriate intrapartum obstetric care is vital in HIV-positive pregnancies. In a randomized controlled trial, published in 1999, the MTCT rate for HIV was reported as 1.8% far planned cesarean section and 10.5% for vaginal delivery (27). Also, the level of maternal viral load at delivery was determined to be a primary factor in MTCT. Although cesarean section remains an essential strategy for those with untreated or poorly controlled HIV, vaginal delivery is now the recommended mode of delivery, as there is no obstetric indication for cesarean section concerning women with a viral load of fewer than 50 copies/mL (28). Concerning the breastfeeding of HIV-positive mothers, and considering the WHO guideline updated in 2016, it is recommended that mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer while being fully supported with anti-retroviral therapy adherence (29).

There were some limitations in the current single-center, the retrospectively designed study that should be noted. First, the inability of knowing the HBV vaccination status in pregnant women, the impossibility of distinguishing whether Anti-HBs positivity is the result of vaccination or a natural immune result obtained as a result of HBV infection, and the inability of knowing the immune status of babies born to pregnant women with positive HBsAg, Anti-HCV, and HIV verification results. Another limitation of our study is that the numbers of pregnant women examined for HBsAg, Anti-HBs, Anti-HCV, and Anti-HIV, respectively, was different. Although HBsAg is routinely requested from pregnant women who present to our hospital for pregnancy in the first or second trimester with the recommendation of the Ministry of Health, other examinations are requested by experts in the outpatient clinic.

In conclusion, pregnant women who present to the pregnancy outpatient clinic for antenatal care should be screened for HBV, HCV and HIV. For HCV and HIV, for which there is no vaccination, early diagnosis and taking necessary precautions during pregnancy is essential.

Declaration of Interest

The authors report no conflicts of interest.

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Türk Kadın Sağlığı ve Neonatoloji Dergisi

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Derleme

COVID-19 pandemisinin maternal-neonatal etkileri ve yönetimi

Maternal-neonatal effects and management of COVID-19 pandemic

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Öz

Coronavirüs hastalığı, SARS-Cov-2 virüsünün neden olduğu solunum yolu hastalığıdır. İnsanlar arasında hızlı bir yayılım gösteren bu virüs pandemi olarak ilan edilmiştir ve tüm dünya sağlığını tehdit etmektedir. Damlacık yolu ve kontamine yüzeyler ile temas sonrası bulaşabilen virüs riskli gruplarda ölümcül olabilmektedir. Bu nedenle gebeler ve yenidoğanlar üzerinde hassasiyetle durulması gereken gruplardandır. Gebelikte ortaya çıkan anatomik ve fizyolojik değişiklikler, yenidoğanın immatür olması COVID-19 pandemisinin ele alınmasını önemli hale getirmiştir. COVID-19 pozitif olan gebelerin intrapartum ve postpartum dönemde yakın izlemi ve koruyucu ekipmanlar ile doğumun gerçekleştirilmesi gerekmektedir. İntrapartum dönemde mutlaka elektronik fetal monitörizasyon izlemi yapılmalıdır. Kullanılan tüm ekipmanların dezenfeksiyonu, en az sayıda sağlık ekibi ile doğumun gerçekleştirilmesi ve multidisipliner bir yaklaşım ile sürecin yönetilmesi gerekmektedir. Ayrıca yenidoğanın ilk bulguları ve APGAR skoru yakından izlenmeli, enfekte anne ile bebeği arasındaki mesafenin korunmasına özen gösterilmelidir. Yenidoğanın resüsitasyon ihtiyacı belirlenmeli, COVID-19 semptomları incelenmeli ve yoğun bakıma transferine karar verilmelidir. Transfer sırasında kullanılan ekipmanların dezenfeksiyonuna özen gösterilmelidir. Yoğun bakımda izlenen bebeklerin, anne ile birlikte negatif basınçlı odada izole edilmesi önerilmektedir. COVID-19'un emzirmeye engel olmadığı, koruyucu önlemler altında emzirmenin en erken sürede başlatılması gerektiği belirtilmektedir. Taburcu edilen olguların on dört gün izlenmesi önerilmektedir. Virüsün maternal ve neonatal etkileri göz önüne alınarak etkili biçimde yönetilmesi gerekmektedir.

Anahtar kelimeler: COVID-19; pandemi; maternal etkileri; maternal yönetimi; neonatal etkileri; neonatal yönetimi; emzirme; izolasyon.

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Abstract

Coronavirus disease is a respiratory disease caused by the SARS-Cov-2 virus. Rapidly spreading among people, this virus has been declared as a pandemic and threatens the health of the whole world. The virus that can be transmitted by droplets and after contact with contaminated surfaces can be fatal in risk groups. For this reason, pregnant women and newborns are among the groups that should be emphasized sensitively. The anatomical and physiological changes that occur during pregnancy and the immature of the newborn have made it essential to handle the COVID-19 pandemic. Pregnant women who are COVID-19 positive should be monitored closely during the intrapartum and postpartum period, and delivery should be performed with protective equipment. Electronic fetal monitoring must be performed during the intrapartum period. Disinfection of all the equipment used, delivery with the least number of healthcare teams and the process should be managed with a multidisciplinary approach. Besides, the first signs of the newborn and the APGAR score should be closely monitored, and care should be taken to maintain the distance between the infected mother and her baby. The need for resuscitation of the newborn should be determined, the symptoms of COVID-19 should be examined, and its transfer to intensive care should be decided. Care should be taken to disinfect the equipment used during the transfer. It is recommended that babies monitored in intensive care are isolated in a negative pressure room together with the mother. It is stated that COVID-19 does not prevent breastfeeding and breastfeeding should be started as soon as possible under protective measures. It is recommended to monitor the discharged cases for fourteen days. The virus needs to be managed effectively, taking into account maternal and neonatal effects.

Key words: COVID-19; pandemic; maternal effects; maternal management; neonatal effects; neonatal management; breastfeeding; isolation

1. Giriş

Coronavirüs hastalığı, hayvanları ve insanları enfekte edebilen, insandan insana yayılım gösterebilen bir solunum yolu hastalığıdır (1, 2). İnsan coronavirüsleri, soğuk algınlığı benzeri hafif semptomlar gösterirken, SARS (Severe Acute Respiratory Syndrome) ve MERS (Middle East Respiratory Syndrome) gibi virüs türevleri daha ağır seyredebilmektedir (1). COVID-19'a neden olan SARS-Cov-2 virüsü ise ilk olarak Çin'de ortaya çıkmış ve hızlı bir yayılım göstererek tüm dünyayı etkilemiştir. COVID-19 ile enfekte kişilerin öksürmesi veya hapşırması ile oluşan damlacıkların insandan insana bulaşması ile yayılım gerçekleşmektedir (2).

COVID-19 virüsü asemptomatik seyredebildiği gibi şiddetli akut solunum yolu semptomlarına yol açabilmektedir (3). Semptomlar arasında sıklıkla ateş, kuru öksürük, nefes almada güçlük ve nefes darlığı yer almaktadır. Bazı vakalarda daha az olmakla birlikte konjonktivit, yorgunluk, baş ağrısı, bulantı/kusma ve diyare gibi semptomlar görülebilmektedir (3, 4). Şiddetli seyreden vakalarda ise pnömoni, akciğer yetmezliği ve ölüm görüldüğü belirtilmektedir (1, 2). Hastalığa ilişkin semptomların ortaya çıkışı, virüse maruziyetten sonraki 2-14 günü kapsamaktadır (2, 5).

Tüm yaş grupları COVID-19 açısından risk altında olmasına rağmen bazı gruplar yüksek riskli olarak kabul edilmektedir. Özellikle ileri yaşta olanlar ve kronik hastalığı bulunanlar (diyabetes mellitus, hipertansiyon, HIV, kalp hastalıkları vb.) riskli gruplardır (4, 6). Dünya Sağlık Örgütü (DSÖ) ve UNFPA (Birleşmiş Milletler Nüfus Fonu) bu gruplar dışında, gebelerin veya doğum yapan kadınların COVID-19 enfeksiyonu açısından yüksek risk grubunda olmadıklarını belirtmektedir. Ancak gebelik döneminde ve postpartum dönemde meydana gelen fizyolojik değişiklikler nedeniyle (bağışıklık, oksijen ihtiyacında artış vb.) komplikasyon riski artmaktadır. Anatomik değişiklikler, torasik kavitedeki değişiklikler ve diyaframın yükselmesi hipoksiye olan maternal toleransı azaltmaktadır (4, 6, 7). Bu nedenle maternal açıdan gebelik, doğum ve doğum sonu döneme ilişkin hassasiyet gösterilmesi ve pandemi açısından gerekli önlemlerin alınması önemlidir (6-8). COVID-19'un vertikal geçişine ve konjenital enfeksiyona yol açtığına ilişkin verilerin kısıtlı olduğu belirtilmektedir (9-12). Fetüsün ve yenidoğanın COVID-19 enfeksiyonuna karşı duyarlı olduğunu gösteren veriler sınırlıdır. Ancak doğuştan gelen bağışıklık fonksiyonlarının immatür olması bu grubu enfeksiyona karşı duyarlı hale getirmektedir (7, 10). Bu nedenle maternal-neonatal değerlendirme, fetüs ve yenidoğana yönelik önlemlerin alınması ve bölümler arasında entegre bir yaklaşımın benimsenmesi önemlidir (6, 13, 14). Sağlık

ekibinin konu ile ilgili güncel bilgiye ve önerilere erişebilmesi enfeksiyon ile mücadelede etkili olacaktır. Bu nedenle COVID-19'un maternal ve neonatal açıdan etkilerinin belirlenmesi ve yönetilebilmesi amacıyla literatür bilgileri derlenmiştir.

2. COVID-19'un Maternal Etkileri

Gebelikte COVID-19 enfeksiyonu ile ilgili sınırlı sayıda vaka olduğu ve bunların büyük bölümünün ciddi bir komplikasyon olmadan taburcu edildiği belirtilmektedir (9, 15). Yapılan bir sistematik incelemede 108 gebenin yer aldığı vakalara yer verilmiştir. Bu gebelerin yaş ortalaması 29-32 ve büyük bölümünün üçüncü trimesterde olduğu belirlenmiştir. Erken gebelik haftasında başvuran gebeler komplikasyon olmadan taburcu edilmiştir. Preeklampsi, gestasyonel diyabet, hipotroidi ve plasental problemler gibi komorbiditeler nedeniyle hastaneye başvuran gebeler olduğu belirtilmiştir. Olguların %92'si sezaryen doğum ile sonuçlanmış ve endikasyon olarak büyük ölçüde fetal distres gösterilmiştir (7). Maternal pnömoni ile ilişkili olarak erken membran rüptürü, preterm eylem ve intrauterin fetal ölüm görülebildiği belirtilmektedir (16). Dokuz gebelik bir olgu serisinde dört hastanın preterm eylem gerçekleştirdiği ifade edilmiştir (17).

COVID-19 enfekte gebelerde sıklıkla yüksek ateş ve kuru öksürük klinik belirti olarak ortaya çıkmaktadır. Bunların yanı sıra halsizlik, dispne ve diyare diğer belirtilerdendir (7). Çin'de dokuz gebenin yer aldığı çalışmada dört kişide öksürük, üçünde miyalji, ikisinde boğaz ağrısı ve halsizlik belirtileri görülmüştür. Ayrıca üç hastada aminotransferaz konsantrasyonunda artış, beş hastada lenfositopeni olduğu belirlenmiştir (17). Ayrıca bazı olgularda yüksek C-reaktif protein konsantrasyonu görülmüştür (7, 17).

Gebelik olgularının yer aldığı bir derlemede üç gebenin yoğun bakım ünitesine alındığı ancak hiç ölüm gerçekleşmediği ifade edilmektedir (7). Yine İran ve Çin'i kapsayan, COVID-19 ile enfekte otuz bir gebenin yer aldığı bir sistematik incelemede iki annenin solunum komplikasyonlarına bağlı olarak öldüğü belirtilmektedir (16). Çin'de dokuz olgunun yer aldığı çalışmada hiç pnömoni ve ölüm olmadığı, tümünün canlı doğum gerçekleştirdikleri belirtilmiştir (17).

COVID-19'un klinik bulguları ve maternal etkileri göz önüne alındığında intrapartum ve postpartum dönemin etkili biçimde yönetilmesi büyük önem kazanmaktadır.

3. İntrapartum ve Postpartum Dönem ve Yönetimi

COVID-19'un gebeler üzerine olan yönetimi MERS veya SARS'ın etkileri ile kıyaslanarak ya da şu an mevcut veriler ışığında enfekte ancak gebe olmayan birine benzer klinik tablo göstermesi üzerine kurulu yaklaşımlar şeklindedir. Fakat gebelik sürecindeki değişimler doğrultusunda daha multidisipliner bir yaklaşım izlenmesi önerilmektedir (6-8,18).

3.1. *İntrapartum dönemde yönetim:* COVID-19 gibi pandemi boyutuna ulaşan enfeksiyon hastalıklarında öncelik tedaviden çok, korunma olması nedeniyle sağlık personeli, gebe ve yenidoğanın koruyucu önlemleri alınmalıdır. Bu konuda sağlık kuruluşlarında genelde poliklinik ve acil servis başvurularında uygulanan triajın, doğumhane gebe kabulünde de yapılması önerilmektedir. Gebenin semptomlarından şüphelenildiği durumlarda mümkünse negatif basınçlı bir odada izole edilmesi önerilmektedir. Bunun mümkün olmadığı durumlarda tek başına izlem yapmaya elverişli bir odada, doğumhaneye kabul edilmeden önce triaj yapılmalıdır (19). COVID-19 pozitif gebenin takibi ve doğumu mümkünse negatif basınçlı odalarda, değilse izole etmeyi sağlayan tek kişilik odalarda gerçekleştirilmelidir. Sağlık personeli triajın yapılamadığı acil olgularda; gebenin temaslı, olası pozitif hasta olup olmadığına bakmaksızın maske, gözlük, önlük, eldiven, siperlik gibi kişisel koruyucu ekipmanları eksiksiz kullanmalıdır. Aerosol bulaşın en sık bulaş yolu olduğu düşünüldüğünde gebenin maske kullanması, tanılı hastalarda ise personelin N95 maske kullanması önerilmektedir (20). COVID-19 virüsünün bazı yüzeylerde 24-72 saat yaşayabildiğini gösteren bulgular nedeniyle, özellikle gebe ile teması olan tıbbı cihazların ve yüzeylerin hijyenine özen gösterilmelidir (21). COVID-19 tanısı almış gebelerin doğum eylemi sırasında yapılacak takibinde, yönetimi etkileyecek en önemli parametrelerden biri maternal hipoksidir. Buna yönelik olarak gebenin yaşamsal bulgularının ölçümlerine ek olarak oksijen saturasyonu ve solunum sayısı yakından izlenmelidir. Bu parametreleri içeren MEOWS (Modifiye Erken Obstetrik Uyarı Skorlaması) skorlaması takip sırasında kullanılabilir. İzlemde oksijen saturasyonu %95 ve üzerinde, solunum hızı dakikada 20 ve altında, ateş 38.5 °C'nin altında olmalıdır. Fetal etkilerin izlenmesi amacıyla Non-Stres Test (NST) takibi dikkatli biçimde yapılmalı, uteroplasental oksijenizasyonu daha iyi sağlaması nedeniyle gebe sol lateralde dekubit pozisyonunda takip edilmelidir (22).

COVID-19 pandemisinde sınırlı verilerle gösterilmekle birlikte genel olarak viral enfeksiyonların etkilerinden biri gebeliğin son trimesterinde preterm eylemdir. Preterm eyleme yönelik olarak, COVID-19 tanılı gebelerde kullanılacak tokoliz ajanlarının etkinliği ve olası yan etkileri ile ilgili çalışmalar devam etmekte olup, çelişkili sonuçlar da mevcuttur. Fakat COVID-19 pozitif gebe preterm eylem nedeniyle doğumhaneye kabul edildiğinde özellikle fetal akciğer maturasyonu için steroid kullanımı sonrası zaman kazanmak amaçlı tokoliz uygulanmaması konusunda görüş birliği mevcuttur

(23). Bazı çalışmalar steroid kullanımını, yoğun bakım olgularında uygulanan kortikosteroidlerin genel etkilerini göz önünde bulundurarak önermemektedir. Ancak yapılan antenatal steroidin betametazon olması, yoğun bakım olgularında uygulanan dozun 1/15-1/80'i arasında olması ve tek doz uygulanması nedeniyle kullanımını öneren çalışmalar mevcuttur (24).

3.1.1. ***Doğum şekli:*** Doğum şekline gebenin takipleri ve maternal-fetal etkiler göz önünde bulundurularak ve obstetrik endikasyonlara göre multidisipliner bir yaklaşımla karar verilmeli, kararlar hastaya özgü olmalıdır (25). Fetal strese yol açtığı düşünülen durumlarda sezaryen doğum endikasyonu konusunda daha esnek karar verilebileceği belirtilmektedir (23). Vajinal doğum ile ilgili özellikle vertikal geçiş ve vücut sıvılarından bulaş olabileceğine yönelik şüpheler mevcuttur. Yapılan çalışmalar sonucunda kanıtlanmış vertikal geçiş olmaması nedeniyle olası veya tanılanmış COVID-19 gebelerde vajinal doğum kontrendike değildir (22). Ancak yeterli kanıt olmaması nedeniyle sezaryen ile doğum tercih edilebilmektedir (6, 11-13). Vajinal doğum sırasında gebenin maske kullanımı, ikinci evrede etkin ıkınmayı olumsuz etkileyeceğinden sağlık personelinin tüm koruyucu ekipmanları kullanması gerekmektedir. Saturasyonun %95 ve üzerinde olması sağlanmalı, gerekliyse oksijen desteği verilmelidir. Saturasyonu düşük olan gebelerde olası pulmoner ödeme yönelik olarak hidrasyon desteği kontrollü yapılmalı ve bolus uygulamalardan uzak durulmalıdır (26). Doğum indüksiyonu amacıyla dinoprost veya oksitosin kullanımında bir kısıtlamama olmamakla beraber kritik olgularda aşırı sıvı yüklemesi ve kardiyovasküler dekompansasyon riski nedeniyle yüksek doz veya bolus şeklinde oksitosin kullanımından kaçınılmalıdır (22). Erken membran rüptürü nedeniyle eylem takibine alınan gebelerde veya eylem sırasında membranların açılması durumunda Penisilin G veya Ampisilin profilaksisi rutinde kullanılabilmektedir. Ayrıca sekonder bakteriyal pnömonide profilaksi amaçlı Seftriakson tercih edilebilir (27). İntrapartum dönemde trombositopeni yoksa, ağrılarla oluşacak hiperventilasyonu önlemek ve acil sezaryen gerektiğinde genel anestezi uygulama ihtiyacını azaltmak amacıyla epidural anestezi önerilmektedir (28). Eylemin ikinci evresinde aktif ıkınmanın maske takılı durumda zor olması, bu süreçte aerosol partiküllerin doğumhane personeline bulaşma riskinin artabileceği göz önüne alınarak ikinci evreyi kısaltılmak için müdahaleli vajinal doğum düşünülebilir (23). Postpartum dönemde rutin prosedürler uygulanmalı, yaşam bulguları yakından izlenmeli ve dikkatli biçimde kanama kontrolü sağlanmalıdır. Kanama kontrolünde uterotonik olarak uygun doz ve sürede uygulanmak üzere oksitosin tercih edilebilir. Misoprostol, prostoglandin E2 ve karbetosin tercih edilmekle birlikte, hemostaz sağlamak için traneksamik asit tercih edilebilir. Bildirilen akut solunum yetmezliği vakaları nedeniyle metilergometrin kullanımının tercih edilmemesi öneriler arasındadır (29). Maternal hipoksi nedeniyle oluşan fetal sıkıntı ve artan yoğun bakım takip ihtiyacı nedeniyle COVID-19 tanılı gebelerde sezaryen doğum oranlarının yüksek olduğu belirlenmiştir (25). Sezaryen doğum gerçekleştirilecek olgularda (acil veya elektif), şüpheli veya pozitif hastalar için önceden belirlenmiş negatif basınçlı ya da HEPA filtreli odalarda doğum gerçekleştirilmelidir. Anestezi, cerrahi ve yenidoğan ekibi uygun koruyucu ekipmanları kullanmalıdır. Ayrıca genel anestezi uygulanacak vakalarda orofarengeal bölgeye müdahalede bulunan personelin N95 maske ve siperlik kullanımı konusunda özenli olması gerekmektedir (30). Sezaryen doğumda, trombositopeni yoksa anestezi uygulamasının rejyonel anestezi şeklinde yapılması önerilmektedir. Fakat bazı vakalarda hızlı hipotansiyon gelişebildiğinden uygulama sürecinde dikkatli olunmalıdır (31). Genel anestezi uygulamasından mümkün olduğunca kaçınılması, maternal solunum fonksiyonlarının bozulması veya acil sezaryen doğum söz konusu olduğunda tercih edilmesi önerilmektedir. Bu durumda personelin kişisel koruyucu önlemleri almasına ek olarak yüz maskesi ile solunum devresi arasına filtre yerleştirilmesi ve video-laringoskopi kullanımı tavsiye edilmektedir. Sezaryen sonrası anne ve bebeğe yönelik uygulamalar ve yapılması gerekenler vajinal doğum sonrası uygulamalarla benzer niteliktedir (28).

3.2. ***Postpartum dönemde yönetim:*** Doğum sonrası hastaların değerlendirilmesi multidisipliner bir ekip tarafından yapılmalıdır. Yoğun bakım ihtiyacı, COVID-19'a yönelik uygulanacak medikal tedavi gerekliliği ve uygun tedavi protokolüne karar verilmelidir. Postpartum takip sürecinde hastaların analjezi ihtiyacına yönelik NSAID uygulamasına yönelik farklı yaklaşımlar mevcuttur. Erken dönemde yapılan çalışmalar uygulanmaması gerektiğini belirtmekte, güncel çalışmalar uygulanmasına engel olmadığını ifade etmektedir. Opioid analjeziklerden olası solunum depresyonu etkisi nedeniyle kaçınılması önerilmektedir (32). COVID-19'a bağlı olarak tromboemboli riski nedeniyle doğum sonrası profilaktik antikoagülan tedavi kullanılabileceği belirtilmektedir (33).

4. COVID-19'un Neonatal Etkileri

COVID-19'un dünyadaki yayılım hızıyla ilişkili olarak yenidoğanlarda virüsün görülme sıklığının arttığı ancak verilerin sınırlı olduğu belirtilmektedir (13). Ayrıca maternal COVID-19 enfeksiyonunun vertikal geçişine ilişkin veriler de

kısıtlıdır. Yapılan araştırmalarda maternal pnömoni ile ilişkili olarak intrauterin gelişme geriliği, intrauterin fetal ölüm ve neonatal mortalite olabilmektedir (11, 16). Sınırlı olan veriler doğrultusunda bir olguda vertikal geçiş olduğu, bir olguda intrauterin ölüm gerçekleştiği belirtilmektedir (7). Ayrıca COVID-19 pozitif annelerin bazılarında preterm eylem görülebildiği ancak bunların enfeksiyon ile ilişkisinin açık olmadığı ifade edilmektedir (34).

Çin'de retrospektif bir çalışmada iki vakada fetal distres görülmüştür. Canlı doğum ile sonuçlanan bu olgularda neonatal asfiksiye rastlanmamıştır. Birinci dakika APGAR skorları 8-9, 5. dakika skorları 9-10 olarak belirlenmiştir. Aynı olgulardan bir yenidoğanın myokard enzimlerinde hafif bir artış olduğu ancak herhangi bir semptom görülmediği belirtilmiştir (17). Yine retrospektif bir çalışmada COVID-19 testi pozitif olan on altı gebe ile negatif olan kırk beş gebenin sezaryen sonrası neonatal sonuçları incelenmiş; fetal distres, mekonyumlu amniyotik mayi ve neonatal asfiksi açısından anlamlı bir farklılık olmadığı belirlenmiştir (35). COVID-19 enfekte annelerin doğum sonuçlarına bakıldığında sınırlı sayıda olguya dayanarak; yenidoğanlarda başlangıç semptomları olarak solunum sıkıntısı, siyanoz, taşikardi, ateş, beslenme intoleransı ve kusma görüldüğü belirtilmektedir (7, 13). İran'da 15 günlük neonatal bir olgu ateş ve letarji semptomları ile kliniğe kabul edilmiş ve öksürük ve gastrointestinal herhangi bir bulgu gözlenmediği belirtilmiştir. Bu olguda taşikardi, taşipne, hafif subkostal retraksiyon görülmüş ve oksijen saturasyonunun %93 olduğu belirlenmiştir (14). Genel anlamda yenidoğanda görülen bu semptomların sıklıkla hafif seyrettiği, ancak bir olguda multipl organ yetmezliği ve DIC (yaygın damar içi pıhtılaşma) nedeniyle neonatal ölüm gerçekleştiği belirtilmektedir (7, 13). Literatürde SARS-CoV-2 IgM antikorları yüksek olan üç yenidoğanın boğaz sürüntü örneklerinde pozitif bulguya rastlanmadığını gösteren olgular da yer almaktadır (36). Virüsün anne sütü ile geçip geçmediğine yönelik kanıt olmadığı, emzirme sırasında damlacık yoluyla yenidoğana bulaşabileceği ifade edilmektedir (16, 37).

COVID-19'un klinik bulguları ve neonatal etkileri göz önüne alındığında bu dönemin ve semptomların etkili biçimde yönetilmesi büyük önem kazanmaktadır.

5. Neonatal Dönem ve Yönetimi

COVID-19'un yönetimi gebelik sürecinde, doğum sırasında ve doğum sonrasında olmak üzere üç aşamada ele alınmalıdır.

5.1. ***Gebelik süreci:*** Özellikle gebelik sürecindeki fizyolojik ve anatomik değişikliklerle ilişkili olarak virüse hassasiyet gelişebilmektedir. Gebeliğin son trimesterinde klinik bulgular görüldüğünde COVID-19 şüphesi ile yaklaşılmalıdır. Annenin pozitif olduğu durumlarda uygulanan tedavi yaklaşımları multidisipliner olarak ele alınmalıdır. Uygulanan tedavinin fetal açıdan etkileri göz önüne alınmalı ve doğuma yönelik olarak neonatal hazırlıklar yapılmalıdır. Yenidoğanın ilk müdahalesini yapacak gerekli ekipmanlar hazırlanmalı, fiziksel koşulların izolasyona uygun biçimde hazırlanması sağlanmalıdır. Ayrıca anne pozitif olgularda yenidoğana mutlaka şüpheli yaklaşılmalıdır (10, 13, 37).

5.2. ***Doğum süreci:*** Doğuma yönelik neonatal yönetim, öncelikle doğum kararının doğru biçimde alınması ile başlamalıdır. Doğum eylemine yönelik adımlar atılırken neonatolog, perinatolog ve anesteziyolog iş birliği sağlanmalı, hemşire ve ebelerin bu süreçteki tüm uygulamalarında multidisipliner bir yaklaşım benimsenmelidir (13). Elektronik fetal monitorizasyon yapılmalı ve fetal kalp atımları yakından izlenmelidir (38). Fetal akciğer maturasyonu sağlamak amacıyla steroid kullanımının COVID-19 açısından risk oluşturduğunu gösteren kanıt olmadığından, preterm doğum olgularında gerektiğinde steroid verilebilmektedir. COVID-19 testi pozitif olan olgularda maruziyeti en aza indirgemek amacıyla az sayıda personel ile doğumun gerçekleştirilmelidir (6, 39). Doğum şekli ve zamanı konusunda UNFPA endikasyon ve annenin doğum tercihi göz önüne alınarak karar verilmesini önermektedir (6, 37). Üçüncü trimesterde negatif bir test sonucuna ulaşana kadar neonatal bir engel yoksa ve mümkünse doğum ertelenmelidir (34). Doğum, izole negatif basınç özelliği bulunan bir alanda gerçekleştirilmeli ve tüm koruyucu ekipmanların kullanımı sağlanmalıdır (13, 37). Tüm müdahalelerden önce eller su ve sabun ile yıkanmalıdır. Şüpheli ve pozitif anne varlığında yenidoğanın resüsitasyon ihtiyacı belirlenmeli, APGAR skorları dikkatlice değerlendirilmeli, saturasyon ve vital bulgular yakından izlenmelidir. Doğumda, yenidoğanın termoregülasyonu sağlandıktan sonra yıkanması, kurulanması önerilmekte ve hasta anne ile yenidoğanı geçici süre ayrı tutmak ve izole etmek gerekmektedir (13, 37, 39). Doğum masası ile radyant ısıtıcı arasında en az iki metre mesafe olmalıdır. Neonatal resüsitasyon gerektiğinde en az sayıda sağlık çalışanı ile N95 maske dahil tüm koruyucu ekipmanlar kullanılarak müdahale gerçekleştirilmelidir (37). Kord klempleme süresine ilişkin herhangi bir kanıt olmamakla birlikte, vertikal geçişin göz ardı edilmemesi ve kordun vakit kaybetmeden klemplenmesi önerilmektedir. Ayrıca ten tene temasın engellenmesi diğer öneriler arasındadır (13, 37). COVID-19 testi pozitif annelerin bebeklerine, doğum sonrası 24-48 saatte test yapılması gerektiği belirtilmektedir (10).

5.3. ***Doğum sonrası dönem:*** Yenidoğanın genel durumu stabil ise, damlacık izolasyon önlemleri alınarak anne ile birlikte aynı odada olacak biçimde servise transfer edilmesinde sakınca olmadığı belirtilmektedir. Bu durumda beş gün boyunca hemşire/ebelerin gözetiminde tutulması ve sonrasında en erken sürede evde izolasyonun sağlanarak taburculuğun gerçekleştirilmesi önerilmektedir. Yenidoğanın resüsitasyon ihtiyacı varsa, ventilasyon sağlandıktan sonra tekrar değerlendirilerek yoğun bakım ya da özel bakım ihtiyacı belirlenmelidir. Yoğun/özel bakım ihtiyacı olmayanların stabilizasyon sonrasında anneleri ile birlikte serviste izole edilebileceği belirtilmektedir (10, 14, 37, 39). Anne ve bebeği rutin olarak izole etme ve birbirlerinden ayırma uygulamasından kaçınılması ve emzirmenin uygun biçimde başlatılması gerektiği vurgulanmaktadır (40).

5.4. ***Yoğun bakıma transfer kararı verilen yenidoğan:*** Bu süreçte ebeveynleri ile temasının önlenmesi, temas ve damlacık izolasyon önlemleri altında ilgili üniteye transferinin gerçekleştirilmesi önerilmektedir (10, 14, 37, 39). Transfer sırasında yenidoğanın mutlaka transport küvöz ile taşınmasına, ambulans kullanımı gereken durumlarda ise ventilatör, monitör ve taşıma ekipmanlarının bulundurulmasına özen gösterilmelidir. Görevli sağlık ekibinin bu süreçte koruyucu ekipmanları eksiksiz kullanması ve transfer öncesinde-sonrasında küvöz, ambulans ve diğer ekipmanların mutlaka dezenfeksiyonu sağlanmalıdır (13). COVID-19 ile enfekte ya da şüpheli yenidoğanın yoğun bakıma kabulü sırasında sorumlu ekip üyeleri koordinasyonu sağlamalıdır. Hasta kabul edilirken koruyucu ekipman kullanılmalı ve aksesuar kullanmaktan kaçınılmalıdır. Ayrıca kullanılan ekipmanları, giysileri ve diğer eşyaları yoğun bakım dışında kullanmamaya özen gösterilmelidir (13). Servise alınan yenidoğan mümkünse negatif basınçlı odada izole edilmeli, değilse ayrı bir odaya alınmalıdır (14, 37, 39). Yoğun bakım ünitesinde kullanılan ekipmanların hastalar ve servisler arasında yer değiştirmesi kısıtlanmalıdır. Kullanılan tüm malzemeler, cihazlar (USG, EKG cihazı vb), küvözler hastadan hastaya geçmeden önce dezenfeksiyon işleminden geçirilmelidir. Tüm invaziv işlemlerden ve numune almadan önce el yıkama ve N95 maske kullanımına özen gösterilmelidir. Alınan numuneler özenle ve doğru biçimde etiketlenmeli, saklanmalı ve koruyucu önlemler altında laboratuvara transfer edilmelidir (13). Tedavi planlaması neonatalog, pediatrist, hemşire, dezenfeksiyon personeli ve diğer sağlık ekibi üyeleri ile multidisipliner bir yaklaşım içerisinde yapılmalıdır. Oksijen tedavisi, sıvı replasman tedavisi, antibiyoterapi, enteral/parenteral beslenme desteği, sürfaktan ve nitrik oksit uygulaması, mekanik ventilasyon gibi tedavi yaklaşımları tercih edilebilmektedir. Ancak COVID-19'a ilişkin etkili bir tedavi yöntemi henüz bulunmamaktadır. Bu nedenle semptomatik ve olgu bazında tedavi uygulamalarının benimsenmesi ve geniş spektrumlu antibiyotiklerin gereksiz kullanımından kaçınılması önerilmektedir (13). Antiviral tedavi yaklaşımına ilişkin olarak klorokin, hidroksiklorokin, kortikosteroid veya intravenöz gama globülin gibi ilaçların karşılaştırılmasına yönelik yeterli klinik çalışma henüz bulunmamaktadır. Enfekte olgularda henüz klorokin/hidroksiklorokin kullanılan neonatal vaka bulunmadığı, destekleyici tedavi yaklaşımının uygulandığı belirtilmektedir (37). Yoğun bakım ünitesinde izlenen yenidoğanların ebeveynleri COVID-19 pozitif ise yoğun bakıma girmelerine müsaade edilmemelidir. Eğer yenidoğanda COVID-19 pozitif ise anne ve bebek izole edilmeli ve ziyaretçi kısıtlaması yapılmalıdır. Bu izolasyon negatif basınçlı bir odada olmalı ve annenin eldiven, maske, gözlük kullanması sağlanmalıdır. Eğer anne ve bebeğin ayrı kalması gerekli ise bu durum aileye açıklanmalı, sosyal ve ruhsal destek unsurları sürece dahil edilmelidir (14, 37). COVID-19 pozitif olan ve yoğun bakımda izlenen yenidoğanlarda taburculuk öncesi testlerin negatifliği doğrulanmalı ve ebeveynler konuya ilişkin olarak eğitilmelidir. Taburculuk sonrasında evde izolasyon devam ettirilmeli ve aileye temas izolasyonuna ilişkin bilgilendirme yapılmalıdır (14). Bulaş riski olan yenidoğanların taburculuk sonrası 14 günlük sürede telefon, yüz yüze görüşme gibi yöntemler ile yakından izlenmesi önerilmektedir (10). Ayrıca 14 gün sonra yenidoğandan kontrol amaçlı farengeal sürüntü örneği alınmalı ve sonuç negatif gelirse 28. günde izlem sonlandırılmalıdır (40).

5.5. ***Emzirme:*** Virüsün anne sütü ile geçişine ilişkin veri olmadığı ve damlacık yoluyla bulaşması nedeniyle koruyucu önlemler altında emzirmenin sürdürülmesi tavsiye edilmektedir. Yapılan araştırmalarda enfekte annelerin sütünde virüse rastlanmadığı ve anne sütünün yenidoğan için antikor kaynağı olması nedeniyle emzirmenin teşvik edilmesi ve en kısa sürede başlatılması önerilmektedir (10, 34, 37). Çin'de COVID-19 pozitif annelerin emzirmelerine tercihen donör süt kullanımı veya formül kullanımını öneren yaklaşımlar yer almakla birlikte bu görüşü destekleyen kanıtlara ulaşılamamıştır. Bu nedenle WHO (Dünya Sağlık Örgütü), CDC (Hastalık Kontrol Önleme Merkezi) ve RCOG (Royal College of Obstetricians and Gynecologists) emzirmeyi desteklemektedir. Ayrıca anne sütünün pastörize edilmesinden kaçınılması gerektiği ifade edilmektedir (40). Emzirme sırasında annenin el hijyeninin ve eldiven, maske, gözlük/siperlik kullanmasının önemli olduğu belirtilmektedir.

Eğer anne sütü pompa ya da elle sağılacaksa el yıkama ve süt saklama konusunda hassas olunması tavsiye edilmektedir. Süt sağma aparatlarının her kullanım sonrasında sıcak su ve sabun ile dezenfeksiyonu yapılmalıdır. Ayrıca ebeveynlere bulaş ve koruyucu önlemler konusunda bilgilendirme yapılmalıdır (10, 34, 37, 39). Annenin COVID-19 testi pozitif olduğu durumlarda semptomlar ve maternal tedavi yaklaşımları doğrultusunda izolasyon yaklaşımları izlenmelidir. Annede şiddetli solunum yolu semptomları ve ateş mevcut ise geçici süre ile anne ve bebek ayrılmalı ancak hijyenik koşullarda süt sağma yoluyla beslenmenin sürdürülmesi sağlanmalıdır (40).

5.6. ***Ziyaretçi uygulaması:*** Anne ve yenidoğan için hastanede kaldıkları süreçte tek bir ziyaretçi olması ve ziyaretçinin servise alınmadan önce COVID-19 semptomları açısından değerlendirilmesi önerilmektedir. Ayrıca ziyaret öncesi ellerin temizliği, koruyucu önlük, maske kullanımı ve oda içerisinde temas kurallarına uyulmasının önemi vurgulanmaktadır (39).

6. Sonuç

Maternal ve neonatal olgularda COVID-19 pozitif veya şüpheli pozitif durumlarda anne, bebek ve sağlık ekibini koruyucu yaklaşımlar benimsenmelidir. Maske, eldiven, gözlük ve önlük gibi koruyucu ekipman kullanımının yanı sıra etkili izolasyon önlemleri alınmalıdır. Doğum eylemi negatif basınçlı izole odalarda ve en az sayıda sağlık personeli ile gerçekleştirilmelidir. Doğum ve doğum sonu dönemde anne ve bebeği mümkün oldukça birlikte izole etmek, buna uygun fiziki koşulları sağlamak, semptomların seyrine göre emzirmeyi başlatmak ve sürdürmek gerekmektedir. Tüm aşamalarda multidisipliner olarak perinatolog, neonatolog, mikrobiyolog, hemşire, ebe, radyolog ve diğer sağlık çalışanlarını kapsayan bir ekip oluşturulmalıdır. Bu ekip üyelerinin izolasyon eğitimleri güncellenmeli ve kişisel koruyucu ekipmanlar tedarik edilmelidir. Tedavi yaklaşımları belirlenirken öncelikle semptomatik ve destekleyici tedavi adımları izlenmelidir. Bu süreçte kullanılan tüm araç-gereç ve tıbbi ekipmanların dezenfeksiyonu sağlanmalıdır. Ayrıca bireyler hastaneye kabul sürecinden başlayarak, taburculuk ve evde izlem sürecine kadar tüm aşamalarda anne, baba ve diğer bakım verenler koruyucu yaklaşımlara, izolasyona, hijyene ve temas kurmaya ilişkin eğitilmelidir. Ayrıca taburculuk sonrası evde izlem sürecinde sağlık ekibinin yakın izlem yapması gerekmektedir.

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Review Article

The place of immunological factors in recurrent pregnancy loss and implantation failures

Tekrarlayan gebelik kaybı ve implantasyon başarısızlıklarında immünolojik faktörlerin yeri

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Abstract

Despite recent advances in assisted reproductive methods and treatments in sustaining fetal viability, recurrent implantation failure (RIF) and recurring pregnancy loss (RPL) still pose significant problems in the context of in vitro fertilization (IVF). Recent studies focused on the role of immunological factors in the etiology of RIF and RPL. They demonstrated that infertile patients might suffer from dysregulated immune system cell activities, including CD4+ T helper (Th1, Th2, Th17, and Tregs), peripheral natural killer (pNK), uterine natural killer (uNK) cells. Researchers have investigated the use and efficacy of immunosuppressant drugs such as glucocorticoids, intravenous immunoglobulin, and TNF-α blockers in achieving successful implantation in infertile women but the efficacy of these treatments remains to be fully established. We conclude that, although the relationship between immunology and infertility is clear, there is still a long way to go to reach a thorough understanding.

Keywords: Infertility; Immunology; IVF; Recurrent pregnancy loss; Recurrent implantation failure

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Öz

Canlı bir gebeliğin devamı için yardımcı üreme teknikleri ve tedavi yöntemlerinde gelişmeler sağlansa da, in vitro fertilizasyon (IVF) sonrası tekrarlayan implantasyon başarısızlığı (TİB) ve tekrarlayan gebelik kayıpları (TGK) büyük problem oluşturmaktadır. Son yıllarda yapılan çalışmalarda TİB ve TGK nedeni olarak immunolojik faktörlerin üzerinde durulmaktadır ve bu hasta gruplarında immun sistem hücreleri olan; CD4+ T-helper (Th1, Th2, Th17, Treg) ve periferik natural killer (pNK) ve uterin natural killer (uNK) hücrelerinin aktivitelerinde dengesizlikler gösterilmiştir. Bu nedenle, bu hasta gruplarında başarılı bir implantasyon ve gebelik devamı için glukokortikoidler, intravenöz immünoglobulin ve TNF-α blokerleri gibi immünosüpresan ilaçların kullanımı ve etkinliği araştırılmıştır. Ancak ilaçların etkinliği ile ilgili net bir sonuç elde edilmemiştir. Sonuç olarak, immunoloji ile infertilite ilişkisi aşikar olmasına rağmen, bu konuda daha katedilmesi gereken uzun bir yol vardır.

Anahtar kelimeler: İnfertilite; İmmunoloji; IVF; Tekrarlayan gebelik kaybı; Tekrarlayan implantasyon başarısızlıkları

1. Introduction

Infertility is defined as the inability of a couple to achieve a viable pregnancy after a year of unprotected regular sexual intercourse. Between 10 to 15% of couples of reproductive age suffer from infertility (1, 2). Despite recent advances in assisted reproductive methods and treatments in sustaining fetal viability, recurring implantation failure (RIF) and recurring pregnancy loss (RPL) still pose significant problems in the context of in vitro fertilization (IVF). RIF is defined as the failure of a woman under the age of 40 to achieve a viable pregnancy after the transfer of at least three fresh or frozen embryos (3). RPL is defined as three or more consecutive miscarriages that occur before 20 weeks of gestation (4). Previous studies investigated genetic causes and uterine structural anomalies, whereas recent studies focused on the role of immunological factors in both RIF and RPL.

The field of reproductive immunology established by Madewar who, in 1953, asked why the semi-allogeneic fetus is not rejected by the maternal immune system (5). Pregnancy is a unique condition that allows the toleration of the embryo, a semi-allogeneic tissue, by the maternal immune system. In order for the mother to be able to tolerate the father's alloantigens, the maternal immune system must develop a balance between tolerance and immunity. Immune imbalance contributes to endometrial implantation failure and miscarriage. Research suggests that infertile patients may suffer from dysregulated immune system cell activities, including CD4+ T helper (Th1, Th2, Th17, and Tregs), peripheral natural killer (pNK), uterine natural killer (uNK) cells (6). These cells and their cytokines participate in blastocyst implantation (**Figure 1**).

This review aims to discuss studies demonstrating an association between NK and T cell counts and ratios, and infertility.

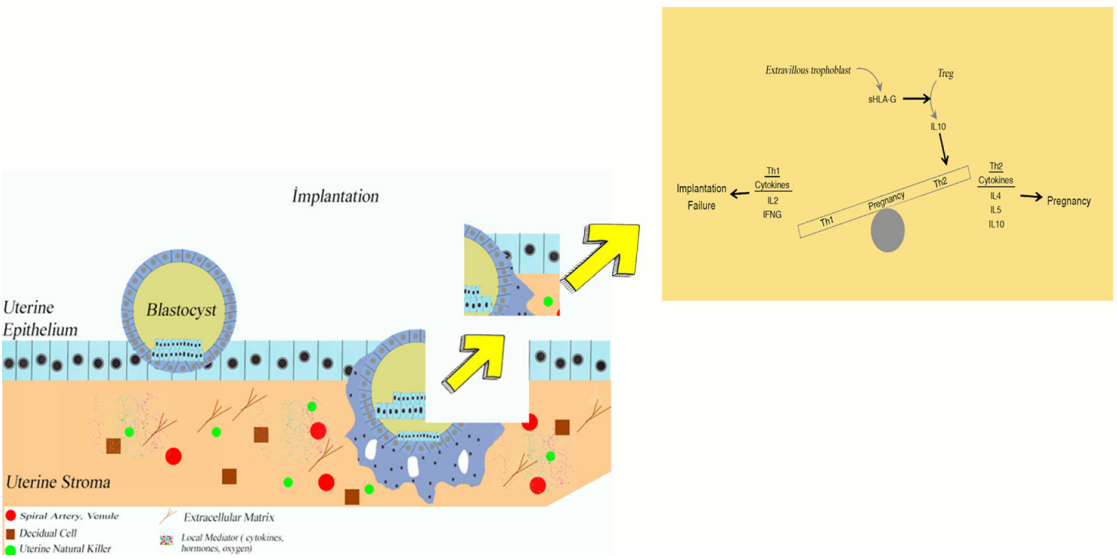

Figure 1. Hormones, oxygen, cytokines, growth factors, and immune system cells effective in blastocyst implantation and placenta formation

2. Methods

Using online databases, we carried out a systematic literature review on the role of immunologic factors in both RIF and recurring pregnancy loss (RPL). The major relevant studies were retrieved mainly from PubMed, Google Scholar, MEDLINE and Web of Science using the keywords 'immunologic factors and infertility', 'immunologic factors and recurrent implantation failure', 'immunologic factors and recurrent pregnancy loss' and 'treatment of immunologic problems for recurrent implantation failure and recurrent pregnancy loss'. Only English-language publications were included in this review.

3. Natural killer cells

A regular functioning immune system is essential for the successful implantation of an embryo (7). Natural killer (NK) cells play a central role in the innate immune system (8, 9). The pNK and uNK cells are phenotypically and functionally different cell types and are distinguished according to their receptor expression intensity, particularly surface CD56 (10). A minority of pNK cells (10%) resemble uNK cells whereas 90% are CD56dim (i.e. highly cytotoxic) and CD16+, while 80% of uNK cells are CD56bright (less cytotoxic) and CD16- (11). The reason why peripheral NK cells are more cytotoxic is twofold: first, the type of surface CD56, and second, the downregulation of CD16 expression by uNK cells, which in turn triggers NK cell antibody-dependent cell-mediated cytotoxicity (11, 12). Hence, uNK cells play a more prominent regulatory role in early implantation. The initiation of embryo implantation is associated with the production of progesterone and interleukin 15 (IL-15) and the stimulation of uNK cells during the luteal phase of the menstrual cycle (11, 13). These cells promote vascular remodelling via endothelial growth factor and are also responsible for trophoblast remodelling and cytokine secretion (10, 14, 15).

The literature contains different methods for NK cell determination, including an endometrial biopsy or lavage sampling, menstrual blood sampling, or placental/decidual sampling (16, 17). NKT cells constitute an important subgroup of lymphocytes that demonstrate both T cell and NK cell-like characteristics (18). NKT cells have two distinct functions in immune responses: pro-inflammatory and tolerogenic (19), leading researchers to speculate that NKT cells may play an important role in implantation and immune intolerance to the fetus (20). Zhou et al. investigated whether peripheral blood NKT-like cells were in any way associated with IVF treatment outcome and showed that patients with higher peripheral NKT-like cell counts had better IVF outcomes (i.e. higher pregnancy and live birth rates). Yuan et al. found elevated pNK cells to be correlated with unexplained recurrent spontaneous abortions (18).

In contrast, one study reported that pNK cell counts were not significantly different but that uNK cells were reduced in patients with RIF (21). In a comparative analysis, Hosseini et al. evaluated NK cell subsets in peripheral and menstrual blood samples of recurring spontaneous abortion patients and found more prominent population differences in NK cell subgroups in the peripheral blood (17). Also, several studies that investigated the efficacy of uNK cells in predicting implantation success after IVF conclude that uNK cell count was not effective in predicting IVF success (22, 23). In reference to these studies, it could be argued that immunomodulatory treatments may be unnecessary in the context of IVF treatments and may only be applied for carefully selected patients. Some studies similarly report no difference in uNK (CD56 and CD16) counts of fertile and infertile women (24), and also that elevated CD16 levels may predict poor prognosis (25). Kofod et al. emphasized that increased CD56 and decreased CD16 levels may predict viable pregnancy outcome in IVF treatment (26). Multiple studies did not find a significant correlation between pNK cell level and pregnancy loss and IVF outcome. On the other hand, the available results on uNK cell levels are contradictory. Regardless, recent studies associate elevated uNK cells with improved IVF outcomes (**Table 1**). Further studies are needed to elucidate the impact of NK cells on pregnancy loss and IVF outcomes.

4. T-helper cells

Cytokines play an important role in successful implantation and the continuation of pregnancy. CD4 T helper cells differentiate into two major subtypes as Th1 and Th2 that are distinguished based on the cytokines they secrete. Th1 cells typically secrete pro-inflammatory cytokines, such as interferon-gamma (IFN-γ), tumor necrosis factor-alpha (TNF-α), and interleukin-2 (IL-2) (27) whereas Th2 cells secrete anti-inflammatory cytokines, such as IL-4, IL-6, and IL-10, and appear to have immunosuppressive effects that are important for the healthy continuation of pregnancy (28). The balance of pro- and anti-inflammatory cytokines depends entirely on the ratio of Th1 and Th2 cells (29). It is possible to measure cytokine levels from serum, plasma, placenta, or endometrial lavage samples (30).

Although the available results on Th cells and cytokines are contradictory, the general opinion is that Th2 dominance is required for successful implantation and pregnancy. Most of these studies included RIF and RPL patients and emphasized the ratios of Th1/Th2 and their cytokines.

It has been demonstrated that the ratios of pro-inflammatory and anti-inflammatory cytokines (i.e. IFN-γ/IL-4, IFN-γ/IL-10, IFN-γ/TGF-β1, IL-6/IL-10, IL-6/TGF-β1, IL-1β/TGF-β1, and TNF-α/TGF-β) in the peripheral blood are increased in RIF patients. These results suggest that the Th1/Th2 ratio may predict prognosis in IVF (31). Kalu et al. similarly demonstrated that Th2 dominance is associated with improved IVF outcomes

Table 1. Studies investigating expression of uNK and pNK cells in samples from different anatomical locations in the context of infertility.

STUDY	SAMPLE TYPE	METHOD	VARIABLES	RESULT
Hosseini et al., 2014 (21)	Uterine and peripheral	Menstrual blood-peripheral blood-flow cytometry	CD56, CD16	uNK counts were higher in RPL patients; no statistical difference in pNK counts
Tohma et al., 2020 (25)	Uterine and peripheral	Uterine lavage- peripheral blood-flow cytometry	CD56, CD16	uNK counts were lower in RIF patients; no statistical difference in pNK counts
Donoghue et al., 2019 (26)	Uterine	Endometrial biopsy-immunohistochemistry	CD56, CD16	No added benefit in predicting the success or failure of implantation after IVF
Kofod et al., 2017 (30)	Uterine	Endometrial biopsy-immunohistochemistry	CD56, CD16	Better IVF outcomes with increased CD56 levels
Giuliani et al., 2014 (29)	Uterine	Endometrial biopsy-immunohistochemistry	CD56, CD16	Higher populations of CD16 may result in increased risk of infertility disorders; no statistical difference in CD56
Matteo et al., 2007 (28)	Uterine	Endometrial biopsy-flow cytometry	CD56, CD16	No differences between infertile and fertile women
Zhou et al., 2013 (24)	Peripheral	Peripheral blood-flow cytometry	CD56, CD16, CD3	Elevated CD3, CD56, and CD16 levels are associated with increased pregnancy and live birth rates in IVF
Yuan et al., 2015 (22)	Peripheral	Peripheral blood-flow cytometry	CD56, CD16, CD3	Elevated CD3, CD56, and CD16 levels are associated with RPL

uNK: Uterine natural killer cells, pNK: Peripheral natural killer cells, IVF: In vitro fertilization, RPL: Recurrent pregnancy loss, RIF: Recurrent implantation failure

Table 2. Studies investigating expression of Th1-Th2 cells and pro/anti-inflammatory cytokines in samples from different anatomical locations in the context of infertility.

STUDY	SAMPLE TYPE	VARIABLES	RESULT
Yuan et al., 2015 (22)	Decidual	Th1 and Th2 cells and pro/anti-inflammatory cytokines	Higher IFN-gamma expression, increased decidual Th1/Th2 ratio, and decreased IL-4 and IL-10 in patients with RPL
Liang et al., 2015 (35)	Plasma	Th1 and Th2 cells and pro/anti-inflammatory cytokines	The ratios of pro-inflammatory and anti-inflammatory cytokines were higher in the RIF patients
Kalu et al., 2008 (36)	Plasma	Th1 and Th2 cells and pro/anti-inflammatory cytokines	The Th1/Th2 ratio was higher in RIF patients
Comba et al., 2015 (34)	Plasma and endometrial tissue	Pro/anti-inflammatory cytokines	Higher IL-12, IL-18, and INF-γ and lower LIF and MIF in RPL patients
Kwak-kim et al., 2003 (37)	Plasma	Th1 and Th2 cells and pro/anti-inflammatory cytokines	The Th1/Th2, INF-γ/IL-4, and TNF-α/IL-4 ratios were higher in RIF and RPL patients
Lee et al., 2013 (38)	Plasma	Th1 and Th2 cells and pro/anti-inflammatory cytokines	The Th1/Th2 ratio was higher in RPL patients

uNK: Uterine natural killer cells, pNK: Peripheral natural killer cells, IVF: In vitro fertilization, RPL: Recurrent pregnancy loss, RIF: Recurrent implantation failure

among RIF patients (32). IFN-γ/IL-4 and TNF-α/IL-4 and Th1/Th2 rates were reported to be increased in RIF and RPL patients (33, 34). Results of decidual and endometrial samples were comparable to those of plasma samples. In RPL patients had elevated decidual IFN-γ levels, and reduced decidual IL-4 and IL-10 levels (18). Another study reported elevated IL-12, IL-18, and IFN-γ levels and reduced leukemia inhibitory factor (LIF) and migration inhibitory factor (MIF) levels in the plasma and endometrial samples of RPL patients (30) (**Table 2**).

5. Human leukocyte antigen (HLA)

The MHC cluster located on chromosome 6 encodes HLA molecules, including HLA Classes I, II and III. HLA Class I proteins are divided into classical antigens (HLA-A, HLA-B and HLA-C) and nonclassical HLA Class Ib antigens, including HLA E, F and G (35, 36). The HLA Class II region contains the HLA-DR, HLA-DQ and HLA-DP loci. HLA and NK cells are the most prominent immunological factors in fertility and might play a crucial role in the incidence and establishment of pregnancy. They can influence pregnancy-

related processes and actors, including embryonic aggregation, gametes, blastocyst formation, fetal growth, trophoblasts, transplantation, and embryonic survival (37).

HLA class I molecules are expressed in all nucleated cells whereas HLA Class II molecules are expressed only in antigen-presenting cells (e.g. dendritic cells, macrophages, B cells) and some non-APC cells (T cells, endothelial cells). On the other hand, trophoblasts have been shown to express the non-classical HLA-G molecule (38). HLA-C molecules, and to a limited degree, the HLA-A, HLA-B, HLA-G and HLA-E molecules, appear to play an important role in pregnancy by binding to the "activating/inhibitory" ligands on the NK and T cell surfaces (39).

The interaction between the "killer immunoglobulin-like receptor (KIR)" molecules on maternal immune cells (uNK/NK and cytotoxic T cells) and the paternal antigens [Human Leukocyte Antigens (HLA)] can determine the course of the pregnancy (38). The literature on the relationship between HLA and non-classical HLA molecules and pregnancy indicates that polymorphic HLA-G derivatives are associated with recurrent pregnancy loss (40).

6. Immunomodulatory Treatment

Researchers have investigated the use and efficacy of immunosuppressant drugs such as glucocorticoids, intravenous immunoglobulin, and TNF-α blockers in achieving successful implantation in infertile women but the efficacy of these treatments remains to be fully established (41).

6.1. Intravenous immunoglobulin

A systematic review and meta-analysis by Li et al. found that intravenous immunoglobulin (IVIG) was associated with increased implantation, clinical pregnancy, and live birth rates in women with unexplained infertility or IVF/ICSI failure when compared to a placebo (42). However, a 2014 Cochrane review, including eight randomized studies on 303 women with recurrent pregnancy loss, concluded that IVIG treatment did not improve live birth rates (43).

6.2. Corticosteroids

The efficacy or utility of corticosteroids in RIF patients is not clearly established (44). Meta-analyses emphasize that corticosteroids do not increase live birth rates in RIF patients (45). However, some studies report better IVF outcomes when corticosteroids are combined with heparin, aspirin, or progesterone (46, 47). It is not clearly understood how these treatments affect immune cells (Th1, Th2, NK) or cytokine release. Further studies that investigate pre- and post-treatment changes in immune cells and cytokines are needed.

6.3. TNF-α blockers

TNF-α blockers (e.g. adalimumab) inhibit TNF-α and reduce the inflammatory response. Despite studies indicating increased pregnancy rates when aspirin or IVIG treatments are combined with TNF-α blockers, this treatment does not significantly increase live birth rates (48). These drugs are thought to act by altering cytokine ratios. It was reported that Th1/Th2 and TNF-α/IL-10 ratios were reduced after TNF-α blocker treatment (49).

6.4. Tacrolimus

The immunosuppressive activity of tacrolimus is achieved by the inhibition of calcineurin, resulting in reduced inflammatory cytokines, including TNF-α, IL-1β, and IL-6 (50). Nakagawa et al. applied tacrolimus therapy to patients with a history of RIF starting two days before embryo transfer until a positive pregnancy test. They reported increased pregnancy and live birth rates in patients who received treatment (51). On the other hand, it was observed that patients with reduced Th1 levels did not have significantly different clinical pregnancy or live birth rates. However, pregnancies were more likely to progress into the second trimester in patients who were treated with tacrolimus and had lower Th1 levels (52). A study of 100 pregnant women with a history of organ transplantation and tacrolimus therapy reported that four fetuses developed congenital anomalies such as meningomyelocele, urogenital defects, hearing defects, hypospadias, multicystic dysplastic kidneys, and cleft palate (53). Further and more extensive and detailed studies are needed concerning tacrolimus treatment applications.

7. Conclusion

In conclusion, numerous articles have recently been published on the relationship between immunology and infertility, resulting in a better understanding of the effects of immunology on implantation failure and recurrent miscarriage. However, there are still many unknowns, and, as of yet, there are no effective treatment methods for any potential immunological problems. Therefore, well-designed randomized controlled trials are needed to determine relevant immunological conditions and to develop treatment modalities for potential problems.

Declaration of Interest

The authors report no conflict of interest.

Ethical approval: This review protocol was approved after obtaining the necessary permissions by the obstetrics and gynecology department of Baskent University. Ethics committee approval was not sought as the study is a review of the previous works of literature.

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Türk Kadın Sağlığı ve Neonatoloji Dergisi

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Case Report

Successful cervical cerclage in a pregnant woman with a large cervical myoma

Dev servikal myomu olan gebelikte başarılı servikal serklaj uygulanması

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Abstract

Cervical insufficiency or early cervical dilation is a fundamental cause of second-trimester pregnancy loss. Cervical cerclage is the principal treatment for women with cervical insufficiency. Uterine myoma is the most common benign gynaecologic tumour, occurring in approximately 20% of reproductive age women, whereas uterine cervical myoma is rare and constitutes 5% of all myomas. One of the most important aetiological factors for premature labour is cervical insufficiency. Emergency cerclage can be effective, although according to the literature cerclage placement as a means of prolonging the duration of pregnancy has provided conflicting results. Here, we aimed to present successful implementation of cerclage process in a pregnant patient with a large cervical myoma.

Key words: Emergency cerclage; cervical myoma; cervical insufficiency

Öz

Servikal yetmezlik veya erken servikal dilatasyon ikinci trimester gebelik kaybının önemli bir nedenidir. Servikal serklaj servikal yetmezlik olan kadınlar için temel tedavidir. Uterin myom üreme çağındaki kadınların yaklaşık %20'sinde görülen en sık benign jinekolojik tümördür, servikal myom ise nadirdir ve tüm myomların %5'ini oluşturur. Prematüre doğum için en önemli etiyolojik faktörlerden biri servikal yetmezliktir. Literatüre göre serklaj uygulamasının gebelik sürelerini uzatmadaki sonuçları çelişkili bildirilmekle birlikte, acil serklaj hamilelik süresini uzatmada etkilidir. Bu olguda, büyük servikal myomu olan gebede başarılı bir şekilde serklaj uygulanmasını sunmayı amaçladık.

Anahtar Kelimeler: Acil serklaj; servikal myom; servikal yetmezlik

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1. Introduction

The concept of cervical insufficiency classically refers to a painless cervical opening in the second trimester. Cervical insufficiency or early cervical dilation is a predominant factor in second-trimester pregnancy loss and preterm birth (1). Cervical cerclage is the principal treatment for women with cervical insufficiency; it is recommended to perform a cerclage in high-risk women when transvaginal sonography shows cervical shortening <25 mm (1). There are two types of cerclage, the McDonald and Shirodkar. There is no consensus on how late the procedure can be performed during pregnancy (2).

Uterine myoma, also known as a leiomyoma or fibroid, is the most common benign gynaecologic tumour occurring in approximately 20% of reproductive age women, whereas uterine cervical myoma is rare and constitutes 5% of all myomas (3). Cervical myomas are classified as type 8 according to the International Federation of Gynecology and Obstetrics classification, arising from the muscular structure of the cervix instead of the uterine corpus. These can grow into both the parametrium and vagina (4). Myometrial prevalence in pregnancy usually ranges from 0.1% to 3.9%, but in some studies is reported as high as 10.7% (5, 6). Although leiomyomas can cause a wide variety of symptoms, they are mostly asymptomatic. Symptoms depend on the location, size and number of leiomyomas (7). Uterine leiomyoma is associated with preterm delivery, stillbirth and ectopic pregnancy. If a leiomyoma is close to the placental region, the incidence of pregnancy-related complications increases. Complications include bleeding, pain, premature labour and postpartum haemorrhage. Small fibroids in pregnancy do not usually cause symptoms, and there is no need for surgery. However, successful myomectomy procedures during pregnancy have been reported (8).

In this case report, we report the use of cerclage in a pregnant woman with a large cervical myoma and discuss the current literature.

2. Case report

A 25-year-old woman was admitted to our clinic with a history of inguinal and abdominal pain in the 21st week of her first pregnancy. The patient permitted her medical data and images to be used if needed. She had experienced pain and brown vaginal spotting for two days. She had no systemic disease or history of surgery but was previously known to have a cervical myoma. Transvaginal ultrasonography detected a large cervical myoma approximately 10 × 11 cm in size (**Figure 1**). Fetal measurements were consistent with a 21-week pregnancy on obstetric ultrasonography. Fetal movements and cardiac activity were positive. The amniotic fluid was normal. The cervical canal length could not be clearly evaluated due to the cervical myoma. On vaginal examination, the cervix was 3 cm dilated and 50–60% effaced. Biochemical and urinalysis tests were within normal limits. No fetal anomaly was detected on ultrasonography, and it was decided to perform an emergency cervical cerclage. The major problem was the large myoma in the cervical canal. A McDonald cerclage technique was performed; the cervix was sutured with a mersilene type cerclage suture at the 4-7-12 positions. Prophylactic antibiotherapy was initiated, tocolysis was administered, and the patient was hydrated. At about 33 weeks gestation, the patient started the early stages of labour, and because the birth canal was closed by the cervical myoma, caesarean section was performed, with the safe birth of a 2250 g baby. The myoma was not removed due to its location and the risk of bleeding during the caesarean section.

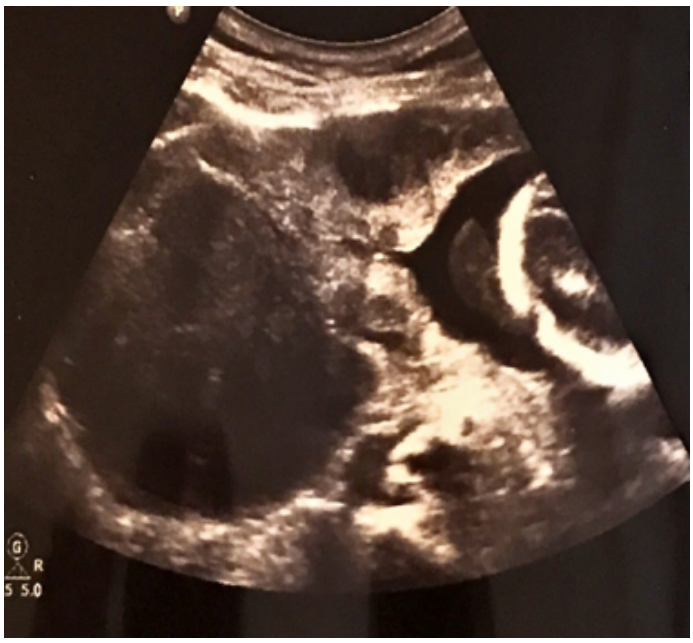

Figure 1. Ultrasonographic image of a 10 × 11 cm myoma in the cervix.

Although the procedure was complicated due to the large cervical myoma in this patient who had developed cervical insufficiency, the McDonald cerclage procedure was successful.

3. Discussion

Reviewing the literature, cerclage procedures for the treatment of cervical insufficiency have varying success rates. A shortened cervix is a strong indicator of preterm delivery in women with singleton and twin pregnancies; the shorter the cervical length, the higher the risk of spontaneous preterm delivery was reported (9). In a systematic review, the perinatal results after

cerclage were more successful in women who did not have a previous history (10). When cerclage results were evaluated, there was an 86% success rate with elective cerclage in 2662 patients in 22 studies (11). In a study conducted by Owen et al. (12), approximately one-third of pregnant women gave birth before 35 weeks gestation, and fewer surgical complications were observed. As Karl and Katz (13) stated that it was vital to place the sutures as high as possible and tight into the cervical stroma. In the presence of a cervical myoma, it becomes challenging to perform the procedure. Tilting the operating table head down and inflating the bladder with 600 mL of saline via a Foley catheter can facilitate the procedure.

Uterine leiomyoma significantly increases the risk of spontaneous abortion. In a study by Buttram and Reiter (7) the rate of abortion was 41% in uterine leiomyoma patients, and this rate decreased to 19% after myomectomy. Uterine leiomyomas tend to grow in pregnancy, display involution in the third month postpartum, and usually return to their pre-pregnancy dimensions (14). Leiomyomas can cause an obstruction and a dysfunctional birth process, leading to presentation anomalies. Postpartum severe bleeding may be seen with submucous leiomyomas, and a hysterectomy may be necessary for control of the haemorrhage. It is crucial to keep in mind that adhesions can cause infertility. Therefore, myomectomy should be performed in selected cases such as spontaneous abortions and premature births if this is considered a cause of infertility (15). In our patient, myomectomy was not performed due to the risk for the patient before pregnancy. However, successful myomectomy operations in pregnancy have been reported (8).

Differences in outcome may be due to inaccurate assessment of the gestational weeks, the selected cerclage technique, timing of the procedure and infection of the amniotic cavity (16, 17). Despite the difficulty of this procedure, cerclage was successfully performed in this 21 weeks pregnant woman at high risk of preterm delivery.

Declaration of Interest

The authors declare no conflict of interest.

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Türk Kadın Sağlığı ve Neonatoloji Dergisi
Turkish Journal Of Women's Health and Neonatology

Yazım Kuralları

Amaç/Aim

"Türk Kadın Sağlığı ve Neonatoloji Dergisi – Turkish Journal of Women's Health and Neonatology" Sağlık Bilimleri Üniversitesi, Etlik Zübeyde Hanım Kadın Hastalıkları Eğitim ve Araştırma Hastanesi'nin süreli bilimsel yayın organı olup, İngilizce/Türkçe yayın kabul eden hakemli, açık erişimli, ulusal bir dergidir ve yılda dört sayı olarak yayımlanır. Kadın doğum ve neonatoloji disiplinleri ile ilgili olabilecek ve tıp gündemini belirleyen güncel konuları içeren yüksek kalitede bilimsel makaleler yayımlamak öncelikli hedefimizdir.

Kapsam/Scope

Başka bir yerde yayınlanmamış, orijinal, güncel konuları içeren tüm çalışmalar dergi kapsamında değerlendirilir. Prospektif/retrospektif klinik-cerrahi ve laboratuvar çalışmaları, olgu sunumları, davet üzerine yazılan derleme, editöre mektuplar, kısa raporlar, cerrahi teknik yazıları dergide değerlendirilir.

Bilimsel Sorumluluk

Tıp dergilerine gönderilecek makalelerin standart gereksinmeleri ile ilgili bilgiler bilimsel yayıncılık standartları açısından Uluslararası Tıbbi Dergi Editörler Kurulu (ICMJE), www.icmje.org internet adresinde bulunabilir.

1. Gönderilecek makalelerde araştırma ve yayın etiğine uyulması zorunludur. Yazıların tüm bilimsel sorumluluğu yazar(lar)a aittir.

2. Makalelerin daha önce hiçbir yerde yayınlanmamış ve/veya yayınlanmak üzere değerlendirme sürecinde olmaması gereklidir. Sorumlu yazar bu ibareyi editöre sunum sayfasında belirtmelidir.

3. Makalenin değerlendirme sürecinin başlaması için, tüm yazarlar tarafından imzalanmış Telif Hakkı Devir Formu gönderilmelidir. Yazar sıralaması için Telif Hakkı Devir Formu'ndaki imza sırası dikkate alınır.

4. Sorumlu yazar, tüm yazarlar adına makalenin son halinin sorumluluğunu taşır.

Etik Sorumluluk

1. "İnsan" öğesini içeren tüm çalışmalarda Helsinki Deklerasyonu Prensipleri'ne (https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/) uygunluk aranır. Bu tip çalışmalarda yazarlar, gereç ve yöntem bölümünde, çalışmayı bu prensiplere uygun yaptıklarını, etik kurul onaylarının bulunduğunu ve çalışmaya katılmış insanlardan "bilgilendirilmiş olur formu" (informed consent) aldıklarını paylaşmalıdırlar.

2. Deney hayvanı çalışmalarında yazarlar gereç ve yöntem bölümünde Guide for the Care and Use of Laboratory Animals (https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf) prensipleri doğrultusunda hayvan haklarını koruduklarını ve etik kurul onaylarının bulunduğunu belirtmelidirler.

3. Etik kurul onayı gereç ve yöntem bölümünde kurul adı, onay tarih ve sayısı bilgileri paylaşılarak belirtilmelidir.

4. Olgu sunumlarında hastalardan kendileriyle ilgili bilgi, belge ve resimlerin isim belirtilmeksizin paylaşılacağına dair "bilgilendirilmiş olur" (informed consent) alınmalıdır.

5. Yazarlar editöre sunum bilgisinde çalışmada her hangi bir kurum, kuruluş ile ticari ilişkilerinin olmadığını belirtmelidirler. Çalışmada ticari bağlantı veya maddi destek veren kurum mevcut ise kullanılan ticari ürün, ilaç, firma vb. ile nasıl bir ilişkisinin olduğunu (konsültan, diğer antlaşmalar) belirtmelidirler. Yazarlar çalışma ile ilişkili olarak kişisel ve finansal tüm ilişkilerin bildirilmesinden sorumludurlar. Çıkar çatışması olmadığına dair beyan mutlaka belirtilmelidir.

6. Makalelerin bilimsel ve etik kurallara uygunluğu yazarların sorumluluğunda olup, editör dergide yayınlanan yazılar için herhangi bir sorumluluk kabul etmez.

Dergi Yazım Kuralları

Yazarlara Bilgi ve On-line makale gönderimi: Tüm yazışmalar ve yazı gönderimleri DergiPark üzerinden yapılmalıdır. Yazı gönderimi için detaylı bilgi DergiPark üzerinden verilen internet adresinden edinilebilir. Yazılar sorumlu yazar tarafından e-posta aracılığıyla DergiPark'ta yer alan linke girilip kayıt olunduktan sonra gönderilmelidir. Gönderilen her yazı için özel bir numara verilecek ve yazının alındığı e-posta yolu ile teyid edilecektir.

Derginin yayın dili Türkçe ve İngilizce olup çalışmalar Türkçe veya İngilizce olarak gönderilebilir. Dergide yayımlanmak üzere prospektif/retrospektif, klinik ve laboratuvar çalışmaları, olgu sunumları, davet üzerine yazılan derleme, editöre mektup, kısa raporlar ve cerrahi teknik yazılar değerlendirilir. Türkçe gönderilen çalışmalarda ayrıca İngilizce Başlık, Abstract, Keywords; İngilizce olanlarda ise Türkçe Başlık, Öz, Anahtar Kelimeler bulunmalıdır. İngilizce makaleler dergiye gönderilmeden önce profesyonel bir dil uzmanı tarafından kontrol edilmelidir. Türkçe yazılarda yazım dilinde Türk Dil Kurumu Sözlük ve Yazım Kılavuzu esas alınarak düzgün-duru bir Türkçe kullanımı önemlidir.

Klinik ve laboratuvar araştırma yazıları giriş, gereç ve yöntem, bulgular, tartışma, kaynaklar, tablolar, resimler ve altyazıları şeklinde sıralanacak şekilde düzenlenerek gönderilmelidir. Öz sayfasından sonraki sayfalar giriş sayfasından itibaren numaralandırılmalıdır. Ön sayfada yazının başlığı, kısa başlığı, yazar adları (ünvan belirtmeksizin), yazı kategorisi (araştırma yazısı, olgu sunumu, derleme, editöre mektup, teknik yazı, kısa rapor) makalenin gönderildiği kurumun açık

adı, sırasıyla yazarların ünvanlarının üst başlıkla belirtildiği açıklamaları, yazışma yapılacak yazarın bilgileri (iletişim adresi, telefon, elektronik posta bilgileri), kelime sayısı verilmelidir. Yazının daha önce herhangi bir toplantıda sunumu gerçekleştirildiyse, toplantının adı, tarihi ve yeri ayrıca belirtilmelidir.

Öz: Türkçe ve İngilizce olarak en fazla 250 kelime sınırına göre düzenleme yapılarak gönderilmelidir. Bütün makale şekillerinde Türkçe ve İngilizce öz gönderilmelidir. Öz, araştırma makalelerinde amaç, gereç ve yöntem, bulgular, sonuç şeklinde düzenlenmelidir. Öz olgu sunumlarında olgu sunumunu özetleyecek şekilde, sunulma nedenini ve olguyu açıklayıcı şekilde yazılmalıdır.

Türkçe ve İngilizce özetlerin hemen ardından hem Türkçe hem İngilizce Index Medicus (http://www.nlm.nih.gov/mesh/MBrowser.html) "Medical Subject Headings"e uygun en az 3 anahtar kelime verilmelidir.

Olgu sunumu: Giriş, olgu sunumu, tartışma başlıkları altında olgu sunumları hazırlanmalıdır.

Yazılar Microsoft Word programı ile çift satır aralıklı ve 12 punto olarak, her sayfanın iki yanında ve alt ve üst kısmında 25 mm boşluk bırakılarak yazılmalıdır. Yazı stili Times New Roman olmalıdır. "System International" (SI) birimler kullanılmalıdır. Şekil, tablo ve grafikler metin içinde refere edilmelidir. Kısaltmalar, kelimenin ilk geçtiği yerde parantez içinde verilmelidir, sonrasında kısaltma şeklinde açıklaması olmaksızın kullanılmalıdır. Türkçe'de ondalık sayılarda virgül kullanılmalı (45,5), İngilizce yazılarda nokta (45.5) kullanılmalıdır. Derleme 4000, orijinal çalışma 2500, olgu sunumu 1200, editöre mektup (Öz ve Abstract içermemelidir ve kaynak sayısı 10'u geçmemelidir) 500 kelimeyi geçmemelidir. Metinde geçen anatomik oluşum, hastalık ve sendrom isimleri özel isim değillerse, Türkçe okunuşları ile yazılmalıdır.

Maddi destek & Çıkar ilişkisi: Yazarlar editöre sunum bilgisinde çalışmada herhangi bir kurum, kuruluş ile ticari ilişkilerinin olmadığını belirtmelidirler. Çalışmada ticari bağlantı veya maddi destek veren kurum mevcut ise kullanılan ticari ürün, ilaç, firma vb. ile nasıl bir ilişkisinin olduğunu (konsültan, diğer antlaşmalar) belirtmelidirler. Yazarlar çalışma ile ilişkili olarak kişisel ve finansal tüm ilişkilerin bildirilmesinden sorumludurlar. Çıkar çatışması olmadığına dair beyan editöre sunum bilgisinde ve makale sonunda **"Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkar dayalı ilişkisi yoktur"** şeklinde mutlaka belirtilmelidir.

Kaynaklar

Kaynak gösterirken en yeni ve güncel yayınlar tercih edilmelidir. Yararlanılan kaynaklar yazıdaki kullanım sırasına göre numaralandırılmalı, numaraları cümle sonunda, nokta işaretinden önce parantez içinde yazılmalıdır. Tüm kaynaklarda, yazar sayısı altı ve altında ise tüm yazarların isimleri yazılmalı, yazar sayısı altıdan fazla ise, ilk üç yazarın ismi yazıldıktan sonra İngilizce makalelerde 'et al', Türkçe makalelerde 've ark' eklenmelidir. Kaynaklar derleme ve özgün makalede en fazla 30, olgu sunumlarında en fazla 10 olmalıdır. Dergi isimleri Index Medicus ve Ulakbim/Türk Tıp Dizini'nde belirtildiği şekilde kısaltılmalıdır. Kaynaklar listesi yazının sonunda ayrı bir sayfaya yazılmalıdır. Kaynakların doğruluğundan yazarlar sorumludur. Farklı yayın türleri için kaynak gösterme biçimleri aşağıdaki örneklerde gösterilmiştir.

Dergiden yapılan alıntı: Yazar(lar)ın soyadları ve ad(lar)ının baş harf(ler)i, makale ismi, dergi ismi, yıl, cilt, sayı ve sayfa numarası belirtilmelidir.

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Kitap Bölümü:

Bölüm yazar(lar)ının soyad(lar)ı ve ad(lar)ının baş harfi, bölüm başlığı, editörün(lerin) soyad(lar)ı ve ad(lar)ının baş harfi, kitabın ismi, kaçıncı baskı olduğu, basım yeri, yayınevi, baskı yılı, bölümün ilk ve son sayfa numarası belirtilmelidir.

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Tez:

Yazarın soyadı, adının baş harfi, tezin başlığı (tez olduğu belirtilmeli), tezin yapıldığı şehir, üniversite adı, yılı.

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Web sitesinin adı, erişim tarihi, web sitesinin adresi.

Cancer-pain.org New York: Association of Cancer Online Resources. Erişim tarihi: 16 May 2002. Available from: www.cancer-pain.org

Diğer kaynak türleri yazımları konusundaki geniş bilgi 'International Commitee of Medical Journal Editors' web sitesinden edinilebilir (www.icmje.org).

Şekil, Tablo, Resim ve Grafikler:

Şekil, tablo, resim ve grafikler ana metin içerisindeki geçiş sıralarına uygun olarak numaralandırılmalı ve metin içinde ilgili cümlenin sonunda belirtilmelidir. Şekil, tablo, resim ve grafiklerin açıklamaları makale sonuna eklenmelidir. Tabloların üzerinde tanımlayıcı bir başlık yer almalı ve tablo içerisinde geçen kısaltmaların açılımları tablo altında alfabetik sıraya göre tanımlanmalıdır. Resimler, grafikler ve fotoğraflar (TIFF ya da JPEG formatında) ayrı dosyalar şeklinde sisteme yüklenmelidir. Görsellerin çözünürlüğü en az 300 DPI olmalıdır.

Türk Kadın Sağlığı ve Neonatoloji Dergisi
Turkish Journal Of Women's Health and Neonatology

Instructions to Authors

Aim

The "Turkish Journal of Women's Health and Neonatology" is the official, scientific publication of Etlik Zubeyde Hanim Women's Health Training and Research Hospital". The journal is open access, national, double-blind journal published four times per year; in March, June, September, and December. Our primary goal is to publish high-quality scientific articles, written in English/Turkish, that may be relevant to the disciplines of obstetrics, gynecology and neonatology including current topics related to the medical agenda.

Scope

Unpublished, original papers including current topics that are not under review for publication elsewhere can be submitted for publication. Original peer-reviewed papers of prospective/retrospective studies, clinical-surgical and laboratory researches, case reports, reviews upon invitation, letters to the editor, short communications, reports on surgical techniques are welcomed and evaluated for publication.

Scientific Responsibility

The standard requirements for the manuscripts submitted to medical journals are listed by the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org).

1. Research and publication ethics should be followed in all submissions. The whole scientific responsibility of the manuscript belongs to the author(s).

2. All submissions should state that neither they have been published already, nor they are under consideration for publication, or in press elsewhere. The corresponding author should make this statement on the page of 'Letter to the Editor'.

3. To start the review process of the submitted manuscript, a 'Copyright Transfer Agreement Form' should be signed by all authors, and sent during the submission. For author ranking, the order of signatures in the 'Copyright Transfer Form' is considered.

4. The corresponding author bears responsibility for the final version of the manuscript on behalf of all authors.

Ethical Responsibilities

1. All studies involving 'human' should follow the principles described in an appropriate version of the 1964 Declaration of Helsinki, as revised in 2013. (https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/). Manuscripts submitted for publication must contain a statement that the study has been reviewed by the appropriate ethics committee and have therefore been performed under the ethical standards described in an appropriate version of the Declaration of Helsinki. It should also be stated clearly in the text that all human subjects gave their informed consent before their inclusion in the study.

2. In experimental animal studies, the authors should indicate in the Material and Method section that the procedures followed were in accordance with animal rights as per the Guide for the Care and Use of Laboratory Animals (https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf) and they should obtain animal ethics committee approval. Experimental animal studies should be presented with the disclosure of the appropriateness to the institutional/national/international ethical guides on the care and use of laboratory animals.

3.Ethical Approval should be stated in the Material and Method section by sharing the name of the approving committee, date and the number of the approval.

4. In case reports, the patients, who were described in the paper, should have given written informed consent to the inclusion of material about themselves, that they acknowledge they are not identified via the paper; and/or fully anonymized.

5. On submission, the author(s) must identify potential competing or conflicts of interest of a financial or other nature with any kind of institution in the cover letter. If there is any commercial connection or financial support from an institution in the study, authors should declare the kind of relationship (consultant or other agreements) with the commercial product, drug, company, etc used. Author(s) are responsible for reporting all personal and financial relationships related to the study. The declaration that there is no conflict of interest should be stated.

6. The compliance of the articles with scientific and ethical rules is under the responsibility of the authors, and the editor does not accept any responsibility for the articles published in the journal.

Submission of Manuscripts

Information to the Authors and On-Line Manuscript Submission: All correspondence and manuscript submissions must be made via DergiPark. Detailed information about the submission of the articles can be obtained from the web address given via DergiPark. Manuscripts should be submitted after registration to the link on the DergiPark via e-mail by the corresponding author. Once a manuscript is submitted through DergiPark, it will be assigned a number, and the corresponding author will be notified by an e-mail.

The publication language of the journal is Turkish and English, and studies can be submitted in Turkish or English. Original peer-reviewed papers of prospective/retrospective studies, clinical-surgical and laboratory researches, case reports, reviews upon invitation, letters to the editor, short communications, reports on surgical techniques are welcomed and evaluated for publication. The studies that are submitted in Turkish should include Title, Abstract, Keywords in English; and those submitted in English should include Title, Abstract, Keywords in Turkish as well. Manuscripts in English should undergo a professional language editing process before submission. It is important to use a proper and clear language based on the "Turkish Language Association Dictionary" and "Turkish Spelling Guide" in the papers submitted in Turkish.

Clinical and laboratory research papers should include introduction, material and methods, discussion, references, tables, figures, and legends. All pages after the abstract page should be numbered consecutively beginning with the abstract page. The title page should contain the title of the article, a running title, authors' names, types of the article (original article, case reports, review articles, letter to the editor, technical writing, short communication), the full name of the institution, academic degrees of the authors, contact information of the corresponding author (including address, telephone number, e-mail address) and number of the words. If the article was presented at a scientific meeting, authors should provide a complete statement including the date and place of the meeting.

Abstract: All types of articles should include abstracts in both Turkish and English that should not exceed 300 words. The abstract of the original articles should be structured with the following headings; aim, material and method, results, and conclusion. The abstract of a case report should include a brief description of the case and the aim of submission. Review articles should also contain a brief description of the aim of the submission.

The authors should list at least three keywords taken from Index Medicus (http://www.nlm.nih.gov/mesh/MBrowser.html) ''Medical Subject Headings'' after Turkish and English abstract.

Case Reports: Should be arranged as follows; introduction, case report, discussion.

Manuscripts should be prepared using Microsoft Word software, written in Times New Roman font, 12 point-type, double-spaced with 25mm margins on the left and right sides. "System International" (SI) units should be used. Figures, tables and graphs should be given in the text. Abbreviations should be defined accordingly in the text in parenthesis when first mentioned and used in the text then, the abbreviated form should be used throughout the article. A comma must be used in decimal numbers in Turkish articles (45,5) and the point must be used in English articles written in English (45.5). Review articles should not exceed 4000 words, original articles 2500 words, case report 1200 words, letter to the editor (should not include abstract and reference numbers should not exceed 10) 500 words. If the anatomical formations, disease and syndrome names, are not special names, they should be written in Turkish readings in the text.

Conflicts of Interest: Authors must provide a statement on the absence of any financial relationship or conflict of interest with any financial/material support. All financial contributions and sponsorships for the study and all financial relationships and conflict of interest areas should be specified. The authors are responsible for reporting all personal and financial relationships related to the study.

Declaration of conflict of interest should be given at presentation information to the editor. If there is no conflict of interest, this section must include a "The authors declare no conflict of interest" statement.

References

When citing the references, the most recent and current publications should be referred to. References should be numbered consecutively in the order in which they are first mentioned in the text, they should be identified with numerals at the end of the sentence, in brackets before the full stop. When there are six or fewer authors, all author names should be listed. If there are 7 or more authors, the expression "ve ark." should be added to Turkish articles and the expression 'et al.' should be added to English articles after the first 3 authors' names. The number of references should be a maximum of 30 in original articles and review articles, a maximum of 10 in case reports. Names of journals should be abbreviated following the style of Index Medicus. The reference list should be written at the end of the manuscript on a separate page. The authors are responsible for the accuracy of the references.

The reference styles for different types of publications are presented in the following examples.

Journal Article: Author(s)' surname and initial(s) of the first name. Title of the article. Name of the journal abbreviated according to Index Medicus. Year; Volume (Suppl. Supplement number): First and last page number.

Example: Schiroli C, Carugati M, Zanini F et al. Exogenous reinfection of tuberculosis in a low-burden area. Infection 2015; 43:647–653.

Book: Author (s)' surname and initial(s) of the first name. Title of the book. Edition number. City of publication; Publisher, Year of Publication.

Example:

Kleinman CS, Seri I. Hemodynamics and Cardiology. Neonatology Questions and Controversies. 2 nd ED. Philadelphia; PA Elsevier, 2008.

Book Section:

Surname and initial(s) of the first name of the author(s) of the chapter. Title of the chapter. In: Surname and initial(s) of the first name(s) of the editor(s) (ed) or (eds). Title of the book. Edition number. City of publication: Publisher; Year of publication: First and last page numbers of the chapter.

Hamvas A. Pathophysiology and management of respiratory distress syndrome. In: Martin RJ, Fanaroff AA, Walsh MC,

eds. Fanaroff and Martin's Neonatal-Perinatal Medicine Diseases of the Fetus and Infant. 9th ed. St. Louis: Elsevier; 2011.p.1106-16.

Thesis:

Author's surname and initials of the first name. Title of the thesis (thesis). City; Name of the university (if it is a university), Year.

Koç F. Amyotrofik lateral sklerozda klinik bulguların dağılımı (Uzmanlık tezi). Adana; Çukurova Üniversitesi, 1999.

Website:

Name of the web site. Access date. Available from: address of the web site.

Cancer-pain.org New York. Association of Cancer Online Resources. Access date: 16 May 2002. Available from:www.cancer-pain.org

Further detail information on writing other types of references is available on the website International Committee of Medical Journal Editors' (www.icmje.org).

Figures, Tables, Photographs, and Graphics:

All figures, tables, photographs, and graphics should be numbered consecutively in the order they are referred to within the main text, which should be stated at the end of the sentence. A descriptive title must be placed above the tables and abbreviations used in the tables should be defined below the tables by footnotes.

Figures and photographs (saved as either TIFF or JPEG format) should be submitted as a separate file. Images must have a resolution of at least 300 dpi.