Accessory Renal Arteries; Clinical Features and Prognosis in Hypertensive Children

Aksesuar Renal Arterli Hipertansif Çocuklarda Klinik Özellikler ve Prognoz

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ABSTRACT

Objective: Accessory renal arteries may be related to the risk of renovascular hypertension. This study aims to evaluate the clinical course of accessory renal arteries in children with hypertension. We also aimed to compare renal function tests, blood pressure loads, frequency of end-organ damage, and prognosis of hypertensive patients who had detected single and accessory renal artery with Magnetic Resonance Angiography.

Material and Methods: From 01 January 2015 to 31 December 2017 medical records of hypertensive patients were retrospectively reviewed and patients who had been evaluated with Magnetic Resonance Angiography for differential diagnosis of renovascular hypertension were selected. Hypertensive patients with single renal arteries and those who had accessory arteries were compared in the terms of findings Doppler Ultrasound, blood pressure load, and presence of end-organ damage, laboratory investigations, treatment modalities, and prognosis.

Results: Of 49 hypertensive patients who underwent Magnetic Resonance Angiography, 26 (51%) showed accessory renal arteries. Despite the normal Doppler Ultrasound, 13 patients were found to have accessory renal artery with Magnetic Resonance Angiography. There was no significant difference between blood pressure load, and laboratory investigations between the patients with single renal arteries and those who had accessory renal arteries. The frequency of end-organ damage was also similar between both groups at the end of follow-up period as well as the number of medications.

Conclusion: Magnetic Resonance Angiography is more successful than Doppler Ultrasound to detect accessory renal artery. It seems that the presence of accessory renal arteries does not affect the prognosis of the disease.

Key Words: Children, Hypertension, Renal artery

ÖZ

Amaç: Aksesuar renal arterler, renovasküler hipertansiyon ile ilişkili olabilir. Bu çalışma, hipertansiyonlu çocuklarda aksesuar renal arterlerin klinik seyrini değerlendirmeyi amaçlamaktadır. Ayrıca, Manyetik Rezonans Anjiyografi ile tek ve aksesuar renal arter tespit edilen hipertansif çocuk hastaların, böbrek fonksiyon testleri, kan basıncı yükleri, hedef organ hasar sıklığı ve prognozunu karşılaştırmayı amaçladık.

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Gereç ve Yöntemler: Hastanemize 01 Ocak 2015- 31 Aralık 2017 yılları arasında başvuran hipertansif çocuk hastaların tıbbi kayıtları retrospektif olarak incelendi ve renovasküler hipertansiyon şüphesi ile Manyetik Rezonans Anjiyografi ile değerlendirilen hastalar belirlendi. Aksesuar renal arterli ve tek renal arterli hipertansif çocuk hastaların laboratuvar tetkikleri, Doppler Ultrasonografi, kan basıncı yükleri, hedef organ hasarı varlığı, tedavi modaliteleri ve prognozları karşılaştırıldı.

Bulgular: Manyetik Rezonans Anjiyografi yapılan 49 hipertansif hastadan 26'sında (%51) aksesuar renal arterler görüldü. Normal Doppler Ultrasonografi'ye rağmen, 13 hastada Manyetik Rezonans Anjiyografi ile aksesuar renal arter olduğu bulundu. Bununla birlikte, aksesuar renal arterleri olan hastalar ile tek renal arterleri olan hastaların laboratuvar incelemeleri ve kan basıncı yükü açısından anlamlı bir fark yoktu. Takip süresi sonunda hedef organ hasarının sıklığı ve kullanılan ilaç sayısı da her iki grup için benzerdi.

Sonuç: Manyetik Rezonans Anjiyografi, aksesuar renal arteri saptamada Doppler Ultrasonografi görüntülemesi ile elde edilenden daha başarılıdır. Ancak, aksesuar renal arterlerin varlığının hastalığın prognozunu etkilemediği görülmektedir.

Anahtar Sözcükler: Çocuk, Hipertansiyon, Renal arter

INTRODUCTION

Renovascular hypertension was shown to be the cause of almost 10% of childhood hypertension (1). Although the prevalence of primary essential hypertension, mostly in older school-age children and adolescents has increased in parallel with the epidemic of obesity, renovascular diseases remain an important factor leading to hypertension in children. Vascular imaging in the diagnostic evaluation of children with hypertension should be considered once hypertension is confirmed. Initial radiological investigations may include Doppler renal ultrasound, 99mTc dimercaptosuccinic acid (DMSA), and followed by CTA or magnetic resonance angiography (2).

Accessory renal arteries are common in 30% of individuals and originate mostly from the abdominal aorta (3). The casual relationship between accessory renal arteries and hypertension in children is not as definite as it is observed in renal artery stenosis. De Jong et al.(4) have addressed the association between accessory renal arteries and hypertension. Various hemodynamic and biochemical mechanisms have been identified to explain the relationship between accessory renal arteries and hypertension (5). Nevertheless, the role of the accessory renal artery is still not clear. This study aims to determine the importance of accessory renal arteries in the etiology of childhood hypertension and also to compare the performance of MRA and renal doppler ultrasound in regard of detecting accessory renal arteries.

MATERIAL and METHODS

Medical records of hypertensive patients admitted to an outpatient clinic of pediatric nephrology department, in a tertiary referral hospital, from January 1, 2015, to December 31, 2017, were retrospectively reviewed and patients who had evaluated with MRA for differential diagnosis of renovascular hypertension were selected. MRA performed the patients who had treated with more than one antihypertensive drug or who had a suspicion of renal artery stenosis or accessory renal artery on Doppler USG imaging. Patients who were admitted with malignant hypertension, syndromic patients, and patients with any chronic illness were excluded.

Patients' data regarding their age, body mass index (BMI), biochemical analysis of blood and urine, Thyroid stimulant hormone (TSH), free T4, renin and aldosterone levels, results of radiologic studies including abdominal USG and renal Doppler USG as well as renal MRA were recorded. Estimated glomerular filtration rates (eGFR) of hypertensive patients were calculated according to the Schwartz formula. Serum was collected for renin and aldosterone levels when the patient is in the supine position during 8:00 am. Renin and aldosterone levels were studied with the radioimmunoassay method. Clinical symptoms, number of anti-hypertensive medications, and results of ambulatory blood pressure monitoring (ABPM) were also recorded. Clinical characteristics of patients at the last visit, presence of end-organ damage, medications, renal function tests, were also recorded. ABPM was performed on all patients who were hypertensive on casual blood pressure measurements with an appropriate-sized cuff for arm circumference and carried out over 24 hours during the patient's routine workday. Blood pressure was measured every 30 minutes during daytime hours (8 am to 12 pm) and every 60 minutes during nighttime hours (12 pm to 8 am). Based on the ABPMs, we analyzed general 24 h systolic and diastolic blood pressure load (BPL), daytime (8 a.m.-12 p.m.) and nighttime (12 p.m.-8 a.m.) systolic and diastolic BP load, and the number of dipper or non-dipper patients. According to ABPM data diagnosis of hypertension is based on the presence of mean systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) >95 percentile and SBP and/or DBP load > 25% (6). Patients with a nocturnal fall > 10% of the nighttime values were accepted as "dippers" while, patients with a nocturnal fall < 10% of the nighttime values were accepted as "non-dippers" (7).

Digital subtraction angiography (DSA) was performed on the patients who had resistant hypertension despite two antihypertensives.

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee No.2, Ankara City Hospital (07.04.2021-E2-21-311).

Statistical analysis

SPSS v.16 was used for statistical analysis. P< 0.05 was considered statistically significant. Student t test, Mann-

Whitney U test and Chi-Square test were used for inter-group comparisons.

RESULTS

Three hundred and eight patients were referred to our pediatric nephrology clinic with the diagnosis and/or suspicion of hypertension in primary care. Forty-nine (16%) of them were found to have had renal MRA because of hypertension that was resistant to treatment with a single agent and with no definable etiologic factor or who had abnormalities suggesting renal artery stenosis or accessory renal artery in Doppler USG. The mean age of patients was 15.3±2.6 years (median: 16 years) and male/female (M/F) was 31/18. The demographic data and the results of laboratory analysis of blood were all given in Table I.

Among those 49 patients with hypertension, 25 of them (51%) were found to have accessory renal arteries. The mean age of patients with accessory renal arteries was 14.8±2.6 years (median: 15). Fifteen of them were males (M/F: 15/10). The mean follow-up time of hypertensive patients with accessory renal arteries is 29±2.8 months and 23.2±3.1 months for patients with a single renal artery (p >0.05). The demographic data of patients with accessory renal arteries were given in Table I.

Table I: Demographic data and results of blood analysis of the study group, and 25 hypertensive patients with accessory renal arteries.

	(n=49) mean±SD	(n=25) mean±SD	p
Age (years)	15.3±2.6	14.8±1.4	>0.05
BMI	26.4±8.1	25.6±7.4	>0.05
eGFR (mL/min/1.73 m^2)	129.4±35.7	127.5±33.6	>0.05
Creatinine (mg/dL)	0.78±0.11	0.79±0.13	>0.05
Na (mmol/L)	137.4±3.6	137.4±1.7	>0.05
K (mmol/L)	4.1±1.9	4.2±0.9	>0.05
Cl (mmol/L)	102.8±2.8	102.9±2.7	>0.05
WBC (µL)	7.7±1.9	7.9±2.1	>0.05
Hg (g/dL)	14±1.5	14±1.5	>0.05
PLT (µL)	281±65	283.4±59.6	>0.05
TSH (µIU/Ml)	1.89±0.9	1.6±0.7	>0.05
f T4 (ng/dL)	0.83±0.1	0.84±0.1	>0.05
Renin (ng/ml/h)	35.7±41	38.1±49.3	>0.05
Aldosterone (ng/dL)	223.7±165.5	190.1±141.5	>0.05

BMI: *Body mass index;* ***eGFR:*** *Estimated glomerular filtration rate;* ***Na:*** *Sodium;* ***K:*** *Potassium;* ***Cl:*** *Chlorine;* ***WBC:*** *White blood cells;* ***Hg:*** *Hemogram;* ***PLT:*** *Platelet;* ***TSH:*** *Thyrotrophin-Stimulating Hormone;* ***f T4:*** *free T4*

Table II: Results of 24-hour ABPM of patients with renal MR angiography.

	n	General evaluation mean±SD			Daytime mean±SD			Nighttime mean±SD		
		MAP	SBPL	DBPL	MAP	SBPL	DBPL	MAP	SBPL	DBPL
Hypertensive children who had MR angiography	49	130/71	55±23	31±22	135/75	53±25	29±20	116/62	50±20	31±26
Hypertensive children with accessory renal arteries	25	128/71	59±27	35±24	135/75	58±27	34±24	115/63	53±27	33±27
Hypertensive children without accessory renal arteries	24	131/71	50±19	27±19	134/74	48±21	24±15	117/61	46±22	29±25

MAP: *Mean arterial pressure;* ***SBPL:*** *Systolic blood pressure load;* ***DBPL:*** *Diastolic blood pressure load*

Table III: MRA and Doppler USG correlation.

	MR Angiography		Total
	SRA	ARA	
Doppler USG			
SRA	15	13	28
ARA	0	5	5
Suspicion of ARA	9	7	16
Total	24	25	49

SR: *Single renal artery;* ***ARA:*** *Accessory renal artery*

Renin and aldosterone levels of all patients were within the normal range. Renin and aldosterone levels were not significantly different between the two groups.

Age, BMI, eGFR, creatinine, sodium, potassium, chloride, leukocyte, hemoglobin, platelet, TSH, free T4 levels also were not significantly differed between groups ($p > 0.05$).

We have compared to groups in terms of ABPM and there was not any significant difference between groups ($p>0.05$). The results of 24-hour ABPM were given in Table II.

Except one patient with a rotational kidney anomaly; all patients had normal ultrasonographic examination. The DMSA scan of this patient revealed normal separate functions. Other patients had normal urinary tract USG.

Renal Doppler USG revealed a suspicion of the accessory renal artery in 16 patients. However, only the diagnosis of 7 patients was correlated with MRA. Despite the normal Doppler USG, 13 patients were found to have accessory renal artery with MRA (Table III).

Eighteen patients were found to have left ventricular hypertrophy (LVH) and 9 patients have had hypertensive retinopathy. Nine of the patients (50%) with LVH were among patients with accessory renal arteries. Five of the patients with hypertensive retinopathy (55%) were found to have accessory renal arteries. The difference between the groups regarding the frequency of end-organ damage was not found to be statistically significant. Proteinuria was not detected in any of our patients.

The mean follow-up time of hypertensive patients with accessory renal arteries is 29±2.8 months and 23.2±3.1 months for patients with a single renal artery. During this time only 4 of them (16%) underwent Digital subtraction Angiography (DSA) because of hypertension which was difficult to treat. All of the patients' DSA were normal.

No patient required surgical intervention. Five of 25 (20%) patients with accessory renal artery and 8 of 24 (33%) patients with a single renal artery were not receiving any antihypertensive drug at the last visit ($p>0.05$). Sixteen patients (64%) with accessory renal arteries and 11 (45%) patients with single renal artery were on treatment with a single antihypertensive drug ($p>0.05$). Four (16%) patients with accessory renal arteries and 5 (20%) patients with single renal arteries were found to be treated with multiple drugs ($p>0.05$). Eight (32%) of patients with accessory renal arteries and 8 (33%) of patients with a single renal artery had LVH at the last visit ($p>0.05$). Two patients in both groups were found to have hypertensive retinopathy at the last control ($p>0.05$).

DISCUSSION

The renal arteries usually originate from the abdominal aorta. In general, each kidney receives a single renal artery (5). Different origins of renal arteries are the most frequent renal vascular anomaly in the general population (6). The frequency of extrarenal arteries reported as much as 35% among the normal population (3,7). In this study, we detected accessory renal arteries in 51% of hypertensive patients. Accessory renal arteries were found to be significantly more prevalent in our hypertensive patients compared to the normal population. We also found that accessory renal arteries were more frequently located on the left side which is convenient with the literature (5).

In terms of diagnosis, there are many types of imaging techniques, such as Doppler USG, Computed Tomography Angiography (CTA), MRA, and DSA (1,8). Doppler USG is a widely available, noninvasive, repeatable, relatively inexpensive, and extremely safe imaging method for the measurement of renal blood flow. Moreover, Doppler USG does not have ionizing radiation. However, despite the use of multiple views, and the experience acquired with practice, accessory renal arteries as well as renal arterial stenosis can be missed by Doppler USG (1). In our study 13 patients who had had normal renal Doppler USG examination were detected to have accessory renal arteries on MRA (Table III). The possibility of detecting the accessory renal artery by renal Doppler USG was considerably lower than MRA.

It is claimed that the accessory renal artery increases the risk of developing hypertension (9). Paige VA et al.(3) have found that 59% of adult patients with resistant hypertension had accessory renal arteries compared to 32% of healthy transplant donors. More studies are confirming this association and proposing that accessory renal arterial stenosis may cause renal ischemia and renin-dependent hypertension (3, 9, 10). Kem et al.(11) have hypothesized that hyperreninism results from inadequate vessel size. High plasma renin activity may accompany accessory renal artery and hypertension (10).

In our study we did not find any difference in terms of renin and aldosterone levels, between hypertensive patients who have an accessory or single renal artery. Glodny B. et al. (10), have shown that plasma renin response to furosemide stimulation in patients with multiple renal arteries was only slightly greater

than the controls. However, in the same study, it was found that plasma renin activity was significantly higher in patients with multiple arteries. It also should be emphasized that they selected patients with imaging evidence of eccentric or concentric narrowing of the accessory renal artery by more than 30% (10). Our results could be affected by antihypertensive medications of patients and/or technical difficulties in measuring plasma renin activity.

Accessory renal arteries usually do not have any impact on the function of the kidneys or any other clinical manifestation. In this study, no significant difference was found between the two groups in terms of renal function tests, serum levels of renin and aldosterone, and results of ABPM as well as estimated GFR. Surprisingly, blood pressure load did not differ between both groups and probably could not be used as a clue to predict the presence of accessory renal arteries. Regarding end-organ damage, we also did not find any difference between the groups. However, studies with a higher number of patients should be conducted to get more precise results.

Some adult studies are demonstrating that patients with multiple renal arteries have a significantly higher blood pressure than patients with normal renal anatomy (3,7,9,10). However, the prognosis of those patients has not been studied well. In our study, we followed-up with our patients for approximately 2 years. At the end of 2 years of follow-up, we did not find any difference regarding the number of medications and frequency of end-organ damage. Five of our patients with accessory renal arteries are free of drugs and 16 of them are still treated with one antihypertensive drug at the end of 2 years. These results did not differ from patients with single renal arteries.

We also conclude that the prognosis of patients with accessory renal arteries is as good as those with a single renal artery. We wanted to draw attention to the fact that the role of renal Doppler USG is quite weak in the detection of the accessory renal artery. However, more evidence is needed to determine the impact of the accessory renal artery on hypertension. To detect the prognosis of the patients with accessory renal arteries and the need for surgical intervention prospective studies with a large number of patients are required.

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Konuşma Geriliği Etiyolojisinde Rol Oynayan Faktörlerin Çocuk Nörolojisi Perspektifinden İncelenmesi

Examining the Factors Playing A Role in The Etiology of Speech Retardation from the Perspective of Child Neurology

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ÖZ

Amaç: Konuşma ve dil gelişimi nöromotor gelişimin bir parçadır ve yaşa uygun gelişim basamaklarını kazanamama organik etiyolojilerle ilişkili olabilmektedir. Zamanında fark edilmeleri ve tanı almaları, zamanında tedavi edilmeleri açısından önemlidir. Bu çalışmada; konuşamama- konuşma geriliği yakınmasıyla çocuk nöroloji polikliniğine başvuran çocukların etiyolojik nedenlerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Temmuz 2011 ve Temmuz 2014 arasında, Samsun Kadın Hastalıkları Doğum ve Çocuk Hastanesi ve Özel Medikal Park Samsun Hastanesi, Çocuk Nörolojisi Polikliniği'ne konuşamama-konuşma geriliği şüphesiyle başvurmuş hastaların verileri retrospektif olarak incelenmiştir.

Bulgular: Çalışmaya alınan 348 hastanın %25.7'si kız (n=89), %74.3'ü erkekti (n=259) ve yaş ortalaması 41.3±15.6 ay (min 14 ay, maksimum 91 ay) olarak saptanmıştır. Çocukların %61'inin ikinci sırada doğduğu, %11.2'inde prematürite öyküsü olduğu ve %42'inde ailede konuşma geriliği olan başka birey olduğu saptanmıştır. Hastaların %32.7'sinde elektro ensefalografilerinde epileptik bozukluk, %21'inde otizm açısından yüksek risk ve %6.5'inde işitme kaybı olduğu görülmüştür. Denver II gelişim testi sonucunda hastaların %20.7'sinde gelişimsel dil geriliği, %52.2'inde ise global gelişme geriliği olarak adlandırılan, gelişim basamaklarının iki ve daha fazla alanında gerilik olduğu görülmüştür. Beyin manyetik rezonans görüntüleme ile %4 oranında anormallik olduğu görülmüştür.

Sonuç: Konuşma geriliği şüphesiyle başvuran çocuklarda öykü, fizik muayene, tarama testleri ve tanısal testlerden oluşan ayrıntılı bir tanısal yönetim yaklaşımının benimsenmesi, sadece konuşma geriliğinin düzeltilmesi için değil, aynı zamanda altta yatan global gelişme geriliği, epileptik bozukluk, otizm ve işitme kaybı gibi klinikopatolojik durumların erken tanısı ve tedavisi açılarından da önemlidir.

Anahtar Sözcükler: Çocuk, Epilepsi, Global gelişme geriliği, Konuşma geriliği, Otizm, Sağırlık

ABSTRACT

Objective: Childhood speech retardation can have significant negative effects on a child's personal, social and later academic and professional life. Determining the risk groups of retardation is important in terms of timely recognition and diagnosis. In this study, it was aimed to reveal the causes of children who applied to our clinic with speech retardation.

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Material and Methods: Between July 2011 and July 2015, data of pediatric patients aged 1-12 years, who were diagnosed with speech retardation and who were admitted to the Pediatric Neurology Outpatient Clinic of Samsun Obstetrics and Gynecology Hospital and Private Medical Park Samsun Hospital, were analyzed retrospectively. analyzed. Descriptive statistics were given as mean, standard deviation and proportions.

Results: Of the 348 patients included in the study, 25.7% were female (n=89), 74.3% were male (n=259), and the mean age was 41.3±15.6 months (min 14 months, maximum 91 months). It was determined that 61% of the children were born in the second row, 11.2% had a history of prematurity, and 42% had another family member with speech retardation. Epileptic disorder was observed in 32.7% of the patients, high risk for autism in 21%, and hearing loss in 6.5%. As a result of the Denver II developmental test, it was observed that 20.7% of the patients had developmental language retardation and 52.2% had retardation in two or more areas of developmental stages, which was called global developmental delay. Brain magnetic resonance imaging showed 4% abnormality.

Conclusion: The adoption of a detailed diagnostic management approach consisting of history, physical examination, screening tests and diagnostic tests in children presenting with suspicion of speech retardation, not only for the correction of speech retardation, but also for early clinicopathological conditions such as underlying global developmental delay, epileptic disorder, autism, and hearing loss. It is also important in terms of diagnosis and treatment.

Key Words: Child, Epilepsy, Global developmental delay, Speech retardation, Autism, Deafness

GİRİŞ

Zamanında konuşma ve dil yeteneği kazanımı bir çocuğun gelişimini gösteren önemli belirteçlerden biridir (1). Konuşma geriliği çocuğun konuşmasının yaşı için beklenenden daha az akıcı olması veya yaşıyla uyumsuz derecede fazla konuşma ve ses hataları içermesi durumu olarak tanımlanır (2,3). Tanı ve tedavi almamış konuşma geriliklerinin yüzde 40-60 oranında kalıcı olabildiği ve bu çocukların sosyal, duygusal, davranışsal ve zihinsel problemler yaşama riskinin diğer çocuklara göre daha yüksek olduğu gösterilmiştir (4,5). Bununla birlikte, çoğu zaman bu durum aileler tarafınca bir problem olarak görülmemekte ve konuşma geriliğinin zamanın geçmesiyle kendiliğinden düzeleceğine inanılmaktadır. Bu geleneksel bakış açısı nedeniyle konuşma gerilikerinin prevalansını doğru olarak tahmin edebilmek de güçtür. Ayrıca, bu bakış açısı nedeniyle tanıda gecikmeler yaşanmakta, bu da tedavide gecikmeye neden olmaktadır.

Konuşma gerilikerinin zamanında tanı alması altta yatabilen olası nedenlerin zamanında saptanması ve tedavi edilmesi açısından da önemlidir. İşitme kaybından epileptik bozukluğa kadar geniş bir yelpazeye yayılan tıbbi risk faktörleri ve nedenlere ek olarak ailesel ve çevresel nedenler de konuşma bozuklukları ile ilişkilendirilmiştir (6). Bu nedenlerden bazıları "geri çevrilemez" nedenlerken, epileptik bozukluk ve orofaringeal anatomik deformiteler gibi bazı tıbbi nedenler ve çevresel nedenler "geri çevrilebilir" niteliktedir.

Nedene yönelik araştırmaların önemli olmasına karşın gerek dünyada, gerekse de ülkemizde bu konu ile ilgili literatür çok sınırlıdır (6,7). Bu çalışmada, konuşma geriliği nedeniyle başvuran çocuklarda etiyolojik araştırma sonucunda elde dilen veriler ışığında ilgili literatüre katkı yapılması amaçlanmıştır.

GEREÇ ve YÖNTEMLER

Temmuz 2011 ve Temmuz 2014 arasında, Samsun Kadın Hastalıkları Doğum ve Çocuk Hastanesi ve Özel Medikal Park Samsun Hastanesi, Çocuk Nörolojisi Polikliniği'ne konuşamama-konuşma geriliği şüphesiyle başvuran, 14-91 ay aralığındaki çocuk hastaların verileri Samsun Eğitim Araştırma Hastanesi, Etik Kurulu' ndan onay (06/2011-191723) alındıktan sonra retrospektif olarak incelenmiştir. Tüm hastaların ebeveynlerinden onam alınmış; yakını onam vermeyen hastalar çalışmaya dahil edilmemiştir.

Tüm hastalar, kliniğimizde rutin olarak uygulanan standart protokol çerçevesinde değerlendirilmiş ve tüm veriler hasta dosyalarına kaydedilmiştir. Ayrıntılı bir anamnez alınmış, fizik muayene ve nörolojik muayene yapılmıştır. Özgeçmiş ve soygeçmişinde: annenin hamilelik sırasında geçirdiği hastalıklar, perinatal travma, infeksiyonlar, doğumda asfiksi, doğumda gebelik haftası, hastanın ailenin kaçıncı çocuğu olduğu, doğum ağırlığı, çocuğun tıbbi hikayesi, ototoksik ilaç kullanımı hikayesi, psikososyal öykü, yeterli/yetersiz uyarılma durumu, çocukla konuşulan dil veya diller, ailede önemli hastalık öyküsü, ailede konuşma geriliği öyküsü sorgulanarak elde edilen bilgiler kaydedilmiştir.

Fizik muayenede çocuğun boyu, ağırlığı ve baş çevresi ölçülmüştür. Genel fizik muayenede saptanan dismorfik özellikler ve anormal bulgular kaydedilmiştir. Görme ve işitme değerlendirmelerini içeren nörolojik muayene yapılmıştır.

Konuşma geriliği genel zihinsel geriliğin bir göstergesi olabildiği için tüm hastaların gelişimleri "Denver Developmental Screening Test II" (Denver Gelişimsel Tarama Testi II) kullanılarak değerlendirilmiştir. Yaşı 72 ayın üzerinde olan 9 hasta ise konuşma yeteneği açısından "Peabody Picture Vocabulary Test-Revised" ile değerlendirilmiştir.

0-36 ay arasındaki hastalar Çocukluk Dönemi Otizm Tarama Ölçeği (M-CHAT) ve 36 aydan büyük hastalar da ODKL (Otizm Davranış Kontrol Listesi) ile değerlendirilmiştir.

Konuşamama- konuşma geriliği şüphesiyle başvuran tüm hastalardan kulak-burun-boğaz (KBB) konsültasyonları istenmiş, odyometri ve timpanometri testleri yapılmıştır.

Tüm hastalara intrakraniyal patolojileri dışlamak için elektroensefalografi (EEG) ve beyin manyetik rezonans (MR) görüntülemesi yapılmıştır.

Veri analizi için Statistical Package for Social Sciences (SPSS) yazılımı (v17) ile birlikte Microsoft Excel programı kullanılmıştır. Tanımlayıcı istatistikler ortalama, standart sapma ve oranlar şeklinde verilmiştir.

BULGULAR

Bu çalışmaya konuşamama-konuşma geriliği yakınması ile polikliniğimize gelen tüm hastalar dahil edilmiştir. Çalışmada yer alan 348 hastanın %25.7'si kız (n=89), %74.3'ü erkekti (n=259) ve yaş ortalaması 41.3±15.6 ay (min 14 ay, maksimum 91 ay) olarak saptanmıştır. Sadece dokuz hasta 72 aydan büyük olduğu için Denver II gelişimsel tarama testi yapılamamıştır. Çocukların %61'i (n=210) ailenin ikinci çocuğu olduğu öğrenilmiştir. Prematüre doğum veya düşük doğum ağırlığı öyküsü %11.2 çocukta saptanmıştır. Hastaların %42'nin (n=145) ailesinde konuşma geriliği olan başka bir birey olduğu öğrenilmiştir. Yapılan testler sonucunda hastaların %32.7'sinde (n=113) elektoensefalografide epileptik bozukluk, %21'inde (n=72) otizm açısından yüksek risk ve %6.5'inde (n=22) işitme kaybı olduğu görülmüştür. Uygulanan Denver II gelişim testi (n=339) sonucunda hastaların %20.7'sinde gelişimsel dil geriliği saptanmıştır. Hastaların %52.2'inde ise (n=177) global gelişme geriliği olarak adlandırılan, gelişim basamaklarının iki ve daha fazla alanında gerilik olduğu görülmüştür. Test sonucu %27.1 (n=92) hastada normal bulunmuştur. Gelişimsel dil geriliği olan hastalar kendi içinde değerlendirildiğinde, %6.5'inde (n=22) ifade edici dil geriliği, %14.2'inde (n=48) hem ifade edici, hem de alıcı dil geriliği saptanmıştır. Beyin manyetik rezonans görüntüleme ile %4 oranında anormallik olduğu görülmüştür. Hastaların demografik bilgileri ve altta yatan nedenlere göre dağılımı Tablo I'de gösterilmiştir.

Tablo I: Hastaların demografik bilgileri ve altta yatan nedenlere göre dağılımı.

Değişkenler	Sonuç
Yaş (en büyük-en küçük)	41.3±15.6 ay (14-91 ay)
Cinsiyet, n (%)	
Erkek	259 (74.3)
Kız	89 (25.7)
Altta yatan neden,n (%)	
İşitme kaybı	22 (6.3)
Global gelişme geriliği	177 (%52,2)
Epileptik bozukluk	113 (32.7)
Yüksek otizm riski	72 (21.0)
Düşük doğum ağırlığı/preterm doğum	10 (2.8)
Orofaringeal deformite	5 (1.4)
Multilingual aile ortamı	25 (7.1)
Aile öyküsü	145 (42.0)
Perinatal travma/ doğumda asfiksi	100 (28.6)
Kronik gürültü	58 (16.7)
Yetersiz uyarılma	133 (38.1)
Doğum sırası(birth order), n (%)	
Birinci	69 (19.5)
İkinci	210 (61.0)
Daha sonraki sıradaki çocuğu	69 (19.5)

TARTIŞMA

Dil, iletişim amacıyla kullanılan, düşünceleri simgeleyen, uzlaşmaya dayalı biçimlerden oluşan bir dizgedir. İnsanlarda bilişsel ve sosyal gelişimin temel öğesi olarak kabul edilen dil gelişimi; genetik, çevresel, kültürel faktörlerin etkileşimi ile şekillenen kompleks bir kognitif süreç olarak tanımlanmaktadır (8). Konuşma ise fonasyon ve artikülasyondan oluşan bir eylem olup, insanlar arasındaki sözel iletişimin en önemli öğesidir ve konuşmaya iletişim diyebilmek için konuşan ve dinleyenin birbirini anlayabilmesi gerekmektedir (9). Gelişimsel olarak bir çocuğun 12. ayında anne ve baba kelimesi yoksa, iki yaşında iki kelimeyi birleştiremiyorsa ya da üç yaşında üç kelimeli cümle kuramıyor veya anlaşılmaz konuşuyorsa konuşma geriliği açısından değerlendirilmesi önerilmektedir (10). Sunderajan ve ark. (6) yaptıkları çalışmada konuşma geriliği saptadıkları çocukların yaş ortalamasını 65.9 ay (5.5 yaş) olarak belirlemiştir. Bu çalışmada hastaların yaş aralığı 14-91 ay, ortalama 25.7-56.9 ay olarak bulunmuştur. Hastaların büyük çoğunluğunda konuşma gecikmesinin geç fark edildiği görülmüştür. Bu durum; hastaların çok sık doktor tarafından görülmelerine rağmen, genel pediatri pratiğinde öncelikli olarak fizik gelişim ile ilgilenildiği ve dil gelişim basamaklarının yeterli değerlendirilmemesi ile ilişkili olarak açıklanmıştır.

Her bireyin motor ve zeka kapasitesi değişiklik göstermektedir. Bu durum konuşmanın başlama zamanı, hızı ve diğer parametrelerinde etkilidir. ABD'nde okul öncesi çocukların %8'i konuşmasının gecikmesi yönünden kalıtsal etkiye sahip olduğunu gösteren bir çalışma yayınlanmıştır (11). Gelişmiş ülkelerden yapılan benzer yayınlarda da bu oranın yüzde 2-8 aralığında olduğu bildirilmiştir (1,12). Başka bir çalışmada da okul öncesindeki 2-5 yaş arasında çocuklarda sadece konuşma kazanımının gecikmesi %2.53 oranında olduğu bulunmuştur (6). Primer dil ve konuşma problemlerinin nedeni konusunda fikir birliğine varılmamış olsa da, bazı risk faktörleri belirtilmiştir. Cinsiyet, bir risk faktörü olarak bilinmektedir (10, 13). Erkeklerde üç kat fazla risk olduğu bilinmektedir. Bu çalışmalar söz konusu bulguyu erkek çocuklarda santral sinir sisteminin kız çocuklarına göre daha geç matüre olmasına bağlamıştır. Ayrıca, ailede konuşma gecikmesi yaşamış bireylerin olması bu riski iki katına çıkarmaktadır (14). Bir diğer risk faktörü ise düşük doğum ağırlığı ve erken doğum olarak belirlenmiştir. İdeal doğum ağırlıklarının %85'inden daha düşük ağırlıkla doğan çocuklarda veya 37 gestasyonel haftadan erken doğan çocuklarda dil ve konuşma gecikmesi riski iki kat fazladır

(11). Bunların yanı sıra çocuğun zeka kapasitesi, sosyal çevresi, ailenin sosyoekonomik durumu, kardeş sayısı, çocuğun kişiliği, çocuğa bakan kişinin tutumu ve eğitim durumu gibi birçok neden konuşma ve dil gelişimi üzerine etki göstermektedir (6). Bizim çalışmamızda da erkek çocuklarında konuşma gerilikleri kızlardan 3 kat daha fazla sıklıkta gözlenmiştir; hastaların yüzde 74'ünün erkek olduğu saptanmıştır. Ayrıca çalışmamızda hastaların yüzde 6.5'inde ifade edici dil geriliği, yüzde 14'ünde ise hem ifade edici hem alıcı dil geriliği saptanmıştır. Dahası hastaların %42'inde aile öyküsü saptanmış olup bu bulgular da literatür ile uyumludur (15). Biz çalışmamızda ebeveynlerin eğitim düzeylerini incelemedik. Ancak ebeveynlerin eğitim düzeyinin ve sosyoekonomik seviyelerinin düşük olmasının diğer bir risk faktörü olan yetersiz uyarılma ile birebir ilişkili olduğuna inanıyoruz. Bu düşüncemiz ile uyumlu olarak, Sidhu ve ark.(1) eğitim seviyesi yüksek olan ebeveynlerin hem çocuklarıyla daha çok verimli zaman geçirdiklerini, hem de bu süre içinde diğer ebeveynlere göre daha çeşitli ve kompleks kelimeler kullanarak çocuğa konuşma gelişimi açısından daha zengin uyaranlar verdiklerini belirtmiştir.

Konuşma geriliklerinin nedenlerini inceleyen çalışmalarda doğum asfiksisi, epileptik bozukluk ve orofaringeal deformitelerin belirgin risk faktörleri olduğu ileri sürülmektedir (6). Bir diğer çalışmada da doğum asfiksisi ile konuşma geriliği arasında güçlü bir bağ olduğu vurgulanmıştır (16). Konuşma geriliğinde EEG'nin tanı değerini araştıran çalışmalarda, dil gelişimini daha iyi anlamak için EEG'nin önemine dikkat çekilmiş, farklı analiz yöntemleri önerilmiştir (17). Ayrıca, konuşma merkezindeki epileptik deşarjların da konuşmayı engelleyebildiği, epileptik atak esnasında santral sinir sisteminin hipoksik kalmasının negatif yönde etkisinin olabileceği ve kazanılmış epileptik afazi olan Landau-Klefner sendromundaki afazinin bu şekilde gelişebileceği öne sürülmüştür. Konuşma gecikmesindeki epileptik bozukluğun, LKS'daki fizyopatolojik mekanizmalara benzediği ancak konuşmanın kazanılmasından önce oluştuğu düşünülmektedir. Epileptik deşarj anında nöron fonksiyonlarının sürdürülemediği bilinmektedir. Dominant hemisferdeki epileptik deşarjların sözel görevleri, non-dominat hemisferdeki epileptik deşarjların ise sözel olmayan görevleri algılamada- uygulamada bozukluk yarattığı saptanmıştır (18). Bir çalışmada, konuşma geriliği olan disfazik çocuklardaki epileptik bozukluk oranı %8 bulunmuş, genel nüfustaki oranın çok üstünde olduğu görülmüştür. Aynı çalışmada, regresyon gösteren hastalarda bu oran %36, epileptik afazi olarak adlandırılan, en yaygın konuşma bozukluğu olan LKS'da ise %58 saptanmıştır (19). Aboufaddan ve ark. (20) konuşma geriliği teşhisi koydukları çocukların yüzde 6.7'sinde epileptik bozukluk saptamışlar ve tahmini rölatif riski (Odds oranı) 5.28 olarak hesaplamışlardır. Bu çalışmada, herhangi bir nöbet geçirme öyküsü olmayan hastalarda, EEG'de %32 oranında epileptik bozukluk saptanmış ve 3/4'ünün sol hemisferde olduğu görülmüştür. Antiepileptik ilaç tedavisi (lamotrigine, valproik asit) ile deşarjlar kontrol altına alınmış ve hastaların %60'ında yaşa uygun konuşma kazanılmıştır. Çalışmamızda orofaringeal deformiteler ise yüzde 1.4 ile düşük oranda saptanmıştır.

Literatürdeki bazı çalışmalar işitme kaybı ile konuşma geriliği arasında güçlü bir neden-sonuç ilişkisi olduğunu bildirmişlerdir (21). Bununla birlikte aksi yönde bulguları olan çalışmalar da mevcuttur (22). Aslında hayatın ilk yıllarında sağlam bir işitme duyusunun olmasının konuşma yeteneğinin gelişmesinde kritik bir rol oynadığı bilinen bir gerçektir (10). Bu bilgi ile uyumlu bir şekilde biz de çalışmamızda hastaların %6.3'ünde işitme kaybı olduğunu belirledik. Bizim düşüncemize göre literatürde bu konuda farklı verilerin olmasının nedeni hastalara yaklaşımdaki farklılıklar olabilir. Biz kendi pratiğimizde konuşma geriliği tanısı koyduğumuz her hastamızı işitme ile ilgili bir yakınma kendisi veya ailesi tarafınca ifade edilsin veya edilmesin, hastanın konuşma geriliğine neden olduğuna inandığımız başka bir klinikopatolojik durumu olsun veya olmasın, işitme açısından değerlendirdik. Bu değerlendirmenin odyometri ve beraberinde timpanometriyi de içerecek şekilde ayrıntılı yapılmış olması da gözden kaçabilecek işitme bozukluklarını teşhis etmemizi sağlamış olabilir. Bu nedenle bizim saptadığımız işitme kaybı oranları, benzer yaklaşım göstermeyen otörlerin bildirdiği oranlardan daha yüksek çıkmış olabilir. Konuşma geriliği tanısı koyduğumuz hastaları işitme açısından ayrıntılı bir değerlendirmeye tabi tutmuş olmamızın bir diğer faydası da hastalarda seröz otitis media (%6.3) saptanmış olması ve hastaların bu hastalık açısından tedavilerine KBB kliniğinde başlanmış olmasıdır. Literatürde de benzer bir şekilde konuşma geriliği ile başvuran çocuklarda altta yatan nedenlerden biri olarak persistan otitis media (%4.8) tanısı konulduğunu bildiren çalışmalar mevcuttur (6).

İşitsel uyaranların kodlanması ve özellikle konuşmanın temporal işlemlenmesinde bozukluk ile seyreden işitsel nöropati hastalıkları, izole olarak görülebileceği gibi Charcot-Marie-Tooth hastalığı, Friedreich Ataksisi, Mohr-Traneberg sendromu, otozomal dominant optik atrofi tablosunun bir parçası da olabilmektedir. Hastaların %40'ında genetik faktörlerin suçlanırken, edinsel sebepler arasında hiperbiluribinemi ilk sırada, anoreksi, viral enfeksiyonlar, demiyelinizan hastalıklar, ilaç reaksiyonları, Guillan-Barre gibi diğer polinöropatiler ve otoimmün hastalıklar da sıralanmaktadır. Bu hastaların sadece %5'inde dil ve konuşma normal olarak gelişmektedir ve bu nedenle de multisipliner yaklaşım (KBB uzmanı, Pediatrik Nörolog, odyolog, konuşma ve dil patoloğu) uygulanmalıdır (23). Bu çalışmada nörolojik muayene ve beyin MR bulgularında işitsel nöropati bulgularına rastlanılmamıştır.

Global gelişme geriliği ve yüksek otizm riski çalışmamızda yüzde %52.2 ve %21 oranlarında saptanmıştır. İki veya daha fazla alanda gelişme geriliği olarak da tanımlanan global gelişme geriliğine ait bu yüksek oranı; uyaran eksikliğine bağlı hafif zihinsel geriliğin, düşük sosyoekonomik düzey ve yetersiz beslenme gibi etkenlerin de katkısıyla toplumda azımsanmayacak bir oranda yaygın olmasıyla açıkladık. Yapılan bir çalışmada, global gelişme

geriliğinin, konuşma geriliği olan çocuklarda kayda değer oranlarda sık olduğu ve daha çok erkek çocuklarda gözlenen bir durum olduğu belirtilmiştir (21). Yine aynı yazarlar otizmin nörolojik temelli bir gelişimsel hastalık olduğunu, konuşma geriliği veya anormal dil gelişimi olan çocuklarda mutlaka akla getirilmesi gerektiğini belirtmişlerdir. Zihinsel geriliğin X'e bağlı kromozom anomalilerinde sık olduğu bilindiğinden, erkeklerde zihinsel geriliğe bağlı konuşma ve dil gelişimi geriliği daha sık görülmektedir. Ayrıca serebral palside de %65 zihinsel gerilik, %46 epilepsi, %15 sensörinöral işitme kaybı olduğu için dil gelişimi geri kalmaktadır (24). Çalışmamızda M-CHAT ve ODKL testleri kullanılarak hastalar otizm riski açısından değerlendirilmiş ve orta ile yüksek risk taşıdığı düşünülen hastalar çocuk ruh sağlığı kliniğine yönlendirilmiştir.

Dilin öğrenilmesi döneminde iki ayrı dil öğrenimine maruz kalan çocuklarda iki dilin birbirine karıştırılması (çift dillilik) gözlenebilmektedir ama bu durum dil gelişimi arttıkça kaybolmaktadır. Bu çocuklar beş yaşından önce her iki dili de öğrenmektedir ancak erken çocukluk döneminde konuşma ve dilin gelişiminde gecikme yaşayabilmektedir. Çift dilli çocukların tek dille yetişenlere oranla kavramsal esneklik açısındandaha avantajlı olduğu düşünülmektedir (25, 26). Bu çalışmada ailelere bu açıdan değerlendirme yapılmamış ve çalışmanın eksik yönlerinden biri olarak kabul edilmiştir.

Sunderajan ve ark.(6) kronik gürültü maruziyetininin konuşma bozukluğu açısından bir çevresel risk faktörü olmadığını saptamışlardır. Bizim hasta grubumuzda ise kronik gürültü maruziyeti yüzde 16.7 oranında görülmüştür. Ancak ilk planda çelişkili gibi görünen bu bulgular değerlendirilirken, bizim çalışmamızda işitme kaybının yüzde 6.3 oranında bulunmasına karşın, Sunderajan ve ark.'nın (6) çalışmasında bu oranın yüzde 2.4 ile sınırlı kaldığını akılda tutmak gereklidir.

Çalışmamızın sonuçları değerlendirilirken akılda tutulması gereken bazı zayıflıkları mevcuttur. Birincisi, çalışmamız retrospektif bir çalışmadır. İkincisi, bir kontrol grubu olmadığından karşılaştırmalı analizler yapma imkanı olmamıştır. Üçüncüsü, hasta sayısı relatif olarak düşüktür. Ayrıca hastaların nedensel araştırma sonrası takip bilgileri eksiktir; bu araştırmaların sonucunda hem bulunan nedenler açısından, hem de konuşma geriliğinin kendisi açısından hastaların nasıl bir prognoz gösterdiği bildirilmemiş, nedensel araştırmanın getirdiği yararlar somut bir biçimde ortaya konmamıştır. Ancak teorik olarak bu araştırmaların ortaya çıkardığı klinikopatalojik durumların en azından bazılarının geri çevrilebilir ve tedavi edilebilir durumlar olduğu açıktır. Bu nedenle zayıflıklarına rağmen çalışmamız çocuklarda konuşma geriliklerinin hem hastaların aileleri, hem de hastayı gören klinisyenler tarafınca zamanında önemsenmesinin ve nedene yönelik araştırmaların belirli bir algoritmaya göre yapılmasının gerekli olduğu sonuçlarına varmaktadır.

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Orta-Ağır Bronkopulmoner Displazide Tek Merkez Deneyimi: Antenatal ve Postnatal Risk Faktörleri

Antenatal and Postnatal Risk Factors for Bronchopulmonary dysplasia: Single-center Experience

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ÖZ

Amaç: Bronkopulmoner displazi (BPD), çok düşük doğum ağırlıklı her üç bebekten birini etkileyen uzun dönem ciddi olumsuz sonuçları olan bir prematüre morbiditesidir. Bu çalışmada orta-ağır BPD için antenatal ve postnatal risk faktörlerini araştırmayı amaçladık.

Gereç ve Yöntemler: Tek merkezli retrospektif kohort çalışmada Ocak 2014-Aralık 2018 tarihleri arasında doğan <32 hafta ve <1500 g bebekler dahil edildi. Orta-ağır BPD tanılı hastalar çalışma grubunu, hafif BPD ve BPD tanısı olmayan hastalar kontrol grubunu oluşturdu. Her iki grup antenatal ve postnatal özellikleri açısından karşılaştırıldı.

Bulgular: 626 bebekten oluşan kohortun ortalama gestasyonel yaş ve doğum ağırlığı sırasıyla 28±1.4 hafta ve 1084±225 g'dı. Orta-ağır BPD tanılı 97 bebeğin (%15.4) ortalama gestasyonel yaş ve doğum ağırlıkları, kontrol grubuna göre anlamlı olarak düşük saptandı (27±1.5 ve 28.3±1.7 hafta; 933±201 ve 1108±256 g sırasıyla; p<0.001). Doğum salonunda ileri canlandırma (OR 2.64, CI [1.57-4.4]), gestasyonel yaş (OR 0.80 CI [0.67-0.95]), hemodinamik anlamlı patent duktus arteriozus (haPDA) (OR 1.78 CI [1.05-3.03]) ve geç tam enteral beslenme (OR 1.05 CI [1.02-1.08]) orta/ağır BPD ile ilişkili bulundu.

Sonuç: Doğum salonunda ileri canlandırma, düşük gestasyon haftası, haPDA ve geç tam enteral beslenme BPD ile ilişkili bulunmuştur. Ancak tam enteral beslenmeye geçiş süresi ve haPDA ile BPD ilişkisinin neden sonuç mu, yoksa BPD'ye gidiş sürecindeki hastalık durumunun bir parçası olup olmadığının ortaya çıkarılması için geniş çaplı prospektif çalışmalara ihtiyaç olduğu düşünülmüştür.

Anahtar Sözcükler: Bronkopulmoner displazi, Enteral beslenme, Prematürite

ABSTRACT

Objective: Bronchopulmonary dysplasia (BPD) is the chronic lung disease of prematurity that affects a substantial proportion of extremely preterm infants. We aimed to find out the antenatal and postnatal risk factors for BPD in a large-scale cohort of preterm infants.

Material and Methods: Records of preterm infants born <32 gestational weeks and <1500 g were included in this single-center retrospective study that was performed between January 2014 and December 2018. While babies with moderate and severe BPD constituted the study group, the control group included those with mild BPD and without BPD. Groups were compared in terms of antenatal and postnatal risk factors.

Results: In the final analysis, data of 626 infants were recorded. The mean gestational age and birth weight of the whole cohort were 28±1.4 weeks and 1084±225 g, respectively. Ninety-seven (15.4%) infants in the study group had

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Yazarların katkısı / Contribution of the Authors*: *ÖZER BEKMEZ B: Araştırma/çalışmanın sorumluluğunu üstlenmek, ilerlemenin seyrini denetlemek, Çalışma için gerekli literatür taramasında sorumluluk almak, Çalışmanın bütününün veya önemli bölümlerinin yazımında sorumluluk almak. ***BÜYÜKTİRYAKİ M:*** Hasta takibinde sorumluluk almak, ilgili biyolojik malzemelerin toplanması, veri yönetimi ve raporlama, deneylerin yürütülmesi. ***SARI FN:*** Araştırma ve/veya makalenin hipotezini veya fikrini oluşturan. ***ALYAMAÇ DİZDAR E:*** Sonuçlara ulaşmak için planlama/metodoloji belirleme. ***TAYMAN C:*** Sonuçların mantıksal olarak yorumlanması ve sonuçlandırılması. ***OĞUZ ŞS:*** Yazım ve dilbilgisi dışında bilimsel olarak gönderilmeden önce makaleyi gözden geçirme.

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significantly lower gestational age and birth weight compared to those in the control group (27±1.5 vs 28.3±1.7 weeks, and 933±201 vs 1108±256 g respectively, p<0.05). Extensive resuscitation in the delivery room (OR 2.64, CI [1.57-4.4]), low gestational age (OR 0.80 CI [0.67-0.95]), hemodynamically significant patent ductus arteriosus (hsPDA) (OR 1.78 CI [1.05-3.03]) and delayed full enteral feeding (OR 1.05 CI [1.02-1.08]) were associated with a higher rate of moderate-to-severe BPD.

Conclusion: Large-scale randomized controlled trials are warranted to elucidate whether the association of hsPDA and delayed full enteral feeding with BPD is a real cause and effect relationship or a component of illness state during the process of evolving BPD.

Key Words: Bronchopulmonary dysplasia, Enteral nutrition, Prematurity

GİRİŞ

Bronkopulmoner displazi (BPD), prematürenin multifaktoriyel etiyolojiyle karakterize kronik akciğer hastalığıdır (1). İlk kez 1967 yılında Northway ve arkadaşları tarafından tanımlanan ve daha büyük prematüre bebeklerde görülen, ön planda kistik değişiklikler ve heterojen havalanma ile karakterize eski BPD yerini daha düşük hafta bebeklerde alveolar ve vasküler gelişim bozukluğunun görüldüğü yeni BPD'ye bırakmıştır (1,2). Antenatal kortikosteroid uygulamaları, yaygın kafein kullanımı ve minimal invaziv surfaktan uygulamaları gibi güncel yaklaşımları da içeren tıbbi hizmetlerin iyileşmesi ile birlikte, aşırı preterm bebeklerin yaşam süresinin artması beklenenin aksine BPD oranlarında bir azalmaya neden olmamış ve BPD sıklığı aynı kalmıştır (3). BPD günümüzde hala çok düşük doğum ağırlıklı bebeklerin %20-40'ını etkilemeye devam etmektedir (4). Bu yeni tip BPD gelişimine neden olan risk faktörleri araştırmacıların ilgisini çekmiş ve etiyolojisini aydınlatmaya yönelik birçok çalışma yapılmıştır.

Genetik yatkınlığın patogenezde önemli bir rol oynadığı gerçeği yanında, birçok antenatal ve postnatal faktör etiyolojide suçlanmıştır (5). BPD gelişiminde en önemli tetikleyici henüz kanaliküler evreden sakküler evreye geçmekte olan akciğer gelişiminin, preterm doğum sonucu duraklaması ve hasarlanmasıdır (5). Bunun yanında intrauterin büyüme kısıtlılığı, koryoamniyonit, preeklampsi, annenin sigara kullanımı BPD için bilinen antenatal predispozan faktörlerden bazılarıdır (3). Bebeğin ilk soluğunu alması ile birlikte BPD gelişimini etkileyebilecek postnatal olaylar zinciri gündeme gelmektedir. BPD ve diğer morbiditeler arasında neden sonuç ilişkisi kurmak oldukça zor olsa da invaziv solunum desteği, ek oksijen kullanımı, sepsis, patent duktus arteriozus ve ekstrauterin büyüme kısıtlılığının BPD ile ilişkili olabileceği düşünülmektedir (3).

Bu çalışmada, geniş bir kohortta orta ve ağır BPD ile ilişkili antenatal ve postnatal faktörlerin ortaya konulması amaçlanmıştır.

GEREÇ ve YÖNTEMLER

Bu tek merkezli retrospektif kohort çalışmaya, Ocak 2014-Aralık 2018 tarihleri arasında doğan 32 gestasyon hafta ve doğum ağırlığı 1500 g ve altında olan hastalar dahil edildi. Orta ve ağır BPD tanısı alan hastalar çalışma grubunu oluşturmaktayken, hafif BPD tanılı hastalar ile BPD tanısı almayan hastalar kontrol grubunu oluşturdu. Major konjenital veya kromozomal anomalisi olanlar ile dosya kayıtlarından verilerine ulaşılmayan hastalar çalışma dışı bırakıldı. Çalışma için Dr. Zekai Tahir Kadın Sağlığı Eğitim ve Araştırma Hastanesi, Klinik Araştırmalar Etik Kurulu'ndan 29.05.2018/24-2018 numaralı onay alınmıştır.

BPD tanısı ve sınıflaması, Jobe AH ve Bancalari E'nin 2001 yılında Ulusal Sağlık Çalıştayı'nda önerdiği sınıflamaya göre yapılmıştır (2). Gebelik haftası 32 hafta bebeklerde hafif BPD; en az 28 gün boyunca ek O2 tedavisi alan ve düzeltilmiş 36 hafta veya taburculuk sırasında ek O2 ihtiyacı olmaması olarak tanımlanmıştır (2). Orta ve ağır BPD ise postmentrüel 36. haftada ya da taburculuk sırasında <%30 ek O2 gereksinimi ve ≥%30 ek O2 veya pozitif basınçlı ventilasyon gereksinimi olarak tanımlanmıştır (2).

Hasta kayıtlarından erken membran rüptürü ve süresi, klinik ve/veya histolojik koryoamniyonit, preeklampsi, diyabetes mellitus, hipertansiyon ve çoğul gebelik varlığını içeren maternal veriler elde edildi.

Neonatal özellikler, gestasyon yaşı, doğum ağırlığı, doğum şekli, cinsiyet, doğum haftasına göre düşük doğum ağırlığı, antenatal kortikosteroid uygulaması vb demografik özellikler yanında, doğum salonunda ileri canlandırma, respiratuar distres sendromu, surfaktan doz ve sayısı, solunum desteği suresi (invaziv mekanik ventilasyon, noninvaziv solunum desteği ve ek O2 suresi), erken ve geç neonatal sepsis, hemodinamik anlamlı patent duktus arteriosus (haPDA), haPDA nedeniyle medikal tedavi ve/veya ligasyon uygulanması, evre 3-4 intraventriküler kanama (6), periventriküler lökomalazi, doğum ağırlığına ulaşılan gün, tam enteral beslenme günü, taburculuk günü ve kilosu, beslenme intoleransı varlığı, nekrotizan enterokolit (modifiye Bell sınıflamasına göre ≥ Evre 2b) (7) spontan intestinal perforasyon, prematüre osteopenisi, prematüre retinopatisi (lazer fotokoagulasyon gerektiren) ve mortalite verileri retrospektif olarak hasta kayıtlarından not edildi.

Doğum salonunda ileri canlandırma; hava yolunu temizleme, taktil uyaran verme ve pozitif basınçlı ventilasyona ilaveten endotrakeal entübasyon, göğüs kompresyonu ve/veya ilaç kullanımı olarak tanımlanmıştır.

Beslenme intoleransı tanısı safralı kusma veya bir önceki beslenme volümünün >%50 gastrik rezidü saptanması; batın

hassasiyeti veya renk değişikliği, 24 saat içinde ≥ 3 kusma ve sonuç olarak bebeğin beslenme planının bozulması durumu olarak tanımlanmıştır (8). haPDA tanısı, klinik ve ekokardiyografik bulgular varlığında neonatolog ve kardiyolog tarafından konuldu. Solunum sıkıntısı, artmış oksijen veya ventilasyon ihtiyacı, takipne, hipoksi veya başka bir nedenle açıklanamayan apne gibi klinik bulgulara ilaveten ekokardiyografi ile tespit edilmiş geniş duktus çapı (>1.5 mm) ve artmış sol atrium:aort kökü oranı (>1.4) varlığında haPDA tanısı konuldu. haPDA tanısı konulan bebeklere farmakolojik tedavi başlandı. Medikal ajan olarak öncelikle oral ibuprofen, ibuprofen için kontrendikasyon varlığında ise intravenöz parasetamol kullanıldı. haPDA bulgularının devam etmesi durumunda klinisyenin kararı doğrultusunda aynı veya farklı ajanlar ile medikal tedavi tekrarlandı. Farmakolojik tedavilerin başarısız olması durumunda kardiyolog ve neonatolog ortak kararı ile ligasyon uygulandı.

Ünitemizde 2010 yılından beri doğum ağırlığı ve postnatal güne göre hazırlanmış parenteral nutrisyon solüsyonları kullanılmaktadır. Kliniğimizde 32 hafta ve 1500 g ve altında doğan tüm bebeklere en kısa süre içerisinde parenteral nutrisyon desteği başlandı, anneler süt sağma konusunda teşvik edildi ve en kısa sürede minimal trofik beslenme başlandı. Bebeklerin beslenme toleransına göre 3-5 gün minimal beslenme devam edildi.

İstatistiksel analiz

Verilerin istatistiksel analizi SPSS 22.0 programı kullanılarak yapıldı. Tanımlayıcı istatistikler ortalama ± standart sapma, frekans dağılımı ve yüzde olarak sunuldu. Devamlı değişkenlerin normal dağılıma uygunluğu görsel (histogram ve olasılık grafikleri) ve analitik yöntemler (Kolmogorov Smirnov/Shapiro-Wilk Testi) kullanılarak incelendi. Kategorik değişkenlerin değerlendirilmesinde Pearson Chi-square test ve Fisher's Exact test kullanıldı. İleri analiz için lojistik regresyon analizi kullanıldı. İstatistiksel anlamlılık düzeyi p<0.05 olarak kabul edildi.

BULGULAR

Bu çalışmada, 626 bebeğin verisi analiz edildi. Grupların demografik özellikleri ve antenatal faktörler Tablo I'de verildi. Tüm kohortun ortalama gestasyonel yaş ve doğum ağırlığı sırasıyla 28±1.4 hafta ve 1084±225 g'dı. Toplam 626 bebekten 97'si (%15.4) orta-ağır BPD tanısı aldı. Orta-ağır BPD tanılı 97 bebeğin (%15.4) ortalama gestasyonel yaş ve doğum ağırlıkları, kontrol grubuna göre anlamlı olarak düşük saptandı (27±1.5 ve 28.3±1.7 hafta; 933±201 ve 1108±256 g sırasıyla; p<0,001). Preterm morbiditeleri Tablo II'de verilmiştir. Tek varyant analizinde orta-ağır BPD için anlamlı risk faktörü olan tüm değişkenler lojistik regresyon analizi modeline dahil edildi. Doğum salonunda ileri canlandırma (OR 2.64 CI [1.57-4.4]), gestasyonel yaş (OR 0.80 CI [0.67-0.95], haPDA (OR 1.78 CI [1.05-3.03]) ve geç tam enteral beslenme (OR 1.05 CI [1.02-1.08]) orta/ağır BPD ile ilişkili bulundu.

TARTIŞMA

Bu çalışma sonucunda tek merkezli geniş kohortlu bir seride gestasyonel yaş, doğum salonunda ileri canlandırma, haPDA ve gecikmiş tam enteral beslenme orta-ağır BPD gelişimi ile ilişkili bulundu.

Çalışmamızda geç tam enteral beslenme lojistik regresyon analizi sonucunda BPD için risk faktörü olarak ortaya konmuştur. Öte yandan, enteral beslenmeye başlama ve doğum ağırlığına

Tablo I: Grupların demografik özellikleri.

Özellik	Orta-Ağır BPD n=97	Kontrol n=529	p
Gestasyonel yaş, hafta*	27±1.5	28.3±1.7	**<0.001**
Doğum ağırlığı, g*	933±201	1108±256	**<0.001**
Erkek cinsiyet, n (%)	50 (51.5)	267 (50.5)	0.47
Sezaryen doğum, n (%)	69 (71)	386 (73)	0.41
Antenatal kortikosteroid, n (%)	61 (62.9)	367 (69.4)	0.12
APGAR 1*	4±2	5±1	**<0.001**
APGAR 5*	6±1	7±1	**<0.001**
SGA, n (%)	76 (78)	460 (86)	0.35
EMR, n (%)	19 (19.6)	102 (19.3)	0.52
Histolojik koryoamniyonit, n (%)	13 (13.4)	60 (11.4)	0.33
Preeklampsi, n (%)	15 (15)	91 (17.2)	0.53
Maternal diabetes mellitus, n (%)	3 (3)	22 (4)	0.50
Çoğul gebelik, n (%)	22 (22.7)	118 (22.3)	0.51

Ortalama ± standart sapma olarak verilmiştir.* ***EMR:* *Erken membran rüptürü,* ***SGA:****gebelik haftasına göre düşük doğum ağırlığı.*

Tablo II: Grupların klinik özellikleri.

Özellik	Orta-Ağır BPD n=97	Kontrol n=529	p
haPDA	66 (68)	207 (39)	<0.001
haPDA için farmakolojik tedavi (2 kür)	28 (28)	58 (11)	<0.001
PDA ligasyonu	7 (7)	10 (2)	0.009
Surfaktan (2 doz)	36 (37)	63 (11.9)	<0.001
İnvaziv ventilasyon süresi*	20±21	3±6	<0.001
Non-invaziv ventilasyon süresi*	22±12	8±8	<0.001
Doğum odasında ileri canlandırma	49 (50)	109 (20)	<0.001
Evre 3-4 İVK	18 (18.6)	29 (5.5)	<0.001
Periventriküler lökomalazi	25 (25.8)	33 (6.3)	<0.001
Erken neonatal sepsis	14 (14.4)	73 (13.8)	0.48
Geç neonatal sepsis	38 (39)	128 (24)	0.002
Doğum ağırlığına ulaşma günü*	15±4	13±6	<0.001
Tam enteral beslenme günü*	20±8	16±7	<0.001
Beslenme intoleransı	52 (53.6)	184 (34.8)	<0.001
Nekrotizan enterokolit	5 (5,2)	7 (1.3)	0.026
Spontan intestinal perforasyon	4 (4)	7(1,3)	0.075
Prematüre osteopenisi	16 (16,5)	33 (6)	0.003
Prematüre retinopatisi	23 (22)	27 (5.3)	<0.001
Mortalite	6 (6)	5 (1)	<0.001

***Ortalama ± standart sapma olarak verilmiştir. Frekanslar n (%) olarak verilmiştir. **haPDA:** hemodinamik anlamlı patent duktus arteriozus, **İVK:** intraventriküler kanama.*

ulaşma günü, BPD tanılı hastalarda daha geç, beslenme intoleransı ve NEK ise anlamlı olarak daha sık görülürken regresyon analizinde bir risk faktörü olarak gösterilemedi. BPD gelişimi ile beslenme ilişkisi birçok çalışmada bildirilmiştir. Malikiwi ve ark. bizim çalışmamıza benzer şekilde BPD tanılı bebeklerde tam enteral beslenmenin geciktiğini ortaya koydu (6). Bunun da düşük gestasyonel yaş ve doğum ağırlığı nedeniyle veya özellikle 2. haftanın sonuna doğru gelişmiş olan haPDA'nın bağırsak perfüzyonunu bozup beslenme intoleransına neden olmasıyla açıklanabileceğini düşünmüşlerdir (9). Yine Wemhoner ve ark. (10) BPD tanılı bebeklerin yaşamlarının ilk iki haftasında daha az enteral beslendiğini ortaya koymuşlardır. Her ne kadar parenteral beslenme ile yeterli kalori ve protein ihtiyacı uygun şekilde kompanse edilmiş olup sağlansa da, BPD gelişiminin önlenmesi için enteral yolla verilmesi gereken makro ve mikronutrient desteğinin belli bir eşiği olduğunu düşündürmüştür (10).

Biz de orta-ağır BPD tanılı bebeklerde parenteral beslenmeden tam enteral beslenmeye geçiş sürecinin daha uzun sürmüş olabileceği, bu durumun da tam enteral beslenmenin gecikmesine ve bu dönemde yetersiz protein ve kalori alımına neden olmuş olabileceği hipotezini kurduk. Bu geçiş dönemindeki beslenme araştırmacıların ilgisini çekmiş, bu periyodda özellikle yetersiz protein alımının ekstrauterin büyüme geriliği için bir risk faktörü olduğu çalışmalarda ortaya konulmuştur (11). Bu bulgular ile uyumlu olarak yetersiz beslenme sonucunda yaşamın ilk dört haftasındaki büyüme kısıtlılığının BPD için risk faktörü olduğu belirtilmiştir (12).

Düşük gestasyonel yaşın BPD için en kritik risk faktörü olması uzun suredir bilinen bir gerçek olmakla birlikte, prematürenin kendisinin mi yoksa prematüriteye neden olan faktörlerin mi BPD ile ilişkili olduğu hala açıklığa kavuşmamıştır (13). Kanaliküler evreden sakküler evreye geçmekte olan akciğerde, preterm doğuma sıklıkla eşlik eden intrauterin büyüme kısıtlılığı, inflamasyon, enfeksiyon ve oksijen toksisitesi gibi etkenlerin de varlığıyla vasküler ve alveolar gelişim durmaktadır (13).

Çalışmamızda orta-ağır BPD tanılı 97 hastanın 49'unun (%50) doğum odasında ileri canlandırma ihtiyacı olduğu gösterilmiştir. Regresyon analizinde orta-ağır BPD ile ilişkisi en güçlü değişkendir. Özellikle solunum desteği olmaksızın geçiş sürecini tamamlayamayan çok düşük doğum ağırlıklı bebeklerde, daha ilk solukla birlikte baro/volütravma ve oksijen hasarı oluşturarak akut akciğer hasarı başlamaktadır (14). Bu nedenledir ki güncel rehberler ilk solukta başlayan akciğer hasarlanması kaskadını azaltmaya yönelik entübasyondan kaçınılması, akciğer koruyucu stratejiler olan nazal CPAP, minimal invaziv surfaktan ve kısıtlı oksijen sunumu gibi uygulamaların rutin hale gelmesini önermektedir (14). Çok düşük ve aşırı düşük doğum ağırlıklı olup doğum salonunda veya yoğun bakım izleminde ileri canlandırma alan bebeklerin dahil edildiği bir sistematik derleme ve metaanalizde, ileri canlandırmanın kronik akciğer hastalığı

için predispozan bir faktör olmadığı ortaya konmuştur (15). Öte yandan bu çalışmada yenidoğan yoğun bakım ünitesinde ve doğum salonundaki canlandırma nedenleri farklı olabileceği, uygun çıkarım yapmak için bunların ayrı değerlendirildiği çalışmalara ihtiyaç olduğu vurgulanmıştır (15). Klinger ve ark. (16) da popülasyon bazlı 1663 BPD tanılı bebeğin dahil edildiği geniş bir seride, bizim çalışmamıza benzer şekilde doğum salonunda ileri canlandırmanın BPD ile güçlü bir şekilde ilişkili olduğunu öne sürmüşlerdir.

Çalışmamızda haPDA varlığının, orta-ağır BPD gelişimi için bir risk faktörü olduğu ortaya konmuştur. İlaveten, haPDA için iki veya daha fazla medikal tedavi alımı ve ligasyon yapılmasının BPD ile ilişkili olduğu gösterilmişse de, lojistik regresyon analizinde anlamlı bir ilişki ortaya konmadı. Bu araştırmacıların en çok ilgisini çeken konuların başında gelmektedir. BPD ile PDA varlığı, büyüklüğü/şant miktarı, süresi, tedavi edilip edilmeme durumu, medikal veya cerrahi tedavi uygulaması ve zamanlaması ilişkisi çok sayıda retrospektif ve prospektif kontrollü araştırmada sorgulanmıştır (17). BPD ile haPDA'nın ilişkili olduğu birçok çalışmada gösterilmesine rağmen, bu ilişkinin gerçek bir neden sonuç ilişkisi mi ya da PDA'nın BPD gelişimine neden olan klinik hastalığın basit bir belirteci mi olduğu konusu hala tartışmalıdır (14). Bizim çalışmamızda haPDA ile BPD ilişkisi ortaya konmuştur. En güncel çalışmalar, medikal tedaviyi birinci haftadan sonraya ertelemenin artmış BPD ve BPD/ölüm ile ilişkili olduğunu göstermektedir (18). Öte yandan, Clyman ve ark. (19) PDA-TOLERATE çalışmasında orta-büyük PDA'da farmakolojik tedavi verilen grup ile konservatif olarak takip edilen hasta grubu arasında BPD insidansı açısından fark göstermemiştir.

Çalışmamızın en önemli kısıtlılığı retrospektif bir çalışma olmasıdır. Nutrisyon detayları (örneğin toplam kalori, protein ve lipid alımı, mayi miktarı), haPDA tanı ve tedavisiyle ilgili (tanı-tedavi günü, şant büyüklüğü, tedavi tipi ve dozu) verilerin olmayışı çalışmamızın en önemli kısıtlılıklarından biridir. Ek olarak kontrol grubunda hafif BPD tanılı hastaların da olması sonuçlar üzerinde etki yaratmış olabilir.

Sonuç olarak bu tek merkezli beş yıllık geniş bir kohortta yapılan çalışmada doğum salonunda ileri canlandırma, düşük gestasyon haftası, haPDA ve gecikmiş tam enteral beslenme BPD ile ilişkili bulunmuştur. Ancak tam enteral beslenmeye geçiş süresi ve haPDA ile BPD ilişkisinin neden sonuç mu yoksa BPD'ye gidiş sürecindeki hastalık durumunun bir parçası olup olmadığının ortaya çıkarılması için, geniş çaplı prospektif randomize çalışmalara ihtiyaç olduğu düşünülmüştür.

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An Assessment of the Knowledge, Attitudes, and Practices of Pediatricians and Pediatric Residents in Duchenne Muscular Dystrophy

Duchenne Musküler Distrofide Pediatri Uzmanları ve Pediatri Uzmanlık Öğrencilerinin Bilgi, Tutum ve Uygulamalarının Değerlendirilmesi

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ABSTRACT

Objective: Pediatric residents and pediatricians play an important role in the management of Duchenne Muscular Dystrophinopathy (DMD) which is the most frequent hereditary muscle disease of childhood. Our study aims to evaluate the knowledge levels and approaches of pediatric residents and pediatricians on DMD.

Material and Methods: In this study, pediatric residents and pediatricians were asked to answer questions on the genetic, pathophysiological, clinical, and laboratory features, in addition, to follow-up and management of DMD. Data acquisition was carried out using an online questionnaire consisting of 17 questions prepared by the authors via Google forms (Google LLC, Mountain View, Ca, USA).

Results: The distribution of 197 responders was as follows: 53.8% were pediatricians, 13.7% were pediatric subspecialty fellows and 32.5% were pediatric residents with a total of 197 responders. 74.6% of the responders gave correct answers on the X-linked inheritance of DMD, 42.6% on the fact that it affected both genders, 93.3% on the fact that the disease is caused by the primary deficiency of dystrophin protein. 91.9% of the responders reported that the patients lost the ability to walk around 9-11 years of age. More than 50% of the responders did not have adequate information on the departments that could participate in the management of DMD patients.

Conclusion: This study has evaluated a wide range of physicians playing important roles in the follow-up and management of pediatric patients and has revealed a necessity for improvement in knowledge about genetic and clinical features of DMD and its management via learning.

Key Words: Attitude, Duchenne muscular dystrophy, Knowledge, Neuromuscular diseases, Rare disease

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Contribution of the Authors / Yazarların katkısı*: *KUTLUK G: Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar. ***YAYICI KOKEN O:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***MIHCI F:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***OZ TUNCER G:*** Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar.

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ÖZ

Amaç: Kronik ve ilerleyici bir seyir gösteren Duchenne Musküler Distrofinopati (DMD), çocukluk çağının en sık karşılaşılan herediter kas hastalığı olup, yönetiminde pediatri uzmanlık öğrencileri ve pediatristler önemli rol oynamaktadır. Bu çalışmada; pediatri uzmanlık öğrencileri ve pediatristlerin DMD hakkındaki bilgi düzeyleri ve tutum özelliklerinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Çalışmamızda pediatri uzmanlık öğrencisi hekimler ve pediatri hekimlerinin DMD'nin genetik, patofizyolojik, klinik ve laboratuvar özellikleri yanısıra izlem ve yönetim özelliklerini kapsayan soruları cevaplamaları istenmiştir. Bu çalışma için veriler Google forms (Google LLC, Mountain View, CA, ABD isimli online tool yolu ile; makale yazarları tarafından hazırlanan 17 soruluk araştırmacılar tarafından tasarlanan bir anket aracılığıyla online ortamda toplanmıştır.

Bulgular: Çalışmaya %53.8'i pediatrist, %13.7'si pediatri yandal uzmanlık öğrencisi, %32.5'i pediatri uzmanlık öğrencisi olmak üzere toplam 197 katılımcı alındı. DMD'nin X-linked geçiş gösterdiği katılımcıların %74.6'sı, her iki cinsiyette de görülebileceği %42.6'sı, distrofin proteinin primer eksikliği sonucu geliştiği bilgisi katılımcıların %93.3'ü tarafından doğru yanıtlandı. Katılımcıların %91.9'u DMD'li hastaların 9-11 yaş civarında yürümeyi kaybettiğini belirtti. DMD'li bir hastanın izleminde rol oynayan pediatri yandalları ve pediatri dışı bölümler açısından katılımcıların %50 ve daha fazlasının yeterli bilgisi olmadığı kaydedildi.

Sonuç: Bu çalışma ile pediatrik hasta takip ve tedavisinde önemli rol oynayan geniş bir hekim grubu değerlendirilerek DMD'nin genetik ve klinik özellikleri ve hastalık yönetimindeki önemli noktaların öğrenim faaliyetleri ile geliştirilmesinin gerekliliği dikkati çekmiştir.

Anahtar Sözcükler: Tutum, Duchenne musküler distrofi, Bilgi düzeyi, Nöromusküler hastalık, Nadir hastalık

INTRODUCTION

Duchenne muscular dystrophies (DMD), also known as dystrophinopathies, are the most common neuromuscular diseases of childhood resulting from X-linked mutations in the dystrophin gene (1-3). The dystrophin gene codes the main skeletal frame protein dystrophin, located on the cytoplasmic surface of the skeletal and cardiac muscle cell membranes. Mutations causing a loss of gene function cause progressive and fatal muscle weakness (1-3). Patients with DMD are followed up by the pediatricians throughout their lifetime for numerous comorbidities such as progressive skeletal muscle weakness starting from the pelvic girdle and cardiac involvement (1-3). These patients are routinely followed up by pediatric neurology and physical therapy and rehabilitation departments for muscle strength and function, and adverse effect management and rehabilitation of sleep disorders. Cardiac functions are followed up by pediatric cardiology while scoliosis, contractures, and bone fractures are followed up by the orthopedics department. Respiratory problems, spirometry evaluation, and sleep studies in addition to ventilator support in the advanced stages of the disease are managed by the department of respiratory pediatrics. The pediatric endocrinology department manages growth, pubertal development, and bone metabolism while the pediatric gastroenterology department is involved in feeding, chewing, swallowing, constipation, gastroesophageal reflux, gastroparesis, and possible gastrostomy placement in the advanced stages of the disease. Pediatrics, social pediatrics and healthy child clinics provide follow up for the continuity of routine health services such as vaccination (1,2)

The medical genetics and/or pediatric genetics department also plays an important role in the detection of carriers and providing genetic counseling to families (1,2). Pediatricians and pediatric clinics are crucial for the management of this chronic-progressive disease which has an early childhood onset and benefits from supportive treatments that have a positive effect on survival and life quality with new gene-based treatment options are discovered every day. Thus, pediatricians and pediatric residents are expected to have detailed knowledge of diagnostic and management features of DMD in addition to the routine treatment options along with the natural course of the disease. The knowledge levels and attitudes towards the disease and coping strategies of the patients and parents on hereditary neuromuscular diseases have been subject to numerous studies (4-6). However, no study concerning the knowledge levels, attitudes, and practices of the medical doctors with the most frequent exposure to this disease – pediatricians and pediatric residents – could be found in the literature. This study aims to identify the knowledge levels, attitudes, and practices of pediatric residents and pediatricians concerning DMD using a structured questionnaire prepared by the authors.

MATERIAL and METHODS

This prospective cross-sectional questionnaire study evaluated Turkish pediatricians and pediatric residents from private hospitals and clinics, government hospitals, and university clinics from 10th to 20th June 2020. The questionnaire was prepared by four researchers to evaluate knowledge, attitude, and practice of pediatric patients with DMD and was submitted via Google Forms (Alphabet, Mountain View, CA, USA). A random sampling method has been used in the study. The questionnaire form was filled in by 197 pediatricians and pediatric residents from all parts of the country. Informed consent was obtained online by adding the "Informed Consent Form" to the questionnaire prepared via Google Forms. The first two questions were about the professional title and the duration of work in that title followed by 15 open-ended, structured, and multiple-choice questions targeted to measure knowledge, attitude, and practice about DMD. Of the questions, 3 were

about the hereditary pattern and genetic features of the disease, 1 was about pathophysiology, 3 were about clinical features, 1 was about laboratory findings, 1 was about vaccination, 5 were about follow-up features and 1 was about treatment. Four of the answers (one question for genetics, one for clinics, one for treatment, one for management) were codified as dichotomous variables, namely as yes/No/unknown or correct/false/unknown responses, or in general (n:11) as categorical variables, when a multiple-choice selection had been requested. To ensure that all questions were answered, a choice for "No opinion" was added and the participants were not allowed to take the next question before answering the current one.

The ethics committee approval was obtained from the Turkish Ministry of Health, Antalya Research and Education Hospital non-interventional studies ethics committee on 06 May 2021 with ethical approval number: 6/19. The study has been conducted in accordance with the Helsinki guidelines.

Statistical analyses

All answers and datas were performed as the number of cases (n) and percentages (%) by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States).

RESULTS

The study was completed with 106 (53.8 %) pediatricians, 27 (13.7 %) pediatrics subspecialty fellows, and 64 (32.5 %) pediatric residents with a total of 197 responders (Figure 1).

The work experience was distributed as follows: 10.7 % (n:21) had less than 6 months, 18.8 % had more than 10 years, 39.1 % (n:77) had more than 5 years. The distribution of work duration in pediatrics was as follows: 7.6 % (n:15) between 6 months and 1 year, 21.3 % (n:42) between 1 and 3 years, 21.3 % (n:42) between 3 and 5 years.

The answers given to three questions concerning the inheritance pattern and genetic features of DMD have been summarized in figure (Figure 2). 97.5 % of the responders knew that it was a genetic disease, 74.6% (n:147) chose X-linked inheritance and 42.6% (n:84) stated that it could affect both genders.

93.3% (n:185) of the responders correctly chose dystrophin to "Which muscle protein deficiency causes DMD?" aimed at questioning the knowledge about the pathophysiological mechansims. On the other hand, 1% (n:2) of the responders chose dysferlin, 1.5% (n:3) chose sarcoglycan while 3.6% (n:7) had no opinion. No responders chose laminin or emerin.

Questions about clinical and laboratory features of DMD patients and answers have been summarized in table (Table I).

The participants were asked "Which of the following is not recommended in the follow-up of DMD patients?" to evaluate the knowledge about vaccination program in DMD patients. Two (1%) of the responders stated that questioning the vaccination history was not necessary at the time of diagnosis, 4 (2%) stated that pneumococcal vaccine was not recommended, 44 (22.3%) stated that the routine vaccination schedule as advised by the ministry of health could not be implanted and 15 (7.6 %) stated that they had no opinion on the vaccination of DMD patients. 131 (66.5%) of the patients believed that it was not necessary to inform the parents and family practitioner about avoiding attenuated vaccines.

Questions concerning bone metabolism, pubertal growth, respiratory and sleep problems, the necessity for genetic

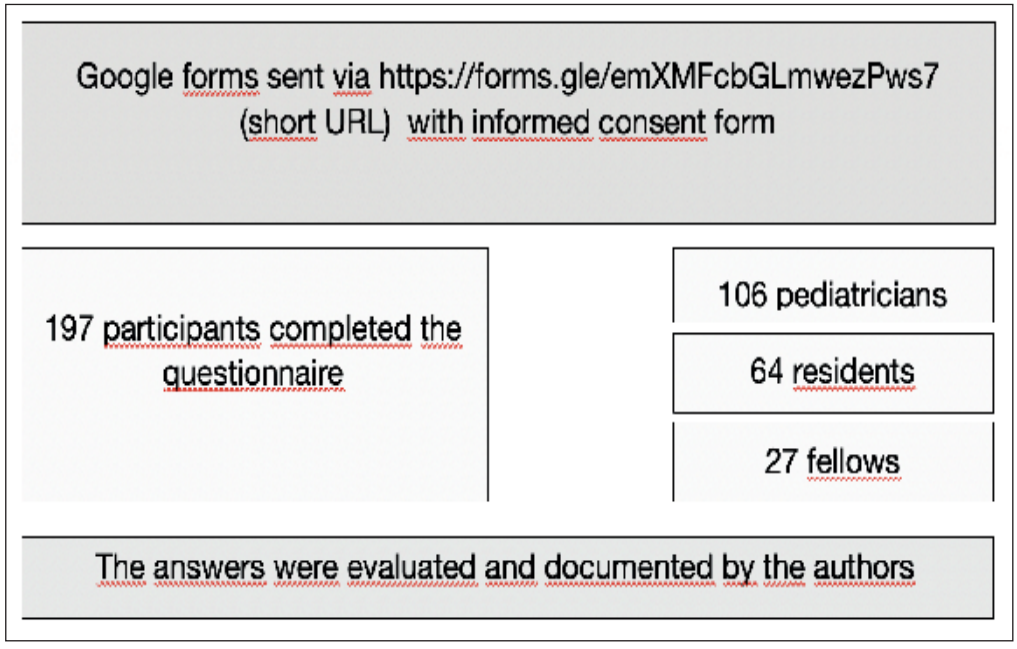

Figure 1: Flowchart of the study.

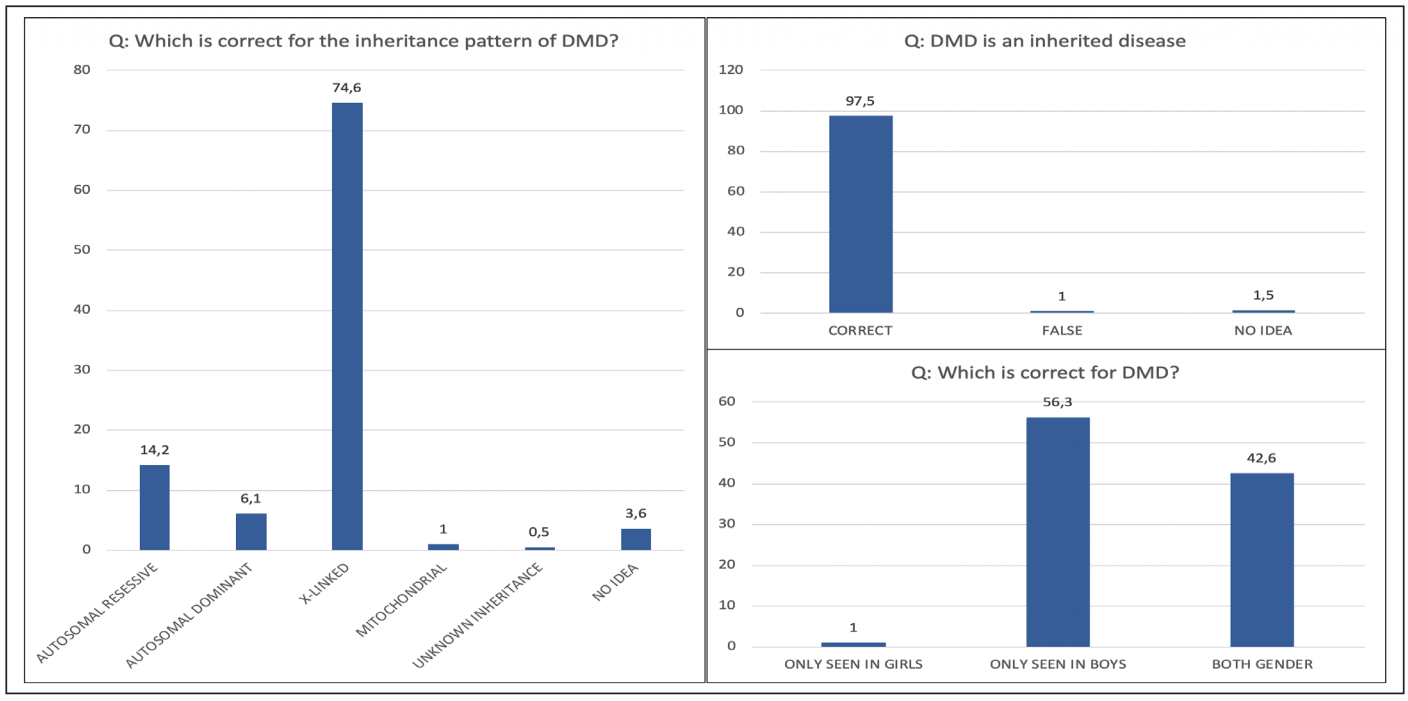

Figure 2: Questions and answers on inheritance pattern and genetic features of DMD.

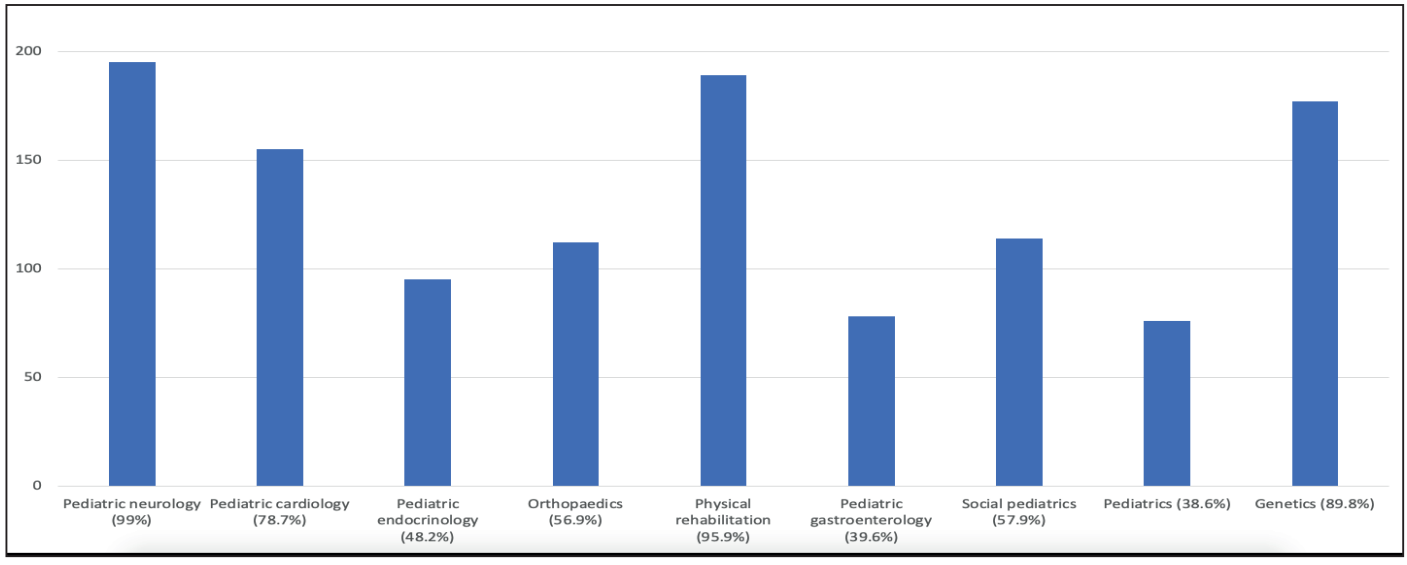

Figure 3: Distribution of answers concerning which subspecialty should follow up patients with DMD.

counseling, and treatment options and their answers have been summarized in table (Table II).

Questions about which pediatric subspecialty should manage DMD and their answers have been summarized in figure (Figure 3). 195 (99%) of the participants agreed on pediatric neurology while the second most popular opinion was physical therapy and rehabilitation with 189 (95.9%) answers. 76 (38.9%) of the responders who consisted of pediatric residents and specialists stated that general pediatrics should also participate in the follow-up.

DISCUSSION

Although rare, DMD is the most frequent hereditary neuromuscular disease and a timely diagnosis decreases future morbidity and comorbidity, while the fact that appropriate management and the consistently increasing number of new treatments increase the quality of life and lower the disease severity point to the importance of guidance by physicians. This survey study has revealed that 26.4% of doctors receiving education on pediatrics could not correctly identify the inheritance pattern of the disease, and 57.3% of them were not aware of the fact

Table I: Questions about clinical and laboratory features of patients with DMD and answers of the participants.

Questions and choices	Answers (%,n)
Which of the following is correct for DMD patients?	
They can never walk	0.5 (n=1)
They can never run	6.6 (n=13)
They can never sit without support	0.5 (n=1)
They lose the ability to walk between 9-11 years of age	91.9 (n=181)
No opinion	0.5 (n=1)
Which of the following is not one of the symptoms and findings of DMD?	
Frequent falls	2 (n=4)
Difficulty climbing stairs	1.5 (n=3)
Difficulty walking	23.9 (n=47)
Fasciculation in the tongue	72.1 (n=142)
Difficulty standing up from sitting position	0.5 (n=1)
No opinion	-
Muscle weakness in DMD starts from the pelvic girdle	
True	68 (n=134)
False	22.8 (n=45)
No opinion	9.1 (n=18)
Which of the following is not a laboratory finding in DMD?	
Elevated serum creatinine kinase (CK)	0.5 (n= 1)
Elevated serum Lactate dehydrogenase (LDH)	1.5 (n= 3)
Elevated serum liver function tests (ALT,AST)	5.1 (n= 10)
Low serum vitamin B12 levels	76.1 (n= 150)
Elevated serum aldolase levels	11.7 (n= 29)
No opinion	5.1 (n= 10)

CK: *Creatinine kinase,* ***ALT:*** *Alanine aminotransferase,* ***AST:*** *Aspartate aminotransferase*

Table II: Questions about bone metabolism, pubertal growth, respiratory and sleep problems, the necessity for genetic counseling, and treatment options of DMD patients and answers of the participants.

Questions and choices	Responses (%,n)
Which of the following is not recommended in the follow up of DMD patients?	
Evaluation of growth every 6 months	1 (n=2)
Evaluation of bone metabolism when the patient loses the ability to walk	71.1 (n=140)
Evaluation of pubertal growth every 6 months	19.3 (n=38)
Evaluation of Vitamin D and calcium intake starting at the time of diagnosis	3.6 (n=7)
No opinion	5.1 (n=10)
Which of the following is incorrect for DMD?	
The most frequent causes of death are lung involvement, infection, and cardiomyopathy	9.1 (n=16)
Cardiac evaluation should be performed at the time of diagnosis	5.1 (n=10)
Lung capacity should continually be evaluated	1.5 (n=3)
Regular rehabilitation, endocrine, gastroenterology, and orthopedic should be performed after diagnosis	6.1 (n=12)
Glucocorticoids should be avoided in DMD patients	70.1 (n=138)
Genetic counselling should be provided to the families of DMD patients	
True	99.5 (n=196)
False	-
No opinion	0.05 (n=1)
Which of the following symptoms in a DMD patient points to a sleep disorder?	
Headache while or after waking up in the morning	1.5 (n=3)
Inactivity and loss of concentration and	8.1 (n=16)
Sweating during night or sleep	1 (n=2)
Loss of appetite	-
All choices point to a sleep disorder	83.8 (n=165)
No opinion	5.6 (n=11)
The curative treatment for DMD has not been found yet	
True	82.7 (n=163)
False	9.6 (n=19)
No opinion	7.6 (n=15)

that it affects both genders. Autosomal recessive inheritance is more common in rare diseases could have misled 14.2% of the participants. On the other hand, this situation may have been caused by the belief that a disease with an X-linked pattern would have resulted in asymptomatic carriers in females. However, DMD can be observed in 1: 50.000.000 live female births (7,8). Girls may be symptomatic carriers when they are affected by homozygous mutations in the dystrophin gene, with the partial or total expression of the abnormal gene and also, carriers are symptomatic due to chromosomal translocations, Turner syndrome, or abnormal X chromosome or X inactivation (1,7). Diagnosis and follow-up of symptomatic/asymptomatic girls is as important as the necessity for genetic counseling for these girls given the fact that they may become mothers in the future (9). 99.5% of the participants of this study have proven their sensibility by stating that genetic counseling was important for these patients.

Although serious progress has been made in the diagnosis and management of DMD in the last decade, there is still a large interval between the onset of symptoms, and genetic confirmation (10,11). In the literature, the mean age of diagnosis of DMD is 4.3-4.11 years and the mean total delay in diagnosis is 19.2-30 months (11). The most important factor that can shorten this interval in our country is the knowledge of pediatricians and pediatric residents on clinical and laboratory findings (11,12). In our study, 91.9% of the responders stated that DMD patients lost their ability to walk around 9-11 years of age, 72.1% stated that tongue fasciculations were not part of the physical examination, 68% stated that muscle weakness originated from the pelvic girdle, while 34.4% reported symptoms which were not part of DMD as symptoms that could be observed and reported that tongue fasciculations which are related to anterior motor horn involvement could

be observed in DMD which is a myopathy. On the other hand, while elevations of enzymes like ALT, AST, aldolase, LDH, and CK are expected and directly related to the diagnosis of DMD, 5.1% of the responders had no opinion and 18.8% reported vitamin B12 deficiency as a laboratory finding directly associated with DMD. This points out the fact that 23.9% of the responders lack sufficient knowledge about laboratory findings associated with DMD. Although not in the screening program of our country, evaluation of CK levels in the first 3 years of life can help early diagnosis which is recommended in other countries (11). Elevated levels of muscle enzymes like AST, ALT, LDH in addition to CK is another finding of the disease (1,2). This points to the fact that CK levels should be evaluated in patients with elevated liver function tests.

In the diagnosis and management guideline by Birnkrant et al, evaluation of pubertal status every six months in addition to vitamin D and calcium supplementation starting at the time of diagnosis is advised (1,2). 71.1% of the responders gave the correct answer about this subject. According to the mentioned guideline, cardiac evaluation should be performed at the time of diagnosis, lung capacity should be regularly measured and routine rehabilitation, endocrinology, gastroenterology, and orthopedic follow up should be initiated However, 5.1%, 1.5% and 6.1% of the responders respectively did not provide the correct response. Additionally, 9.1% of the responders are not correctly informed about the fact that the most frequent cause of death in DMD is pulmonary involvement-infection and cardiomyopathy. This is important about the importance of follow-up concerning pulmonary infection, respiratory, and cardiac functions. The frequency of sleep disorders in children and adolescents with DMD has been reported as 20-65% which is higher than the healthy population (13). Thus clinicians should question the DMD patients and their families on sleep disorder symptoms. However, due to the design of the study, we were not able to evaluate if the clinicians questioned the patients on sleep disorder-related symptoms. 83.3% of the responders were familiar with these symptoms.

More than 90% of the responders believed pediatric neurology and physical therapy and rehabilitation departments should manage these patients. However, the responders had a low level of awareness about the fact that departments such as pediatric cardiology, endocrinology, gastroenterology and orthopedics should also participate in the management.

Treatment of DMD is centered on glucocorticoids, prevention of contractures, and medical care of cardiomyopathy, and respiratory compromise. However, nearly 30% of the responders believed that glucocorticoids should be avoided in patients with DMD. This points to a low level of awareness concerning the use of glucocorticoids which has been extensively researched and found to help pulmonary functions, slowed the progress of cardiomyopathy, delayed the onset of scoliosis and reduced mortality (1,2,14). Until the last decade, hereditary neuromuscular diseases including DMD were believed to be incurable and the aim was to provide supportive therapy to reduce morbidity and mortality. With the advancement of molecular diagnosis and targeted treatment, the necessity of increased competency within the physicians who play the primary role in the diagnosis and treatment of these patients become more evident.

On the other hand, we would like to emphasize that this study can not fully evaluate all knowledge and attitudes of the clinicians. The responses were limited to the knowledge questioned or the choices provided in the survey since the questions were close-ended and most of them had multiple choices. Such questions provide an easier assessment since they are easy to answer and less time-consuming thus provide coherent and regular responses. However, the studies encompassing a wider range of physicians which question knowledge and management with open-ended questions are necessary. Our study shows that pediatricians and pediatric fellows should read more material on routine management and follow-up in DMD and more time should be allocated to this disease in learning activities.

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Evaluation of Kidney Function Parameters in Children with Vitamin B12 Deficiency

Vitamin B12 Eksikliği Olan Çocuk Hastalarda Böbrek Fonksiyon Parametrelerinin Değerlendirilmesi

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ABSTRACT

Objective: Vitamin B12 is crucial for cell metabolism, deoxyribonucleic acid synthesis and cell proliferation. Hematological and neurological systems are known to be affected in vitamin B12 deficiency. The aim of this study was to research the effects of vitamin B12 deficiency on kidney function parameters.

Material and Methods: Thirty-four children with vitamin B12 deficiency and 36 sex and age-matched healthy controls were included in the study. Complete blood count, serum urea, creatinin, vitamin B12, holotranscobalamin, methyl malonic acid, homocysteine, ferritin, folate and estimated glomerular filtration rate were recorded. Additionally, spot urine protein, microalbumin and neutrophil gelatinase-associated lipocalin were measured.

Results: Kidney function parameters were normal for childrens that participated the study. Serum kidney function parameters adjusted for age also showed no significant difference between the two groups. No correlation was found between serum vitamin B12 and neutrophil gelatinase-associated lipocalin; however, a negative correlation was detected between neutrophil gelatinase-associated lipocalin and holotranscobalamin ($r = -0.24$, $p = 0.045$). Holotranscobalamin was substantially lower in the group with vitamin B12 deficiency ($p<0.001$).

Conclusion: No negative influence of B12 deficiency on kidney function was found in non-anemic children.

Key Words: Child, Holotranscobalamin, Kidney function, Vitamin B12 deficiency

ÖZ

Amaç: Vitamin B12, hücre metabolizması, deoksiribo nükleik asit sentezi, hücre proliferasyonu için yaşamsal öneme sahiptir. Vitamin B12 eksikliğinde nörolojik ve hematolojik sistemin etkilendiği bilinmektedir. Bu çalışmada da, vitamin B12 eksikliğinin böbrek fonksiyonları üzerine etkisinin incelenmesi amaçlandı.

Gereç ve Yöntemler: Vitamin B12 eksikliği olan 34, yaş ve cinsiyet özellikleri açısından benzer özellikler gösteren 36 sağlıklı çocuk çalışmaya dahil edildi. Hastalara ait tam kan sayımı, serum üre, kreatinin, vitamin B12, holotranskobalamin, metil malonik asit, homosistein, ferritin, folat düzeyleri ve tahmini glomerüler filtrasyon hızı kaydedildi. Ayrıca, idrarda protein, mikroalbumin ve nötrofil jelatinaz ilişkili lipokalin değerleri ölçüldü.

Bulgular: Çalışmaya katılan çocukların böbrek fonksiyonlarını gösteren parametreler normal değerlerdeydi. Böbrek fonksiyonları ile ilgili parametreler açısından vitamin B12 eksikliği olan ve olmayan hastalar arasında anlamlı fark yoktu. Her iki grup arasında vitamin B12 ve nötrofil jelatinaz ilişkili lipokalin arasında korelasyon bulunmadı, ama holotranskobalamin ve nötrofil jelatinaz ilişkili lipokalin arasında negatif korelasyon saptandı ($r = -0.24$, $p = 0.045$). Holotranskobalamin vitamin B12 eksikliği olan grupta anlamlı derecede düşüktü ($p<0.001$).

Sonuç: Anemisi olmayan çocuklarda vitamin B12 eksikliğinin böbrek fonksiyonları üzerine belirgin olumsuz etkisi bulunamamıştır.

Anahtar Sözcükler: Çocuk, Holotranskobalamin, Böbrek fonksiyonu, Vitamin B12 eksikliği

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Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. This study was approved by the Ethics Committee of Kecioren Training and Research Hospital with the number 24.01.2018/2012-KAEK-15/1583.

Contribution of the Authors / Yazarların katkısı*: *BELDER N: Planning methodology to reach the Conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***GURLEK GOKCEBAY D***: Constructing the hypothesis or idea of research and/or article, Organizing, supervising the course of progress and taking the responsibility of the research/study,Reviewing the article before submission scientifically besides spelling and grammar.

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INTRODUCTION

Vitamin B12 (cobalamin) is one of the most important water-soluble complex vitamins. Vitamin B12 is vital for nucleic acid synthesis in cell metabolism and protein biosynthesis. Deficiency of vitamin B12 is common in childhood period, especially in infancy and adolescence along with multiple nutritional deficiency. The frequency of vitamin B12 deficiency was found to be 22% to 65% in studies conducted in regions with low socioeconomic level (1, 2).

Strict vegetarian nutrition of the mothers of breast-fed infants and dietary vitamin B12 deficiency often cause vitamin B12 deficiency in the children. Absorption disorders also cause vitamin B12 deficiency in childhood. Congenital pernicious anemia, juvenile pernicious anemia and transcobalamin 2 transport deficiency are among the most frequent B12 absorption disorders. Because of vitamin B12 role in cell proliferation, hematological and neurological problems including megaloblastic anemia, peripheral neuropathy, posterior spinal cord degeneration and developmental delay can be observed in children with B12 deficiency (3).

It is important to start the treatment early in children with B12 deficiency to have a better clinical course. Because measurement of the serum total vitamin B12 level quantitates both the inactive forms(transcobalamin I and transcobalamin III bound) and active form (transcobalamin II-bound) of B12, it may not exactly represent real vitamin B12 status (4). Elevated plasma levels of methyl malonic acid (MMA) and homocysteine in combination with low vitamin B12 level are more reliable markers of vitamin B12 deficiency.

Urinary neutrophil gelatinaseassociated lipocalin (uNGAL) is a biomarker reflecting renal tubular damage, and it has been shown to be increased urinary excretion in renal damage (5). Although there are many studies in the literature on the neurological and hematological effects of vitamin B12 deficiency, there are scarce data investigating the effect on renal functions (6-8).

The aim of this study was to research the effects of vitamin B12 deficiency on renal function parameters.

MATERIALS And METHODS

Patients admitted to our Pediatric Hematology and Oncology Department between February 2018 and 2019 with vitamin B12 deficiency were evaluated prospectively in this study. Children aged 2-18 years with a body weight of 3-97 percentile and a vitamin B12 level of <200 pg/ml without any chronic illness or infection were included in the study. Children with chronic illness including hypothyroidism, diabetes, obesity or malnutrition, iron or folate deficiency and signs of dehydration (serum urea/creatinine > 20, urine density> 1020) were excluded from the study. The study group was consisted of a total of 34 patients. Thirty-six sex and age-matched healthy children who accepted outpatient clinics for routine control formed the control group. This study was approved by the local ethics committee by the number of 24.01.2018/2012-KAEK-15/1583. The study complied with the Decleration of Helsinki, and the informed consent was obtained from the all patients and/or their parents. Patient demographics, blood pressure, height and weight percentiles, physical examination were recorded. Complete blood count including hemoglobin (Hb), white blood cell count (WBC), red blood cell count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and platelet count (PLT) were registered. Anemia was described as a Hb concentration below cut off levels established by the World Health Organization (WHO) (9). Serum urea, creatinine(Cre), urinalysis and microalbumin in spot urine, serum vitamin B12, ferritin, folate levels of all subjects; additional homocysteine and MMA levels of the patients with B12 deficiency were recorded. Diagnosis of vitamin B12 deficiency was declared as a serum level of vitamin B12 below 200 pg/ml and eleveated plasma homocysteine and/or MMA with the outside of other causes of anemia (10). Urine samples of 2 ml was taken directly into the Eppendorf tubes and stored at -80ºC until measurement of uNGAL by enzyme linked immunosorbent assay (ELISA) method. The cut off values of the uNGAL were determined on the values reported in the manufacturer's book and 131.70 ng/ml was accepted as upper limit. Two ml of venous blood sample was drawn and centrifuged at 1500 rpm for 10 minutes, the serum was separated and stored at -80 ºC until measurement of holotrascobalamin by Abbot Architecht i2000 (Abbott Park, IL, USA). The values of the holotranscobalamin below 35 pmol/l was accepted as B12 deficiency according to manufacturer's book. The estimated glomerular filtration rate (eGFR) was calculated with serum creatinine according to Schwartz formula for children (11).

Statistical Analysis

The distributions of continuous variables were analysed with Kolmogorov-Smirnov or Shapiro-Wilk tests based on normality of distribution. Descriptive statistics were defined as mean ± standard deviation, and median (minimum-maximum). Categorical data was compared using chi-square and Fisher's exact tests. To compare independent groups, students-t test and Mann-Whitney U test was used based on normality of distribution. Pearson or Spearman correlation analysis was used to test relationships between variables. Statistical analyses were performed using SPSS version 15.0 (SPSS Inc.s, Chicago, IL, USA). When $p \leq 0.05$ was considered as statistically significant.

RESULTS

A total of 34 children (9 girls, 25 boys) with vitamin B12 deficiency and 36 healthy controls (17 girls, 19 boys) were analysed in the study. There was no difference between the groups in terms of median age [13 (range, 4-17) vs. 12.5 (range, 5-17)]. Physical examination was unremarkable in all subjects participated in

Table I: Comparison of complete blood count parameters of the subjects (mean ± SD).

Parameters (mean ± SD)	Vitamin B12 deficient group (n = 34)	Control group (n = 36)	p
Hb (g/dl)	14.40 ± 1.32	13.80 ± 1.18	0.064
MCV (fL)	85.30 ± 4.72	81.50 ± 3.36	< 0.001
RDW(%)	13.80 ± 1.51	13.50 ± 1.12	0.939
MCH (pg)	30.50 ± 8.90	28.00 ± 1.27	0.002
MCHC (g/dL)	34.00 ± 1.33	34.20 ± 0.88	0.638
RBC (x10^6/µl)	5.00 ± 0.45	5.00 ± 0.43	0.780
WBC (x10^3/µl)	7.00 ± 14.30	8.00 ± 2.26	0.032
PLT (x10^3/µl)	284.50 ± 52.34	308.00 ± 59.87	0.084

Hb: *hemoglobin,* ***MCH:*** *main corpuscular hemoglobin,* ***MCHC:*** *mean corpuscular hemoglobin concentration,* ***MCV:*** *mean corpuscular volume,* ***PLT:*** *platelet,* ***RBC:*** *red blood cell,* ***RDW:*** *red cell distribution width,* ***WBC:*** *white blood cell*

Table II: Homocystein end MMA levels in patients with vitamin B12 deficiency.

Patients with vitamin B12 deficiency (n=34)	Increased	Normal
Homocystein	27 (79%)	7 (21%)
MMA	8 (24%)	26 (76%)

MMA: *Metil malonic acid*

the study. Hypertension was detected in none of the patients. No significant difference was found in body mass index (BMI) between the two groups. Mean vitamin B12 levels were 147 ±30 pg/ml in the vitamin B12 deficient group and 411±168 pg/ml in control group. There was a negative correlation between age and vitamin B12 levels of the patients (r=-0.31, p=0.008).

Comparison of complete blood count parameters between children with vitamin B12 deficiency and control group is shown on Table I. Hemoglobin levels, RBC and PLT counts were not different between the two groups, but MCV was higher in the vitamin B12 deficient group (p<0.001). A weak-moderate negative correlation was found between MCV and vitamin B12 levels (r=-0.31, p=0.008), but no correlation was found between MCV and holotranscobalamin. Platelet counts and vitamin B12 levels of the subjects were positively correlated (r= 0.36, p=0.002). White blood cell counts was also statistically significantly lower and MCH was higher in the vitamin B12 deficient group (p=0.032, and p=0.002 respectively). White blood cell count showed a positive correlation with B12 levels of the subjects (r=0.35, p=0.003).

Homocystein levels were found to be increased in the 79% of the vitamin B12 deficient patients (Table II). No correlation was found between homocystein and holotranscobalamin levels. Additionally, there was no correlation between homocystein and uNGAL. Methyl malonic acid were increased in 24% of the vitamin B12 deficient patients, yet, no correlation was found between MMA and uNGAL levels.

Comparison of biochemical and nutritional parameters showed no meaningful difference between the two groups (p> 0.05) (Table III). Serum creatinine adjusted for age also showed no remarkable difference between the two groups.

Median spot urine microalbumin level of the vitamin B12 deficient group was 7.20 mg/l (0.18-29 mg/l) while median spot urine microalbumin level was 6.10 mg/l (0.20-29.0 mg/l) in the control group. Proteinuria was not found in urinalysis obtained as the first urine sample in the morning in all subjects. No significant difference was found in terms of microalbuminuria between the two groups (p=0.630).

Median uNGAL was 8.90 ng/ml (1.10-121.00 ng/ml) in the patient group with vitamin B12 defiency. In the control group,

Table III: Comparison of Biochemical and Nutritional Parameters of the subjects (mean ± SD).

Parameters (mean ± SD)	Vitamin B12 deficient group (n = 34)	Control group (n = 36)	p
Urea (mg/dL)	21.00 ± 5.94	22.60 ± 4.22	0.855
Creatinine (mg/dL)	0.68 ± 0.09	0.64 ± 0.12	0.960
Albumin (g/dl)	4.50 ± 0.33	4.20 ± 0.32	0.112
ALT (IU/L)	12.50 ± 4.94	12.20 ± 4.69	0.568
AST (IU/L)	19.50 ± 4.49	21.50 ± 5.79	0.078
Ferritin (ng/ml)	39.20 ± 21.20	34.80 ± 12.10	0.658
Folate (ng/ml)	6.80 ± 1.85	7.60 ± 2.06	0.811
eGFR (mL/min / 1.73m^2)	102.60 ± 13.59	93.90 ± 8.70	0.309

ALT: *alanine amino transferase,* ***AST:*** *aspartate amino transferase,* ***eGFR:*** *estimated glomerular filtration rate*

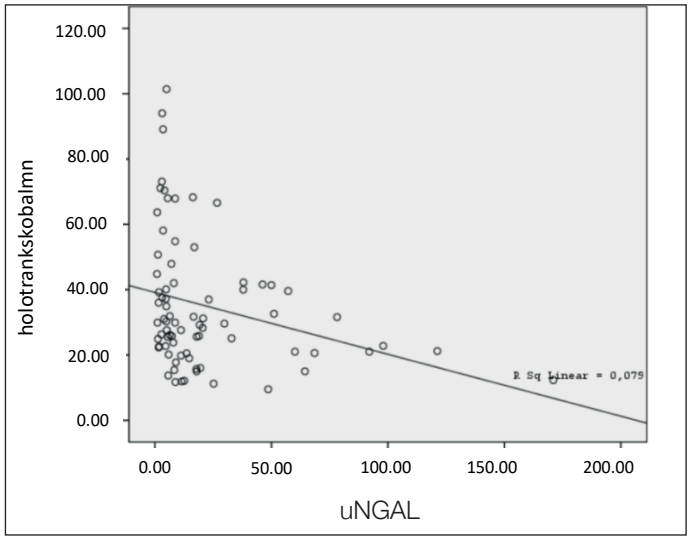

Figure 1: Correlation between holotranscobalamin and uNGAL levels of the subjects.

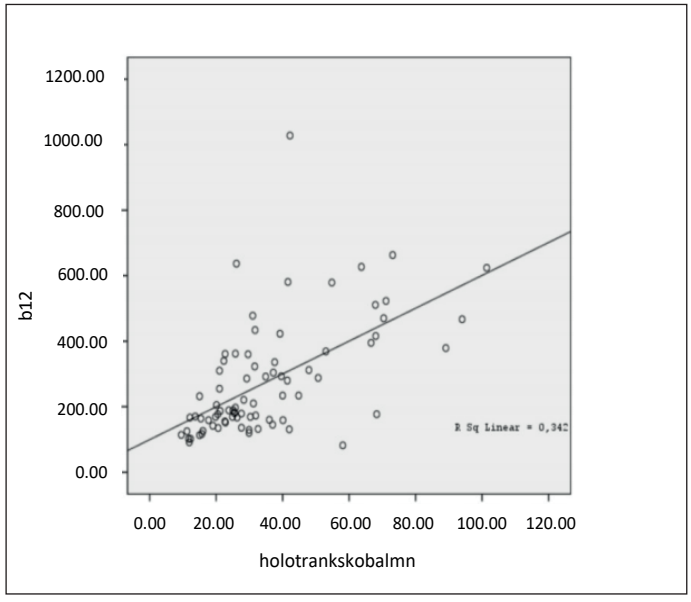

Figure 2: Correlation between vitamin B12 and holotranscobalamin of the subjects.

median uNGAL was 6.1 ng/ml (0.90-92.00 ng/ml). None of the patients included in the study showed no pathological level of NGAL excretion in the urine, but the NGAL level was close to the upper limit in some patients. There was no significant difference between the two groups in terms of uNGAL levels (p=0.290). No significant correlation was found between vitamin B12 and uNGAL; however, there was a weak negative correlation between uNGAL and holotranscobalamin levels (r= -0.24, p =0.045) (Figure 1).

Median holotranscobalamin level was 24.30 pmol/ l(9.50-68.30 pmol/l) in the patient group and 39.80 pmol/l (20.00-101.40 pmol/l) in the control group. Holotranscobalamin levels were found to be low (<35 pmol/l) in 28 patients in the vitamin B12 deficient group and 14 patients in the control group. Holotrascobalamin levels were significantly lower in the vitamin B12 deficient group than the controls (p <0.001). A positive correlation was also found between vitamin B12 and holotranscobalamin levels (r=0.57, p <0.001) (Figure 2).

DISCUSSION

Vitamin B12 is for cell metabolism, nucleic acid synthesis and cell proliferation. This study revealed that no negative effects of vitamin B12 deficiency on renal functions in non-anemic children. Vitamin B12 is needed more during periods that cell regeneration is rapid growth and development like infancy and adolescence. For this reason, its deficiency is most frequently seen in the periods when the need is not adequately met with nutrients. Frequency of vitamin B12 deficiency in adolescents was reported to be %10.5 in our country (12). In our study, the median age of vitamin B12 deficient group was 13 years, and 27 of 34 patients (80%) were between the ages of 12 and 18 years that, they were in adolescence period likewise that study. We found also a negative correlation between the age of patients and vitamin B12 levels.

Deficiency of vitamin B12 results in hyperhomocysteinemia and increased MMA levels in the plasma. Kumagai et al.(13) analysed the renal effects of hyperhomocysteinemia, and showed increased arterial and arteriolar wall thickness and focal tubulointerstitial fibrosis in the kidneys of rats. They reported a negative correlation between creatinine clearance and homocysteine levels. In the present study, comparison of kidney functions between the groups with and without vitamin B12 deficiency revealed no significant difference in urea, creatinine, GFR and albumin levels, although hyperhomocysteinemia was present in 79% of those with vitamin B12 deficiency patients.

Miliku et al.(8) also investigated the effects of maternal and fetal B12 and homocysteine levels on the renal function of children, they observed high GFR values in those with high fetal B12 values. It has been concluded that those with higher levels of homocysteine may also have smaller kidney sizes and decreased GFR values.

Serum creatinine is a late indicator of kidney damage, however uNGAL can provide the earliest detection of renal damage. Zappitelli et al.(14) detected the development of acute kidney injury in critically ill children earlier by uNGAL evaluation. Gunes et al. Analysed human kidney injury molecule-1 (KIM-1), liver-type fatty-acid binding protein (L-FABP) and N-acetyl-bD-Glocosaminidase A (NAG) in addition to uNGAL to detect early renal damage in children with B12 deficiency. Evaluation of these markers and urine electrolytes were found to be similar in the vitamin B12 deficient and control groups. However, the rate of NGAL, KIM-1, L-FABP and NAG proteins in urine to creatinine was found to be higher in patients with vitamin B12 deficiency compared to controls. This difference suggests the presence

of a subclinical renal injury in patients with B12 deficiency. They concluded that hypoxia may develop secondary to anemia and renal damage may developed accordingly (6). In our study, uNGAL values were found within normal limits in all patients. In 34 children in this study group, vitamin B12 deficiency did not cause a pronounced anemia. No significant difference was found in terms of uNGAL values between the vitamin B12 deficient and the control groups. However, there was a negative correlation between holotranscobalamin and uNGAL. This negative correlation isn't enough evidence to said that supports the entity of a chronic process that kidney injury increases parallel to severity of vitamin B12 deficiency. In our study, urinary creatinine couldn't analyses, so the rate of uNGAL to creatinin in urine couldn't be compared. This is a important deficiency of the study.

The transcobalamin, which enables the transport of vitamin B12 in the plasma, is bound to vitamin B12, then holotranscobalamin is formed. Holotranscobalamin is the component of vitamin that reaches the cells, therefore it shows the adequacy of the metabolic function of vitamin B12 and called active B12. Studies showed that holotranscobalamin is a more sensitive marker than serum vitamin B12 in defining vitamin B12 deficiency (15,16). In the study conducted by Bamonti et al.(17), a strong correlation was found between holotranscobalamin and vitamin B12 values. In our study, in accordance with the literature, holotranscobalamin was found to be positively correlated with vitamin B12 levels.

The most important limitation of the study is that urinary creatinine can not be studied. Urine creatinine to uNGAL ratio could provide a more sensitive result to compare renal damage. Another limitation is small sample size. Additionally, vitamin B12 deficient patients were not anemic, which may have prevented hypoxia-induced renal damage.

CONCLUSION

In conclusion, vitamin b12 deficiency seems to no effect on kidney functions in non-anemic children. Further large scale studies are warranted to evaluate the indicators of renal damage in vitamin B12 deficiency.

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İnsan İmmün Yetmezlik Virüsü ile İnfekte Anne Bebekleri ve Perinatal Geçisin Değerlendirilmesi

Evaluation of Infants of Mothers Infected with Human Immunodeficiency Virus and Perinatal Transmission

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ÖZ

Amaç: Tüm dünyada ve ülkemizde HIV/AIDS hem bireysel hem de toplumsal sonuçları ağır olan önemli bir halk sağlığı sorunudur. Gelişmekte olan ülkelerde, HIV ile enfekte çocukların %90'ından fazlasında virüs anneden bebeğe bulaşmaktadır. Her yıl tüm dünyada HIV pozitif 1.3 milyon kadın gebe kalmakta ve anneden çocuğa HIV geçişi küresel olarak yeni HIV enfeksiyonlarının %9'unu oluşturmaktadır. Bu çalışmada HIV ile enfekte annelerden doğan bebeklerin ve perinatal geçişi önlem için uygulanan yöntemlerin sonuçlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Ocak 2015- Aralık 2020 tarihleri arasında Çocuk Enfeksiyon Hastalıkları kliniğinde izlenen HIV ile enfekte annelerden doğan bebeklerin klinik ve laboratuvar özellikleri retrospektif olarak incelendi.

Bulgular: Çalışmamızda 6 yıllık süreçte HIV'li anneden doğan 22 bebek izlendi. Bebeklerin 14'ü (%63.6) erkekti. Bir bebek 34 haftalık prematür diğerleri miad doğumdu. 12 (%54.5) anne gebe kalmadan önce HIV olduğunu biliyordu. 10 anne gebelik sırasında taramalarda tanı almıştı. Bunların 4'ü (%40) ilk trimestirde, 6'sı (%60) son trimestirde idi. 19 (%86.4) anne gebelik sırasında antiretroviral tedavi (ART) aldı. Doğum sırasında annelerin HIV RNA sonucu 14 (%63.6) negatif, 7 (%31.8) pozitif ve 1 (%4.5) bilinmiyordu. 7 (%31) anneye doğum sırasında ART profilaksi verildi. Bebeklerin 19'u (%86.4) sezaryen ile doğdu ve hiçbiri anne sütü almamıştı. Hastaların 20'si (%90.9) doğar doğmaz yıkanmıştı. 21 bebeğe doğum sonrası ilk 24 saat içinde oral antiretroviral profilaksi başlandı. 19 hastaya sadece zidovudin, 2 hastaya zidovudin ve nevirapin ikili profilaksi başlandı. Bebeklerinin hiçbiri HIV ile enfekte olmadı.

Sonuç: Çalışmamızda antiretroviral profilaksi ve bir takım önlemler ile HIV'li anne bebeklerinin hiçbirinin enfekte olmadığı saptandı. HIV ile enfekte çocukların %90'dan fazlasında virus vertikal yolla bulaş sonucu kazanılmaktadır. HIV pozitif gebelerin erken tanısı ve gebelerde antiretroviral tedavinin kullanımının artması, sezaryen ile doğum, bebeğe doğum sonrası antiretroviral profilaksi, anne sütü verilmemesi, doğar doğmaz yıkama gibi bir takım önlemler ile anneden bebeğe HIV geçişini önlemek mümkündür.

Anahtar Sözcükler: AIDS, Anneden bebeğe geçiş, HIV, Gebelik, Profilaksi

ABSTRACT

Objective: HIV/AIDS is an important public health problem with severe individual and social consequences all over the world and in our country. Every year, 1.3 million women become pregnant worldwide, and mother to child transmission of HIV accounts for 9% of new HIV infections globally. In this study, it was aimed to evaluate infants born to HIV-infected mothers, and to evaluate the results of the methods applied to prevent perinatal transmission.

Material and Methods: The clinical and laboratory characteristics of infants born to HIV-infected mothers, who were followed up in the Pediatric Infectious Diseases clinic between January 2015 and December 2020, were analyzed retrospectively.

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***Etik Kurul Onayı / Ethics Committee Approval*:** Bu çalışma Helsinki Deklarasyonu İlkelerine uygun olarak yapılmıştır. Çalışma için Çukurova Üniversitesi, Tıp Fakültesi, Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'ndan onay alındı (No 108, 12/02/2021).

Yazarların katkısı / Contribution of the Authors*: *ÇAY Ü: Araştırma ve/veya makalenin hipotezini veya fikrini oluşturan, Sonuçlara ulaşmak için planlama/metodoloji belirleme, Hasta takibinde sorumluluk almak, ilgili biyolojik malzemelerin toplanması, veri yönetimi ve raporlama, deneylerin yürütülmesi, Sonuçların mantıksal olarak Yorumlanması ve sonuçlandırılması, Çalışma için gerekli literatür taramasında sorumluluk almak, Çalışmanın bütününün veya önemli bölümlerinin yazımında sorumluluk almak. ***TAPAÇ NN:*** Araştırma/çalışmanın sorumluluğunu üstlenmek, ilerlemenin seyrini denetlemek. ***ÖZGÜR GÜNDEŞLÜOĞLU Ö:*** Araştırma/çalışmanın sorumluluğunu üstlenmek, ilerlemenin seyrini denetlemek. ***ALABAZ D:*** Yazım ve dilbilgisi dışında bilimsel olarak gönderilmeden önce makaleyi gözden geçirme.

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Results: In our study, 22 infants born to HIV-infected mothers were followed over a six-year period. 14 (63.6%) of the infants were male. One infant was 34 weeks premature and the others were term. 12 (54.5%) mothers knew they had HIV before they became pregnant. 10 mothers were diagnosed during pregnancy scans. Four (40%) of these were in the first trimester and six (60%) were in the last trimester. 19 (86.4%) patients received antiretroviral therapy (ART) during pregnancy. The HIV RNA result of the mothers at the time of delivery was found to be 14 (63.6%) negative, seven (31.8%) positive and one (4.5%) unknown. Seven (31%) mothers were given ART prophylaxis during delivery. 19 (86.4%) infants were delivered by C-section. None of them had been breastfed. 20 (90.9%) of the patients were bathed as soon as they were born. Oral antiretroviral prophylaxis was started in 21 infants within the first 24 hours after delivery. 19 patients were started only on zidovudine, and 2 patients were started on dual prophylaxis with zidovudine and nevirapine. None of the infants were found to be HIV-infected.

Conclusion: It was determined that none of the infants of HIV-infected mothers followed up in our study were infected. In more than 90% of HIV-infected children, the virus is acquired as a result of vertical transmission. Prevention of HIV transmission from mother to infant is possible with some measures such as early diagnosis of HIV-positive pregnant women, increase of antiretroviral therapy in pregnant women, Cesarean delivery, postpartum antiretroviral prophylaxis, avoidance of breastfeeding and bathing the infant as soon as it is born.

Key Words: AIDS, Mother-to-child Transmission, HIV, Pregnancy, Prophylaxis

GİRİŞ

Tüm dünyada ve ülkemizde HIV/AIDS (Human immunodeficiency virus; HIV, Acquried-immunodeficiency syndrome; AIDS) hem bireysel hem de toplumsal sonuçları ağır olan önemli bir halk sağlığı sorunudur. Günümüzde, çocukluk çağında HIV enfeksiyonunun ortadan kaldırılması yönünde büyük ilerlemeler kaydedilmesine rağmen, pediatrik HIV 'in küresel yükü özellikle gelişmekte olan ülkelerde önemli bir halk sağlığı sorunu olmaya devam etmektedir. 2018 yılı verilerine göre 15 yaşından küçük 160.000 çocukta yeni HIV enfeksiyonu bildirilmiş olup, HIV/AIDS tanısı olan çocuk sayısı 1.7 milyona ulaşmıştır (1). Her yıl tüm dünyada HIV pozitif 1.3 milyon kadın gebe kalmakta ve anneden çocuğa HIV geçişi küresel olarak yeni HIV enfeksiyonlarının %9'unu oluşturmaktadır (2,3). HIV ile enfekte çocukların büyük çoğununa virus anneden bebeğe gebelik sırasında, doğum sırasında veya postnatal emzirme yoluyla bulaşmaktadır (4,5).Bu nedenle, pediatrik HIV epidemiyolojisi anneden bebeğe bulaşın önlenmesi üzerine temellendirilmelidir. Perinatal HIV bulaşının önlenmesinin daha iyi anlaşılması,son 25 yılda ilaç geliştirmedeki illerlemeler ışığında HIV'li gebe kadınların yönetiminde önemli ölçüde gelişmiştir. Amerika Birleşik Devletleri ve Avrupa'da, anneden bebeğe HIV bulaşma riski, antiretroviral ilaçların kullanımıyla tarihsel olarak düşük seviyelere gerilemiştir (6,7). Bu başarılı önleme çabasına katkılar arasında hamile kadınlarda HIV enfeksiyonu için tarama testleri, sezaryen ile doğum (uygun olduğunda) ve emzirmeden kaçınma yer alır. Anneden bebeğe HIV geçişini azaltmakta erken tanı esastır ve bunun için gebelikte veya öncesinde HIV testi yapılması önerilmektedir. Antiretroviral tedavi (ART)'ye ulaşımın artması ile anneden bebeğe HIV geçişinin %18 oranında azaldığı bu oranın 2010 yılında %9 olduğu bildirilmiştir (8). HIV ile enfekte kadınlar ve bebeklerde uygun önlemler alındığında anneden bebeğe HIV geçişin %1'in altına düşürülebilmektedir (9).

Bu çalışmada HIV ile enfekte annelerden doğan bebeklerin klinik, laboratuvar özelliklerinin belirlenmesi, perinatal geçişi önlem için uygulanan yöntemler ve sonuçların değerlendirilmesi amaçlanmıştır.

MATERYAL ve METOD

Çukurova Üniversitesi Tıp Fakültesi Balcalı Hastanesi'nde Ocak 2015- Aralık 2020 tarihleri arasında Çocuk Enfeksiyon Hastalıkları bölümünde izlenen HIV ile enfekte annelerden doğan bebekler çalışmaya dahil edildi. Hastaların dosyaları retrospektif olarak incelendi. Hastaların cinsiyet, şuanki yaşı, başvuru tarihi, doğum haftası, doğum kilosu, doğum şekli, anne sütü alma durumu, doğar doğmaz yıkanma durumu, bebeğe verilen antiretroviral profilaksi, ilk profilaksi doğumdan kaç saat sonra aldığı, profilaksi süresi, ilaç yan etkisi, doğumda, ikinci haftasında, ≥1 ay, ≥4 ay HIV RNA sonuçları, annelerin HIV enfeksiyonuna ve gebelik seyrine ait bilgiler, gebelikte kullandığı ART, doğum sırasında HIV RNA durumu, doğum esnasında profilaksi alma durumu föylere kaydedildi.

Antiretroviral profilaksi zidovudin > 35 hafta üzerinde doğanlarda 4mg/kg/doz günde iki kez, 30-35 hafta arası doğandoğum-2 hafta arası: 2 mg/kg/doz, günde iki kez, 2-4/6 hafta arası: 3 mg/kg/doz, günde iki kez oral başlandı. En az 6 hafta devam edildi. Bulaş riski yüksek olan durumlarda ikili profilaksi zidovudin ve nevirapin verildi. Yenidoğanın ilk haftasında 3 doz nevirapin (doğumda, ilk dozdan 48 saat sonra ve ikinci dozdan 96 saat sonra, Nevirapin: doğum kilosuna 1.5-2 kg ise her doz için 8 mg, 2 kg> ise her doz için 12 mg). HIV bebekte kesin HIV dışlanma kriteri emzirilmeyen bebekte iki ya da daha fazla negatif virolojik test (NAT, RNA veya DNA) (birisi ≥1 aylıkken, diğeri ≥4 aylıkken) veya iki ayrı örnekte iki negatif HIV antikor testi (≥6 aylıkken) olarak belirlendi (10). Takipte kalan negatif virolojik testlere sahip olgularımızda 12-18. ayda anti-HIV antikoru bakıldı. HIV-RNA testlerinden birinin pozitif çıkması, HIV enfeksiyonunun olarak kabul edildi. Pneumocystis jirovecii pnömonisi (PCP) için profilaksi HIV enfeksiyonu durumu belirlenemeyen bebeklere doğumdan sonraki 4-6. haftada başlandı. Emzirilmeyen bebekte; 14 günlükten ve 4 haftalıktan sonra 2 negatif nükleik asit testi varsa PCP için profilaksi başlanmadı.Çalışma için etik uygunluk yerel etik kuruldan alındı (No 108, 12/02/2021).

İstatistiksel analiz

İstatistiksel analiz için SPSS 23.0 versiyonu kullanılmıştır. Kategorik ölçümler artı ve yüzde olarak, sürekli ölçümler ise ortalama, sapma ve minimum-maksimum olarak özetlendi

BULGULAR

Çalışmamızda 6 yıllık süreçte 18 HIV'li anneden doğan anneden doğan 22 bebek takip edildi. 6'si (%36.4) kız, 14'ü (%63.6) erkek, 1(%4.5) hasta Suriyeliydi. Bir bebek 34 haftalık prematür diğer bebekler miadında doğmuştu. 12 (%54.5) anne gebe kalmadan önce HIV olduğunu biliyordu. 10 anne gebelik esnasında yapılan taramalarda tanı almıştı. Gebelik esnasında tanı alanların 4'ü (%40) ilk trimestirde, 6'sı (%60) son trimestirde ydi. Son trimestirde tanı alanların biri doğum esnasındaydı. 19 (%86.4) anne gebelik sırasında ART almıştı. Doğum sırasında annelerin HIV RNA sonucu 14'ü (%63.6) negatif, 7'si (%31.8) pozitif ve 1'i (%4.5) bilinmiyordu. Doğum sırasında sonucu pozitif olanların HIV RNA değerleri 110-63600 copy/mL arasında, bunların üçünün >1000 copy/mL üzerindeydi. Bu 7 gebeye doğum sırasında intravenöz zidovudin verildi. Bebeklerin 19'u (%86.4) sezaryen ile doğdu ve ortalama doğum ağırlığı 3157.5 (1960-3700) gramdı. Hiçbiri anne sütü almadı. bebeklerin 20'si (%90.9) doğar doğaz yıkandı, 2 (%9.1) bilinmiyordu. 21 bebeğe doğum sonrası ilk 24 saat içinde oral antiretroviral profilaksi başlandı. 19 bebeğe zidovudin, 2 bebeğe zidovudin ve nevirapin, başlandı. Nevirapin 3 doz, zidovudin 6-8 hafta devam edildi. Annesi son trimestirde tanı alan 1 bebek bize 19 günlük iken başvurmuştu. Doğar doğmaz yıkanmıştı ve anne sütü almamıştı. ART profklaksi verilmemişti. Antiviral profilaksi alan bebeklerin 2'sinde (%9.1) nötropeni gelişti. İlaç kesildikten sonra normale döndü. Ölü doğum, konjenital anomali perinatal ölüm görülmedi. Bebeklerin son kontrol yaşları ortalama 56 ay (aralık 5-120 ay) olarak belirlendi. Bu çalışmada; HIV'li annelerin bebeklerinin hiçbirnin enfekte olmadığı tespit edildi.

Tablo I: HIV tanılı anne ve bebeklerinin verileri.

	n* (%)
Cinsiyet	
Erkek	14 (63.6)
Kız	8 (36.4)
Etnik Köken	
Türkiye Cumhuriyeti Vatandaşı	21 (95.4)
Suriye	1 (4.6)
Gebede HIV Tanısının Zamanı	
Gebelik öncesi	12 (54.5)
Gebelik esnasında	9 (40.9)
Doğum sırasında	1 (4.5)
Gebelik esnasında ART durumu	
Almıyor	3 (13.6)
Lopinavir/Ritonavir-Tenofovir Disoproksil/Emtrisitabin	9 (40.9)
Tenofovir Disoproksil/Emtrisitabin - Raltegravir	5 (22.7)
Abakavir-Zidovudin – Dolutegravir	3 (13.6)
Tenofovir Disoproksil/Emtrisitabin - Dolutegravir	1 (4.6)
Tenofovir /Emtrisitabin Elvitegravir/Kobisistat	1 (4.6)
Doğum sırasında HIV RNA	
Negatif	14 (63.6)
Pozitif	7 (31.8)
Bilinmiyor	1 (4.6)
Gebe doğum sırasında ART Proflaksi	
Aldı	7 (31.8)
Almadı	15 (68.2)
Doğum Şekli	
C/S	19 (86.4)
NSVY	3 (13.6)
Doğum Haftası	
Premature	1 (4.6)
Miad	21 (95.4)
Doğar doğmaz yıkanma	
Evet	20 (90.9)
Bilinmiyor	2 (9.1)
Anne sütü alma durumu	
Almadı	22 (100)
Aldı	0
Antiretroviral Profilaksi	
Zidovudin	19 (86.4)
Zidovudin +Nevirapin	2 (13.6)
Bebeğin HIV ile enfekte olma durumu	
Enfekte	0
Enfekte olmadı	22 (100)

*****n=22, **ART:** Anti retroviral tedavi, **C/S:** sezeryan, **NSVY:** Normal servikal vajinal yol

TARTIŞMA

İlk anneden bebeğe HIV bulaşma vakaları 1980'lerin başında Amerika Birleşik Devletleri'nde (ABD) tespit edilmesi ile birlikte yapılan kapsamlı araştırmalar sonucunda, anneden-bebeğe geçiş için risk faktörleri, potansiyel bulaş mekanizması ve bulaş zamanlaması dahil olmak üzere küresel pediatrik HIV salgınının epidemiyolojisi daha iyi anlaşılmasına yol açmıştır (11). Pediatrik HIV enfeksiyonunun ortadan kaldırılması yönünde büyük ilerlemeler kaydedilmesine rağmen, pediatrik HIV'in küresel yükü, özellikle gelişmekte olan ülkelerde önemli bir halk sağlığı sorunu olmaya devam etmektedir. ART kullanılmasından önce perinatal HIV bulaşma riski, maternal risk faktörlerine ve emzirmenin uygulanıp uygulanmadığına bağlı olarak %15 - %45 arasında olduğu bildirilmiştir (12). Antiretroviral ajanların HIV bulaşmasını engellemek için kullanımına ilişkin çalışmalar 1990'ların başında ABD ve diğer kaynak zengini ülkelerde başlatılmıştır. Ayrıca bu ülkelerde emzirmeden kaçınmanın yanı sıra kapsamlı HIV ve gebelik bakım hizmetlerine erişim kolaylığı ile birleştiğinde, perinatal geçiş oranı %1-%2'ye düşmüştür (13-15).

HIV ile enfekte anneden bebeğe bulaş, ART öncesinde uterin %25-40, doğum esnasında ya da erken emzirme döneminde %50, geri kalanı ise emzirme döneminde olmaktadır (4). Bu

nedenle gebelik öncesi danışmanlık, antenatal HIV taraması, ART ve perinatal takibe kolay erişim anneden bebeğe geçisin temel önleyici tedbirleridir. Tedavi edilmeyen HIV enfeksiyonu ile anneden bebeğe bulaşma riski arasında güçlü bir ilişkisi vardır (16). Ayrıca Brezilyada yapılan bir çalışmada HIV vakalarının çoğunun yoksulluk, genç yaşta doğum ve düşük eğitim düzeyi ile ilişkili olduğu ve kadınlarda HIV teşhisi konulmadan gebelik geçirme riski daha yüksek olduğu tespit edilmiştir(17).Brezilya 1996-2016 yılları arasında HIV ile yaşayan insanlara evrensel, ücretsiz, ART ve genel sağlık bakımı sağlanması, HIV hızlı testlerini ücretsiz yapılması, gebe ve emziren kadınlarda anne sütü yerine geçen mamaları karşılanması sağlık politikalarına eklenmesi sonucunda son 20 yılda anneden bebeğe HIV geçişini %50 azaltıldığı bildirmiştir (17). Ülkemiz HIV/AIDS açısından hastalığın az sıklıkta görüldüğü ülkeler arasında yer almakla birlikte son yıllarda özellikle 2010 yılından sonra yeni tanı sayısında önemli oranda artış olup HIV tanılı hastaların % 18.95'i kadınlardır.HIV/AIDS yayılımı için risk oluşturan faktörlerle savaşım, her bireyin tanı, tedavi, bakım ve desteğe eşit ulaşımını sağlayarak toplumun sağlığını korumak ve geliştirmek misyonu altında ülkemizdeki HIV/AIDS çalışmalarına yol haritası oluşturmak amacıyla "Türkiye HIV/AIDS Kontrol Programı, 2019-2024" hazırlanmıştır. Bu kapsamda yeni HIV ile enfekte olgu sayısının %75 azaltılması ve HIV ile enfekte yenidoğan sayısının sıfır olması hedeflenmektedir(18).Ülkemizden bildirilen 2 çalışmada anneden bebeğe geçiş oranı %6.7-%8.3 olarak bildirilmiştir (19,20). Bizim çalışmamızda bu oran %0'dı. Kontrol programı sonrası bu oranların tüm ülkede %1 altına düşmesi ümit edilmektedir.

HIV bulaşını önlemede gebelik öncesi tarama büyük öneme sahiptir ancak çoğu merkez tüm hamile kadınları ilk trimesterlerinde ve doğumda test edilmektedir. ülkemizde Sağlık Bakanlığı, 2018 yılında doğum öncesi bakım yönetimi kılavuzlarında ilk kontrolde hamile kadının onayı ile HIV tarama testi yapılmasını önermektedir (21). Ülkemizden bildirilen bir çalışmada gebelik sırasında %31.43 (10/32), doğum sırasında %21.8 (7/32) tanı aldığı bildirilmiştir (19). Bir başka çalışmada gebelik sırasında %15.4 doğum sırasın %7.7 tanı almıştır (20). Bizim çalışmamız ise gebelik sırasında %40.9 (9/22), doğum sırasında % 4.5 (1/22) tanı almıştı. Sonuç olarak üreme çağındaki kadınlarda gebe kalmadan önce tanı konulması, tedavi ve bebeğe bulaşı önleme açısından büyük öneme sahip olduğu görüşünü ortaya koymaktadır. Bu kapsamda HIV testi cinsel açıdan aktif tüm kadınlara gebelik öncesi ve doğum öncesi rutin bakılması önerilmektedir (22).

Anneden bebeğe bulaşmadaki en önemli risk faktörü annenin plazma ve sütündeki viral yük ayrıca annenin immünolojik durumu, klinik evresi gelmektedir (11). HIV RNA'sı ≤1000 kopya/mL olan gebelerde, bebeğe HIV bulaşma insidansı düşüktür (11). Anneden bebeğe geçişi önlemek için zidovudin denenen çalışmalarda viral yük seviyelerinin analizlerinde, Tayland, Batı Afrika Uganda ve Kenya'dan yapılan çalışmaların tümü, maternal plazma viral yükü ile bebeğe bulaşma riski arasında doğrudan pozitif bir korelasyon olduğunu göstermektedir (23-27). Townsend ve ark. (28) yaptığı 12486 HIV tanılı gebenin analiz edildiği çalışmada, doğuma yakın viral yükü <50 kopya / mL olan kadınlar arasında, daha yüksek viral yüke sahip olanlara kıyasla daha düşük geçiş olduğu gösterilmiştir.

Fransa'da 2000-2011 yılları arasında antepartum ART uygulanan HIV'li 8075 kadın üzerinde yapılan bir çalışmada, doğumda viral yükü 50-400 kopya/mL olan kadınlar ile viral yükü <50 kopya/mL olanlar karşılaştırıldığında 4 kat daha yüksek için perinatal bulaşma olasılığı saptanmış ve viral yükü > 400 kopya/mL olan kadınlar arasında bulaşma oranı %2.8 tespit edildiği bildirilmiştir (29). Bu veriler ART kullanımını desteklemektedir. Ortak Birleşmiş Milletler HIV / AIDS Programı (UNAIDS), anneden bebeğe geçişin önlenmesine yönelik antiretroviral programlarının 21 öncelikli ülke arasında 2009'da %36'dan 2015'te %80'e yükseldiğini bildirdi (30). Gebelik öncesi ya da ilk trimestirde tanı tedavi ve doğumdan önce HIV viral yükünün <50 kopya /mL tutulması önlemede ana unsurlardan biri olduğu gerçeği ortaya çıkmaktadır.

Doğum öncesi HIV RNA sonucu doğum şeklini belirlemede büyük öneme sahiptir. Bu nedenle gebeliğin hangi döneminde tanı konulursa konulsun ART başlanmalı PCR takibi yapılmalıdır.

Ayrıca perinatal geçişin önlenmesinde doğum şekli büyük öneme sahiptir. Eskiden tüm gebelere elektif sezaryen önerilirken günümüzde anne viral yüküne göre karar verilmektedir. Bu nedenle anne viral yükü, doğum şekli ve zamanlamasına ilişkin karara yardımcı olmak için 34-36. gebelik haftalarında da değerlendirilmelidir (10). Doğuma yakın viral yük ≥ 1000 kopya /ml ise, mebran rüptürü ve doğum eylemi başlamadan önce perinatal geçişin önlenmesi için 38. gebelik haftasında planlanmış sezaryen ile doğum önerilmektedir (10,31). Planlı sezeryan eyleminin anneden bebeğe bulaşı %10.8'den %1.5 düşürdüğü gösterilmiştir (31). Viral yük, doğuma yakın < 1000 kopya/ml ise özel obstetrik nedenler olmadıkça normal doğum önerilmektedir (33). Bizim çalışmamızda gebelerin %86.4 (19/22) sezaryen ile doğum yaptırılmıştı. Doğum sırasında sadece 3 hastanın HIV RNA >1000 üzerinde olmasına rağmen sezaryen oranının bukadar yüksek olmasının nedeni Türkiye'de HIV oldukça az görülüp son yıllarda artmasına bağlı medikolegal endişelerden dolayı olabileceği tahmin edilmektedir.

Doğum eylemi sırasında intravenöz zidovudin ve bebeğe zidovudin proflokside kullanılması önerilmektedir. Doğum sırasında tanı alan ya da ART kullanan doğum sırasında HIV RNA >50 kopya/ml üzerinde olan gebelerde profilakside IV zidovudin önerilmektedir (34). Bizimde çalışmamızda %31.8 (7/22) gebenin HIV RNA >110 kopya/ml olması üzerine intrapartum profilaksi uygulandı. HIV annelerden doğan tüm yenidoğanların en kısa zamanda, ideali doğumdan sonra ilk 12 saat içerisinde monoterap ya da kombine antiviral profilaksi uygulması bebekte HIV bulaşma riskini azaltmaktadır. Düşük riskli bebeklerde tekli zidovudin 4- 6 hafta boyunca önerilmektedir. Doğum sırasında tanı alan, gebelikte ART almayan ya da sadece intrapartum

ART alan,doğum önceki 4 hafta içinde HIV RNA ≥ 50 kopya / ml olan gebelerden doğan bebekler yüksek riskli olup kombine antiretroviral profilaksi önerilmektedir (34). Bizim çalışmamızda 21 hastaya oral profilaksi başlanmıştı. 7 (%31.8) hastamızda doğun esnasın HIV RNA yüksek olmasına rağmen sadece 2 hastaya zidovudin + nevirapin kombine profilaksiprofilaksi verildi. 1 hasta 19 günlükken başvurdu ve profilaksiprofilaksi almamıştı. Buna rağmen HIV enfekte olan bebek olmadı.

Anne sütünde, kolostrumdaHIV RNA tespit edilmiş ancak bulaş mekanizması tam aydınlatılamamıştır. Dünya sağlık örgütü, HIV'li olduğu bilinen anneler için, bulaşmayı önlemek emzirmeden kaçınmayı ve alternatif güvenli beslenme kaynakları sağlamayı önermektedir (35). Biz çalışmamızda bebeklerin tümüne anne sütü vermedik. Bebeklerimizden birinin annesidoğum sırasında tanı almıştı. Sezaryen ile doğum ve anne sütü verilmemesi dışında ek önlem alınmamıştı. Buna rağmen HIV bulaşı olmadı. Anne sütünün verilmemesinin anneden bebeğe geçişini önlemede önemli yeri olduğunun desteklemektedir. Öte yandan kaynakları sınırlı ülkelerde malnutrisyon ve uygun olmayan beslenme koşulları nedeniyle enfeksiyonlara yol açabilmektedir. HIV ile enfekte olmamış bebeklerin anne sütü almaması mortalite ile ilişkilendirilmiştir. Bu nedenle bu ülkelerde anneye ART verilerek emzirmeye teşvik sağlanabilir (36).

ART öncesindebebeklere bulaş yaklaşık %25-40 intrauterin dönemde olmaktadır (37). İntrauterin bulaşın büyük oranda 3.trimestirde (28-36 haftalar) olduğu düşünülmektedir (37,38). Nadirende erken intrauterin dönemde olabilir.Bulaşma mekanizmalarının plasentanın bütünlüğünün bozulmasıyla viremik maternal kanın plasentadan fetüse mikro geçişine yol açtığı düşünülmektedir (39). Çalışmalar genital sistem enfeksiyonlarının ve plasental inflamasyonun, özellikle koryoamniyonitin intrauterin HIV geçişinde artabileceğini göstermiştir (40). Tawiandan yapılan 39 gebe ile yapılan çalışmada %2.6 (1/39) intrapartum, %28.2 (11/39) antepartum tanı almış ve 3 trimestir tanı alıp %16.7 (6/39) ART başlanmış ve hiçbir bebeğe bulaş olmadığı bildirilmiş (41). Bizim hastalarımızın 6'sı 3 trimestir de tanı almıştı ve doğum esnasında viral yük 110 kopy/mL üzerinde olmasına rağmen bulaş olmadığı görüldü. Çocuk HIV vakalarının önlenmesinde ana faktör HIV'lı kadınların erken tespiti, antepartum ve peripartum dönemde ART kullanması kritik öneme sahiptir. Ne kadar erken aylarda ART başlanırsa bulaş oranı o kadar azalmaktadır.

Çalışmamızın temel kısıtlılığıvaka sayısının azlığı retrospektif ve tek merkezli olmasıdır. Ülkemizdeki durumun bildiren kesin sonuçlar için ulusal çapta ortak çalışmalara gereksinim vardır.

Sonuç olarak, HIV ile enfekte çocukların büyük çoğunluğu virüsu uterin ve intrapartum almaktadır. Tüm ülkelerde HIV pozitif gebelerin erken tanısı ve gebelerde antiretroviral tedavinin kullanımının artması, sezaryen ile doğum, bebeğe doğum sonrası antiretroviral profilaksi, anne sütü verilmemesi gibi bir takım önlemleri içeren etkin programlar oluşturulmalıdır. HIV gebeler mutlaka multidispiliner yaklaşımın gereksinimi nedeniyle perinatolog, erişkin ve çocuk enfeksiyon hastalıklarının olduğu merkezlerde takip edilmelidirler.

KAYNAKLAR

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COVİD-19 Pandemisi Çocuk Sağlığı İzlemlerini Nasıl Etkiledi?

How Has The COVID-19 Pandemic Affected Child Health Tracks?

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ÖZ

Amaç: COVID-19 Pandemisi'nde Sağlam Çocuk İzlemlerinde yaşanan aksaklıkların tespit edilmesi amaçlanmıştır.

Gereç ve Yöntemler: Ülkemizde sokağa çıkma yasaklarının başladığı 14 Mart 2020 tarihinden itibaren 31 Mart 2021 tarihine kadar geçen zamanda hastanemiz Sağlam Çocuk Polikliniği'ne başvuran hastaların dosyaları retrospektif olarak incelendi.

Bulgular: Bu dönemde çocuk sağlığı izlemleri için 5036 hasta başvurdu. Bu hastaların %1.44'ünün (n=73) izlemlerinde eksiklikler olduğu saptandı. Hastaların %35.6'ı Türkiye Cumhuriyeti vatandaşı, %32.9'u Suriyeli, %31.5'i Iraklı mültecilerdi. Hastaların %78.1'i demir profilaksisi almamaktaydı. Kalça ultrasonografisinin %72.6 (n=53) hastada yapılmadığı saptandı. Hastaların %80.8'inde aşı ve beraberinde eksik diğer izlemler varken, %31.5'inin sadece aşısının eksik olduğu diğer taramaların yapıldığı saptandı. Hastaların %38.3'ünün birden fazla aşıyı yaptırmadığı, %12.3'ünün ise aşı reddi nedeni ile doğumdan itibaren hiçbir aşıyı yaptırmadığı saptandı. Eksik takipler açısından Türkiye Cumhuriyeti vatandaşı ile Suriye veya Iraklı vatandaşlar arasında fark saptanmadı (p=0.213). Aşılardaki eksiklikler açısından bakıldığında Suriye ve Iraklı mültecilerin aşılamada eksikliklerinin daha fazla olduğu saptandı (p<0.001).

Sonuç: Sağlıklı çocuklar yetiştirebilmek için bu izlemlerin aksamaması konusunda halkımızın bilgilendirilmesi, eksik takiplerin saptandığı her durumda hastaların geciktirilmeden yönlendirilmesi gerektiği düşünülmektedir.

Anahtar Sözcükler: Aşı, COVİD 19, Sağlıklı Çocuk, Takip

ABSTRACT

Objective: It is aimed to detect the disruptions experienced in Healthy Child Follow-ups in the COVID-19 Pandemic.

Material and Methods: The files of the patients who applied to the Healthy-Child Outpatient Clinic of our hospital from March 14, 2020, when the curfews began in Turkey, until March 31, 2021, were reviewed retrospectively.

Results: During this period, 5036 patients applied for healthy-child follow-ups. It was found that 1.44% (n=73) of these patients missed some of their follow-ups. Of these patients, 35.6% were citizens of the Republic of Turkey, 32.9% were Syrian, and 31.5% were Iraqi refugees. 78.1% of the patients were not taking iron prophylaxis. Hip ultrasonography was not performed in 72.6% of the patients. It was found that 80.8% of the patients were missing vaccination and other follow-ups, while 31.5% were only missing vaccination while other follow-ups were complete. It was determined that 38.3% of the patients did not have more than one vaccination, and 12.3% did not have any vaccination since birth due to vaccine rejection. There was no difference between Turkish citizens and Syrian or Iraqi citizens in terms of missing follow-ups (p=0.213). In terms of missing vaccinations, it was determined that Syrian and Iraqi refugees missed more vaccinations (p<0.001).

Conclusion: In order to raise healthy children, it is thought that public should be informed about the importance of follow-ups, and patients should be guided without delay in every case of missing follow-ups.

Key Words: Vaccine, COVID 19, Heathy Child, Follow up

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***Yazarların katkısı / Contribution of the Authors*: YALAKİ Z:** Araştırma ve/veya makalenin hipotezini veya fikrini oluşturan, Sonuçlara ulaşmak için planlama/metodoloji belirleme, Araştırma/çalışmanın sorumluluğunu üstlenmek, ilerlemenin seyrini denetlemek, Hasta takibinde sorumluluk almak, ilgili biyolojik malzemelerin toplanması, veri yönetimi ve raporlama, deneylerin yürütülmesi, Sonuçların mantıksal olarak Yorumlanması ve sonuçlandırılması, Çalışma için gerekli literatür taramasında sorumluluk almak, Çalışmanın bütününün veya önemli bölümlerinin yazımında sorumluluk almak, Yazım ve dilbilgisi dışında bilimsel olarak gönderilmeden önce makaleyi gözden geçirme.

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GİRİŞ

Sağlıklı bir bireyin gelişimi için doğumdan başlayarak düzenli olarak büyüme ve gelişiminin izlemi ile birlikte koruyucu önlemlerin alınması gerekmektedir. Bu amaçla gerçekleştirilen Çocuk Sağlığı İzlemlerinin zamanlaması ve sıklığı, çocuğa, ailesine, büyüme-gelişme dönemleri ile aşılama programına göre belirlenir (1). Sağlam Çocuk İzlemi'nde (SÇİ) hem anne sütünün desteklenmesi hem de büyüme gelişmenin en hızlı olduğu dönem olması nedeni ile ilk altı ayda aylık takiplerin yapılması önerilmektedir. Altı aydan sonra üç ayda bir kontrol önerilmekle birlikte tamamlayıcı beslenmenin değerlendirilebilmesi için izlem aralığının daha sık da olabileceği ifade edilmektedir (1, 2).

Sağlam Çocuk İzlemi'nde, koruyucu sağlık hizmetleri içerisinde en önemli uygulamalardan birisi çocukluk çağı aşılamalarıdır. Aşılama ile çocuk ciddi morbiditesi ve mortalitesi olan hastalıklara karşı korunmuş olur. Ülkemizde Genişletilmiş Bağışıklama Programı ile aşılama oranları 2018'de %92-98 iken, 2019'da %96-99'a yükselmiştir (3). Aşılama oranları ile enfeksiyon kaynaklı ölüm nedenleri azalmaktadır ve bu durum Türkiye İstatistik Kurumu 2019 verilerinde bir yaş altında bebek ölüm hızının %0.9'a düşmesine katkı sağlamıştır (4).

Koruyucu sağlık hizmetleri içerisinde yer alan önemli uygulamalardan birisi de tarama programlarıdır. Taramalar, bir sağlık sorununun belirti vermeden önce saptanmasına yönelik sağlık hizmetleridir. Bu sayede sorunun kalıcı bozukluklara yol açmadan tanınıp düzeltilmesi amaçlanır. Ülkemizde de bu amaçla yenidoğan döneminden itibaren yapılan taramalar (fenilketonüri, konjenital hipotiroidi, biotinidaz eksikliği, kistik fibrozis, işitme taraması, doğumsal kalça displazisi (DKD), göz muayenesi, anemi taraması vb) bulunmaktadır (1, 2). Sağlıklı çocuk izlemlerinde bu taramaların ve düzenli izlemlerin yapılması, sağlıklı bireyler yetişmesi açısından önemlidir.

İlk olarak Çin'in Wuhan Eyaleti'nde ortaya çıkan ve daha sonra tüm dünyaya yayılarak 11 Mart 2020'de pandemi olarak ilan edilen yeni koronavirüs hastalığı (COVID-19) tüm dünyayı birçok yönden olumsuz etkilemiştir ve etkilemeye devam etmektedir (5). Dünya genelinde COVID-19 Pandemisi nedeniyle yetkililer tarafından virüsün kontrol altına alınmasına yönelik ciddi önlemler alınmakta ve uyarılar yapılmaktadır. Virüsün belirtilerine ilişkin belirsizlik durumu, yüksek bulaş, ölüm oranları, salgının sonuçları, süresi ile ilgili belirsizlik durumu insanlarda tehdit algısı ve süreğen kaygıya neden olmaktadır (6). Bu süreçte ailelerin kendilerini ve çocuklarını korumak amacı ile evlerinden dışarı çıkmamaları, hastanelerin riskli olacağını düşünmeleri nedeni ile özellikle 0-2 yaş grubundaki çocukların SÇİ'de ve aşılarının yapılmasında eksiklikler veya gecikmeler olabileceği düşünülmüştür.

Bu nedenle çalışmamızda pandemi döneminde Sağlam Çocuk Polikliniği'ne gelen ve SÇİ'de eksiklikleri olan hastaları belirlemeyi amaçladık.

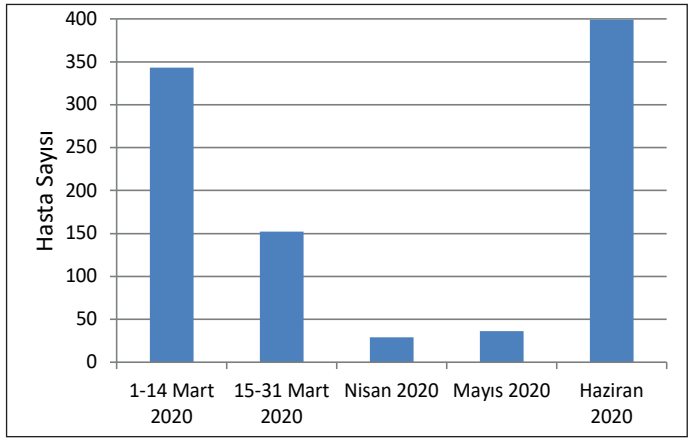
GEREÇ ve YÖNTEMLER

Çalışma için hastanemiz Sağlam Çocuk Poliklinik başvurularındaki aylık değişimleri saptayabilmek amacıyla Şubat 2020-Mart 2021 arasındaki başvuru sayılarının geriye dönük olarak taraması yapıldı. Sonrasında COVİD-19'un pandemi ilan edildiği ve ülkemizde uygulanan sokağa çıkma yasaklarının başladığı 14 Mart 2020 tarihinden itibaren 31 Mart 2021 tarihine kadar geçen zamanda hastanemiz Sağlam Çocuk Polikliniği'ne başvuran hastaların dosyaları retrospektif olarak incelendi. Sağlam Çocuk İzlemlerinde aşı ve taramaların yoğun olduğu ilk iki yaştaki çocukların sosyodemografik özellikleri, aylarına uygun aşı ve taramaların yapılıp yapılmadığı, aylarına uygun vitamin kullanıp kullanmadıkları dosya verilerinden kaydedildi. Çalışma için, Ankara Hastanesi Klinik Araştırmalar Etik Kurulu'ndan 93471371-514.10 sayı ve 29/7/2021 tarih ile izin alınmıştır.

Çalışmanın istatiksel analizi için SPSS-20 paket programı kullanılmıştır. Sürekli ve kesikli sayısal değişkenlerin dağılımının normale yakın olup olmadığı Kolmogorov Smirnov testiyle araştırılmıştır. Tanımlayıcı istatistikler sürekli ve kesikli sayısal değişkenler için dağılımları ortanca (en küçük – en büyük) şeklinde, kategorik değişkenler ise olgu sayısı ve "%" biçiminde gösterilmiştir. Kategorik değişkenler Pearson'un Ki-Kare testiyle değerlendirilmiştir. İstatistiksel anlamlılık düzeyi $p<0.05$ olarak kabul edilmiştir.

BULGULAR

Sağlam Çocuk İzlemleri'nin yapıldığı polikliniğimize Şubat 2020'de 769 hasta gelirken, 1-14 Mart 2020 arasında 343 hastanın başvurduğu, 14 Mart 2020 tarihinden sonra başvuruların azaldığı, 14-31 Mart 2020 arasında 152, Nisan 2020'de 29, Mayıs 2020'de 36 hastanın başvurduğu, yasakların kaldırılıp normalleşme sürecinin başlamasıyla birlikte başvuruların tekrar artarak Haziran 2020'de 399 olduğu saptandı. Şekil 1'de pandemi döneminde Sağlam Çocuk Polikliniğimize başvuran hastaların dağılımı gösterilmiştir.



Şekil 1: Aylara göre hasta başvuruları.

Tablo I: Çalışmaya alınan hastaların sosyodemografik özellikleri.

	n (%)
Cinsiyet	
Kız	29 (9.7)
Erkek	44 (60.3)
Milliyet	
TC	26 (35.6)
Suriye	24 (32.9)
Irak	23 (31.5)
Doğum şekli	
Normal doğum	58 (79.5)
Sezeryan	15 (20.5)
Anne eğitim düzeyi	
Okuma-yazma yok	31 (42.5)
İlkokul	21 (28.8)
Ortaokul	9 (12.3)
Lise	9 (12.3)
Üniversite	3 (4.1)
Baba eğitim düzeyi	
Okuma-yazma yok	22 (30.1)
İlkokul	28 (38.4)
Ortaokul	10 (13.7)
Lise	8 (11.0)
Üniversite	5 (6.8)
Annenin mesleği	
Ev hanımı	71 (97.3)
Çalışıyor	2 (2.7)
Babanın mesleği	
İşsiz	12 (16.4)
İşçi	40 (54.8)
Serbest meslek	18 (24.7)
Özel	3 (4.1)
Akrabalık	
Var	32 (43.8)
Yok	41 (56.2)
Gebe takiplerine düzenli gidilmiş mi?	
Evet	60 (82.2)
Hayır	13 (17.8)
Çocuk sayısı	
Tek	14 (19.2)
2	16 (21.9)
≥3 (3-7 çocuk)	43 (58.9)
Aile tipi	
Çekirdek aile	26 (35.6)
Geniş aile	47 (64.4)
Sosyoekonomik düzey	
≤Asgari ücret	61 (83.6)
≥Asgari ücret -5000 TL	7 (9.6)
≥5000TL	5 (6.8)

Hastanemiz Sağlam Çocuk Polikliniği'ne, 14 Mart 2020-31 Mart 2021 tarihleri arasında çocuk sağlığı izlemleri için 5036 hasta başvurmuştur. Bu hastaların %1.44'ünün (n=73) izlemlerinde eksiklikler olduğu saptanmıştır. Çocuk Sağlığı İzlemleri'nde eksiklik saptanan hastaların yaş ortancası 5.5 ay (1-36) ve %60.3'ü (n=44) erkekti. Bu hasta gruplarının %35.6'sı (n=26) Türkiye Cumhuriyeti (TC) vatandaşı, %32.9'u (n=24) Suriyeli, %31.5'i (n=23) Iraklı mültecilerdi (p=0.233). Hastaların %19.2'i (n=14) ilk çocuktu ve

Tablo II: Çalışmaya alınan hastaların özellikleri.

	n (%)
Beslenme şekli	
Anne sütü	33 (45.2)
Anne sütü+ek gıda	13 (17.8)
Ek gıda	12 (16.4)
Anne sütü+mama	7 (9.6)
Mama+ek gıda	5 (6.8)
Mama	3 (4.1)
D vitamini kullanıyor mu?	
Evet	43 (58.9)
Hayır	30 (41.1)
Demir kullanıyor mu?	
Evet	16 (21.9)
Hayır	57 (78.1)
Kalça USG yapılmış mı?	
Evet	20 (27.4)
Hayır	53 (72.6)
Eksik olan takipler	
Aşı	23 (31.5)
Aşı+kalça USG+vitamin	10 (13.7)
Hepsi	9 (12.3)
Aşı+kalça USG	8 (11.0)
Kalça USG	7 (9.6)
Aşı+vitamin	6 (8.2)
Kalça USG+işitme taraması	4 (5.5)
Aşı+işitme taraması+kalça USG	2 (2.7)
İşitme taraması	2 (2.7)
Topuk kanı	1 (1.4)
Aşı+göz kontrol+anemi taraması	1(1.4)
Eksik aşılar	
Birden fazla sayıda aşı	28 (38.3)
Eksik aşı yok	14 (19.2)
Tek aşı	13 (17.9)
Hepsi (sadece doğumdaki aşı var)	9 (12.3)
Aşı reddi	9 (12.3)
Takiplerdeki aksama sebepleri	
COVID nedeni ile gitmeme	55 (75.4)
Aşı reddi	9 (12.3)
Bilmiyordum	6 (8.2)
Unuttum	3 (4.1)

%64.4'ü (n=476) geniş ailede yaşamaktaydı, %79.5'i (n=58) normal doğum ile doğmuştu. Doğum haftası ortancası 39 hafta (36-42)'di. Tablo I'de hastaların sosyodemografik özellikleri verilmiştir. Annelerin yaş ortancası 26 yaş (17-45) ve babaların yaş ortancası 31 yaş (18-54)'di. Annelerin %17.8'inin (n=13) gebe takiplerine düzenli gitmediği saptandı.

Çalışmaya alınan hastaların %45.2'i (n=33) yalnız anne sütü ile beslemekteydi. Hastaların %58.9'u (n=43) D vitamini alırken, %78.1'i (n=57) demir profilaksisi almamaktaydı. Kalça ultrasonografisinin %72.6 (n=53) hastada yapılmadığı saptandı. Hastaların %80.8'inin (n=59) aşı ve beraberinde eksik diğer izlemlerinin olduğu, %31.5'inin ise (n=23) sadece aşısının eksik olduğu diğer taramaların yapıldığı saptandı (Tablo II). Aşılardaki eksiklikler değerlendirildiğinde; %17.9'unun (n=13) bir aşıyı yaptırmadığı, %38.3'ünün (n=28) birden fazla aşıyı yaptırmadığı,

Tablo III: Hastaların vatandaşlık durumlarına göre eksik takipleri (n (%)).

	Aşı	Kalça USG	İşitme testi	Aşı+ vitamin	Aşı+ kalça USG	Topuk kanı	Aşı+göz+ anemi taraması	Kalça USG+ işitme	Aşı+işitme kalça USG	Aşı+ kalça USG +vitamin	Hepsi	Toplam
Türkiye Cumhuriyeti	9 (34.6)	6 (23)	2 (7.7)	3 (11.5)	1 (3.8)	0 (0)	0 (0)	2 (7.7)	0 (0)	1 (3.8)	2 (7.7)	26
Suriye	7 (29.2)	0 (0)	0 (0)	2 (8.3)	2 (8.3)	1 (4.2)	0 (0)	1 (4.2)	1 (4.2)	6 (25)	4 (16.7)	24
Irak	7 (30.4)	1 (4.3)	0 (0)	1 (4.3)	5 (21.7)	0 (0)	1 (4.3)	1 (4.3)	1 (4.3)	3 (13)	3 (13)	23
Toplam	23 (31.5)	7 (9.6)	2 (2.7)	6 (8.2)	8 (11)	1 (1.4)	1 (1.4)	4 (5.5)	2 (2.7)	10 (13.7)	9 (12.3)	73

p=0.213 ***USG:*** *Ultrasonografi*

Tablo IV: Hastaların vatandaşlık durumlarına göre eksik aşıları (n (%)).

	Yok	1 ve 2. ay	2. ay	2 ve 4. ay	4. ay	9. ay	1. yaş	Hepsi	Çoklu aşı	Aşı reddi	Toplam
Türkiye Cumhuriyeti	10 (38.5)	1 (3.8)	1 (3.8)	0 (0)	1 (3.8)	0 (0)	0 (0)	0 (0)	4 (15.4)	9 (34.6)	26
Suriye	2 (8.3)	2 (8.3)	3 (12.5)	1 (4.2)	0 (0)	0 (0)	1 (4.2)	7 (29.2)	8 (33.3)	0 (0)	24
Irak	2 (8.7)	4 (17.4)	5 (21.7)	1 (4.3)	1(4.3)	1 (4.3)	0 (0)	2 (8.7)	7 (30.4)	0 (0)	23
Toplam	14 (19.2)	7 (9.6)	9 (12.3)	2 (2.7)	2 (2.7)	1 (1.4)	1 (1.4)	9 (12.3)	19 (26.1)	9 (12.3)	73

p<0.001

%12.3'ünün (n=9) sadece doğumda yapılan aşıyı yaptırıp diğer hiçbir aşıyı yaptırmadığı, %12.3'ünün (n=9) ise aşı reddi nedeni ile doğumdan itibaren hiçbir aşıyı yaptırmadığı saptandı (Tablo II). Aşı reddi nedeni ile aşı yaptırmayanlar TC vatandaşı olan ailelerdi. Hastaların sadece %19.2'sinin (n=14) aşılarının tam olarak yapıldığı saptandı. Sağlam Çocuk İzlemleri'ndeki bu eksikliklerin sebeplerinin %75.4'ünün (n=55) 'COVİD-19 nedeni ile hastaneye gelinmek istenmemesi' olarak dosyalara kaydedildiği, %12.3'ünün (n=9) 'aşı reddi' nedeni ile %8.2'inin (n=6)'aşı olması gerektiğini bilmediği' için, %4.1'inin (n=3) 'unuttuğu' için aşıları yaptırmadığının kaydedildiği görüldü (Tablo II). Eksik takipler açısından TC vatandaşı ile Suriye veya Iraklı mülteciler arasında fark saptanmadı (p=0.213) (Tablo III). Aşılardaki eksiklikler açısından bakıldığında Suriye ve Iraklı mültecilerin aşılamada eksikliklerinin daha fazla olduğu saptandı (p<0.001) (Tablo IV).

TARTIŞMA

Sağlam Çocuk İzlemi, 0-18 yaş arası tüm çocukların fizik muayenesinin, büyüme ve gelişmesinin değerlendirildiği, bağışıklama, tarama testleri ve sağlık danışmanlığının da yapıldığı önemli bir temel sağlık hizmetidir (7). Bu izlemler birinci basamak olarak tanımladığımız Aile Sağlığı Merkezleri'nde (ASM), hastanelerin Sağlam Çocuk veya Sosyal Pediatri Poliklinikleri'nde, özel sağlık merkezlerinde yapılabilmektedir. Çocuk Sağlığı İzlemi, doğumdan itibaren çocuğun mevcut kapasitesinin arttırılması ve en iyi şekilde gelişebilmesi için gereken çocuk sağlığı uygulamaları olarak da tanımlanır. Çocuğun muayenesinin yanısıra koruyucu önlemlerin ağırlıkta olduğu uygulamalar içerisinde riskli durumları belirlemek, bunlara uygun yaklaşımlarda bulunmak, aşılama programını uygulamak, sağlıklı beslenmeyi sağlamak, büyüme-gelişmeyi izlemek, çocuk ile ilgili endişe ve sorunları saptamak, erken tanı-tedaviyi sağlamak yer almaktadır (8). Ülkemizde SÇİ'nde ilk altı ayda ayda bir, sonraki aylarda üç ayda bir takipler önerilmektedir. Bununla birlikte çocuğun özel bir durumu varsa çocuk ve ailesine göre izlem sıklığında değişiklik yapılabilmektedir (1, 2).

Sağlam Çocuk İzlemleri'nde yakın takipler ile çocukların aşılaması ve bebeklik dönemi tarama testleri yapılarak mevcut önlenebilir hastalıkların erken tanısı konulabilir ve gelecek nesillerin daha sağlıklı yetişmesi sağlanabilir. Bu nedenle hasta olmadan da sağlık kuruluşlarının normal SÇİ'ni yapması çok önemlidir. Dünya Sağlık Örgütü (DSÖ), gelişmekte olan ülkelerde yaşamın ilk üç yılı daha önemli olmak üzere, beş yaşından küçük her çocuğun büyümesinin izlenmesinin gerektiğini belirtmektedir (1,9). Çocuğun yaşına göre fenilketonüri, hipotiroidi, DKD, görme ve işitme taramaları, anemi, idrar değerlendirmesi, kan basıncı ölçümü yapılmalıdır (1, 2, 9). Yine çocuğun ayına göre TC Sağlık Bakanlığı aşı şemasındaki aşılamanın yapılması gereklidir (10).

Ülkemizde yakınması olmadan Sağlam Çocuk İzlemi amacıyla başvuranlar, çocukların 1/3'ünden daha azını oluşturmaktadır (11). Ailelerin sağlık güvencelerinin olmaması, SÇİ hakkında yeterli bilgi sahibi olmamaları çocukları düzenli kontrollere götürmemelerinin önemli nedenlerinden biri olabilmektedir (11, 12). Goedken ve ark'nın (13) yaptığı çalışmada, 0-2 yaş aralığındaki çocukların %60'ının, 3-5 yaş aralığındaki çocukların %40'ının kendi referans merkezlerinin önerilerinden daha az kontrole götürüldükleri bildirilmiştir. Bazı ailelerin de aşılama dışında bir sorun olmadıkça hekime gitmenin gerekmediğini düşünmeleri nedeni ile Sağlam Çocuk İzlemleri'nin önemini bilmediği ve takiplerini yaptırmadığı saptanmıştır (11, 13).

Sağlam Çocuk İzlemleri'nde bu gibi nedenlerle zaten düzenli takipler istenen oranlarda sağlanamazken, Mart 2020'de ortaya çıkan pandemi ve sonrasında alınan önlemler, uyarılar, çocukların

evde tutulması ve sadece hastalandığında veya gerektiğinde doktora götürülmesi şeklinde verilen mesajlar sonucu aileler COVİD-19 korkusu nedeniyle çocuklarının rutin 'Sağlam Çocuk' muayenelerini ertelemeye, aşılarını yaptırmamaya başlamışlardır (6). Ülkeler toplu bulunulan yerlerin kapatılması (restoran spor salonları, AVM'lerin kapatılması vb), toplu taşıma ile ilgili değişiklikler yapılması, zorunlu bir durum olmadıkça evlerden dışarı çıkılmaması gibi önlemler almışlardır (14, 15). Kolcu ve ark. (16) yaptığı çalışmada pandeminin ülkemizde ilk görüldüğü Mart ayından itibaren inceledikleri ASM verilerinde bebek ve çocuk takiplerinde yaklaşık %20'lik bir azalma olduğunu bildirmişlerdir. Mart-Nisan-Mayıs ve Haziran 2019-2020 dönemlerinin bebek ve çocuk takiplerini karşılaştırdıkları çalışmalarında; Mart 2019-2020 dönemlerinde %18'lik, Nisan 2019-2020 dönemlerinde %14.9'luk, Mayıs 2019-2020 dönemlerinde %27.3'lük ve Haziran 2019-2020 dönemlerinde %3'lük bir azalma olduğu saptanmıştır. Bizim çalışmamızda da Şubat 2020'de Sağlam Çocuk Polikliniği'ne düzenli takiplere gelen hastaların sayısının sokağa çıkma yasaklarının uygulanmaya başladığı 14 Mart 2020 tarihinden sonra belirgin olarak azaldığı, normalleşme adımlarının atıldığı Haziran 2020'de ise tekrar arttığı saptandı. İzlemlerdeki azalmanın Kolcu ve ark'nın (16) çalışmasındaki gibi Nisan ve Mayıs aylarında belirgin olduğu gözlendi.

Sağlam Çocuk İzlemleri'ndeki aksamalar ile milyonlarca çocuğun aşı ile önlenebilir ölümcül hastalıklarla karşı karşıya kalma riski artmaktadır. DSÖ 2020 yılının ilk dört ayı ön verilerini açıkladığı basın toplantısında tüm dünyada çocukluk çağı aşılamasında azalma olabileceği ve bu konuda dikkatli olunması için uyarılarda bulunmuştur (17). Amerika Birleşik Devletleri'nde (ABD) pandeminin başlarında nisan ayının ilk iki haftasında aşı dozlarının bir önceki yıla göre yüzde 68 azaldığı bildirilmiştir. Minnesota Eyaleti'nde ise kızamık, kabakulak ve kızamıkçık aşısı dozlarının Mart sonuna doğru yüzde 71 oranında düştüğü saptanmıştır. Yine benzer şekilde ABD'de sağlık kayıtlarının karşılaştırmasına göre; Nisan ayında kızamık, kabakulak, kızamıkçık aşı uygulamasında %50, difteri ve boğmaca aşılarında %42, HPV aşılarında %73'lük bir düşüş olduğu bildirilmiştir (18). Pandemi ile mücadele edilirken birçok ülke çocukluk çağı aşılamalarını durdurmuş, ertelemiş veya yeniden düzenlemeye almıştır (19). Aşılama verilerinin mevcut olduğu 129 ülkenin yaklaşık yarısı Mart-Nisan 2020 döneminde aşılama hizmetlerini aksattığını veya tamamen durdurduğunu bildirmiştir. Örneğin Vietnam'da 1-15 Nisan 2020 arasında rutin aşılamaların tamamen kesildiği, Hindistan'da rutin aşıların kesintiye uğradığı, Pakistan'da çocuk felci aşılamasının 1 Haziran 2020'ye ertelendiği bildirilmiştir. Bazı ülkelerde de salgının ilk beş ayında rutin çocukluk çağı aşılarından bazılarını erteledikleri bildirilmiştir (inaktif polio, oral polio, tifo, sarı humma, kızamık, Td gibi) (19, 20). Bu nedenlerle aşılama ile sağlanmış olan hastalığı önleme başarısı sekteye uğramış ve tekrar bazı ülkelerde aşı ile önlenebilir hastalıklar görülmeye başlanmıştır (21). Dünya Sağlık Örgütü ve Birleşmiş Milletler Çocuklara Yardım Fonu (UNİCEF) tekrar tüm ülkeleri en az 80 milyon çocuğun difteri, kızamık ve çocuk felci gibi hastalıklar için riski altında olabileceği yönünde uyarmış, aşıların ertelenmemesini istemiştir (20, 22).

Kolcu ve ark'nın (16) dört ASM verileri ile yaptığı çalışmada; bebek ve çocukların izlemlerinde azalma görülmesine rağmen aşılama oranlarında azalma olmadığı aşılamanın %98-100 arasında yapıldığı bildirilmiştir. Bu kadar etkin aşılamanın sebebinin, ülkemizdeki ASM çalışma sistemi, birinci basamak sağlık profesyonellerinin aşı konusundaki yüksek duyarlılığı, halkın aşıya karşı yüksek duyarlılığı ve devletin sağlık politikası olarak ASM'lerde uyguladığı aşı oranlarına endeksli performans sistemi olduğu düşünülmüştür. Bununla birlikte bizim çalışmamızda izlemlerinde eksiklik saptanan 73 hastanın %80.8'inin aşılarında da eksiklik olduğu saptandı. Bu grubun %31.5'inde sadece aşılarda eksiklik bulunmaktaydı. Geriye kalan %49.3'ünde aşılarla beraber bebeklik döneminde yapılması gereken taramalar/vitamin kullanımlarında da eksiklikler mevcuttu.

Çalışmamızda sadece Türk vatandaşlar bulunmamaktaydı. Mültecilerin çocukları da çalışma kapsamındaydı ve mültecilerin aşılamada daha fazla eksikliği olduğu görüldü. Mültecilerin dil probleminin olması, SÇİ hakkında bilgilerinin olmaması gibi nedenlerle aşı ve takiplerde daha fazla eksiklik saptamış olabileceğimiz düşünülmüştür.

Ülkemizde Suriyeli mültecilere barınma merkezlerinde, poliklinik ve hastaneye sevk, acil sağlık hizmetleri, bağışıklama, aşılama, bebek ve gebe takip sistemi, bulaşıcı hastalık takibi gibi pek çok alanda sağlığı hizmetleri sunulmaktadır (23). Bu amaçla birçok ilde Göçmen Sağlığı Merkezleri kurulmuştur. Hastanelere mültecilerin ulaşımları, hizmet alımları sağlanmıştır. Bununla birlikte mültecilerin bu sağlık hizmeti alımlarında en sık karşılaştıkları sorunun dil problemi olduğu saptanmıştır ve görüşümüzü destekler niteliktedir (24). Bu durum bebek takiplerinde aksaklıklara yol açabilmektedir.

Aşıların günümüzde etkinliği, faydaları ve güvenliği bilinmektedir. Buna rağmen nadir gözlenen yan etkileri veya içerisindeki maddeler ön plana çıkarılarak aşı karşıtlığı oluşturulmaya çalışılmaktadır (25). Aşılara güven duyanlar olumlu bakanlar (%55-75) çoğunluğu oluşturmakla birlikte, tereddüt eden, kararsız olanların oranı bilinmemektedir. Tüm aşılara karşı çıkan grupların ise (<%2) küçük bir yüzde de olsa sayıları her yıl giderek artmaktadır (26, 27). Dünyadaki aşı reddi vakalarının son yıllarda giderek artması nedeni ile 2019'da DSÖ çözüme kavuşturmayı planladığı 10 küresel sağlık sorunları arasında aşı karşıtlığına da yer vermiştir. (28). Ülkemizde 2016 yılında aşıyı reddeden aile sayısı 12000'den fazla, 2017 yılında ise 23000'den fazla olmuştur (29). Bizim çalışmamızda da aşı reddi ile karşılaşılmıştır. Aşı reddinin olması sadece aşı yapılmayan çocuk için değil aynı zamanda halk sağlığı için de önemli bir sorun teşkil etmektedir. Bu nedenle aşılama ve etkileri konusunda yapılan bilimsel çalışmaların sonuçları hakkında toplumun doğru bilgilendirilmesi ve bilinçlendirilmesinin çok önemli olduğu düşünülmüştür.

Sonuç olarak; Mart 2020'den itibaren hayatımıza giren COVID-19 Pandemisi nedeni ile SÇİ'de ve aşılamalarda aksaklıklar olduğu saptanmıştır. Sağlıklı çocuklar yetiştirebilmek için bu izlemlerin aksamaması konusunda halkımızın bilgilendirilmesi, eksik takiplerin saptandığı her durumda hastaların geciktirilmeden yönlendirilmesi gerektiği düşünülmektedir. Ayrıca hassas grupta yer alan mülteci çocuklarının polikliniklere farklı nedenlerle başvurularında SÇİ ve aşılama durumları ile ilgili bilgi edinilmesinin ve gerekli takiplerinin yapılmasının önemli olduğunu düşünüyoruz.

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Evaluation of Psychiatric Symptoms in 2-5 Years Old Children Who Are Followed and Treated with the Diagnosis of Wheezing during the COVID-19 Pandemic and Depression, Anxiety, and Stress Levels of Mothers

COVİD-19 Pandemisi Döneminde Hışıltılı Çocuk Tanısıyla Takip ve Tedavi Edilen 2-5 Yaş Grubu Çocuklarda Psikiyatrik Belirtiler ve Annelerin Depresyon, Kaygı ve Stres Düzeylerinin Değerlendirilmesi

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ABSTRACT

Objective: The impact of COVID-19 on the mental health of children and adults is a candidate to be one of the most current issues in healthcare in the near future. This study aimed to determine the clinical course of patients diagnosed with wheezing, to make emotional, behavioral, social, and psychiatric evaluations, and to investigate the possible effect of the pandemic on disease follow-up and treatment by evaluating the psychiatric conditions of their mothers.

Material and Methods: The study included 58 patients diagnosed with a wheezy infant aged 2-5 years. Data regarding the sociodemographic characteristics and wheezing history of the patients were recorded. 'Test for Respiratory and Asthma Control in Kids (TRACK)' was applied to evaluate their current clinical condition. For psychiatric evaluation, the 'Strengths and Difficulties Questionnaires (SDQ)' was applied to the patients, and the 'Depression Anxiety Stress Scale 21 (DASS 21)' and 'The Brief Resilience Scale (BRS)' were administered to their mothers.

Results: In our study, it was observed that our patients experienced emotional, behavioral, peer, and social problems at varying rates (17-43%) during the pandemic period. It was especially noteworthy that emotional problems were seen more frequently in girls. It has been shown that there is a positive relationship between depression scores in mothers and SDQ Total Scores of their children. On the other hand, it was observed that current disease control status, hospitalization history, and whether or not being symptomatic during the pandemic period did not contribute to mental impairment in mothers.

Conclusion: The detection of high overall difficulty scores in children of mothers with high depression scores indicates that there is a need to evaluate maternal and child mental health together. Psychological influence is multifactorial and varies between societies. There is a need for studies on a larger scale that take familial and individual variables into account.

Key Words: Children, COVID-19, Mental health

0000-0001-7648-0352: EMEKSIZ ZS
0000-0002-9393-7497: BUYUK YAYTOKGIL S
0000-0002-8383-6350: KARATMACA B
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0000-0001-8451-0099: COP E
0000-0002-7869-5338: UNERI OZ
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Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by the T.R. Ministry of Health and Ankara City Hospital Clinical Research Ethics Committee (decision number: E1-20-879).

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ÖZ

Amaç: COVİD-19'un çocukların ve yetişkinlerin ruh sağlığı üzerindeki etkisi, yakın gelecekte sağlık hizmetlerinde en güncel sorunlardan biri olmaya adaydır. Bu çalışma ile hışıltılı çocuk tanılı hastaların pandemi dönemindeki klinik seyirlerini belirlemek, duygusal, davranışsal, sosyal ve psikiyatrik değerlendirmelerini yapmak, ayrıca annelerinin de psikiyatrik durumlarını değerlendirerek pandeminin hastalık takip ve tedavisi üzerine olan olası etkisinin araştırmak amaçlanmıştır.

Gereç ve Yöntemler: Çalışmaya 2-5 yaş arası 58 hışıltılı çocuk tanılı hasta dahil edildi. Hastaların sosyodemografik özellikleri ve hışıltı geçmişlerine ait veriler kaydedildi. Güncel klinik durumlarını değerlendirmek üzere Çocuklar İçin Solunum ve Astım Kontrol Testi uygulandı. Psikiyatrik değerlendirme amacıyla hastalara Güçler ve Güçlükler Anketi (SDQ), annelerine ise Depresyon Anksiyete Stres Ölçeği 21 (DASS 21) ve Kısa Psikolojik Sağlamlık Testi uygulandı.

Bulgular: Çalışmamızda pandemi döneminde hastalarımızın değişen oranlarda (%17-43) duygusal, davranış, hiperaktivite, akran ve sosyal açılardan problem yaşadığı gözlemlenmiştir. Kız çocuklarda duygusal problemlerin daha sık görülmesi özellikle dikkat çekmiştir. Annelerdeki depresyon skorları ile çocuklarının SDQ toplam skorları arasında pozitif ilişki olduğu gösterilmiştir. Buna karşılık güncel hastalık kontrol durumunun, hospitalizasyon öyküsünün ve pandemi döneminde semptomatik olup olmamanın annelerde mental etkilenmeye katkıda bulunmadığı gözlenmiştir.

Sonuç: Depresyon puanı yüksek olan annelerin çocuklarında genel güçlük puanlarının yüksek saptanması, anne ve çocuk ruh sağlığının birlikte değerlendirilmesine ihtiyaç olduğunu göstermektedir. Psikolojik etki çok faktörlüdür ve toplumlar arasında farklılık gösterir. Bu konuda ailesel ve bireysel değişkenlerin göz önüne alındığı daha büyük ölçekli gelecek çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Çocuklar, COVİD-19, Ruh sağlığı

INTRODUCTION

Wheezing is an expiratory high-vibration sound caused by turbulent airflow passing through bronchi that are narrowed due to inflammation, bronchospasm, and mucosal edema. It is one of the most common respiratory symptoms in childhood and is a major reason for presenting to the hospital, especially in early childhood (1). Wheezing that begins in the early stages of life is associated with a group of diseases that have heterogeneous phenotypes and are different in terms of pathophysiology. It can start and end as a single attack, be prolonged, or be seen as recurrent attacks. The term "wheezing child" is used for children whose wheezing lasts longer than a month and/or recurs three or more times. While most cases are due to viral lower respiratory tract infections, some have an atopic background and are among the first symptoms of childhood asthma (2). Although this clinical picture can be controlled with appropriate treatments, attacks, and loss of control can occur, especially when treatment compliance diminishes and there are intervening triggers. Recent studies have shown that wheezing can have negative effects on the quality of life and mental health of both patients and their families due to the need for regular outpatient check-ups, regular medication use, and the need for emergency services when an attack occurs (3).

Coronavirus disease (COVID-19) is a serious medical condition caused by the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It emerged as a case of treatment-resistant pneumonia of unknown cause in the Chinese city of Wuhan, Hubei province, in December 2019 (4). The first case in Turkey was reported on March 11. It began to impact the population, and a series of public health measures, including social isolation, were declared to prevent it from progressing. The pandemic period has affected all chronic patient groups as well as the population of recurrent wheezing patients and their families. It was observed that patients and their parents experienced concerns about issues like experiencing COVID-19 more severely due to their existing diseases or the medication they used and the risk of SARS-CoV-2 transmission during hospital admissions. The intense experience of emotions, such as anxiety of contracting the disease, fear of death, and feeling helpless, can have mental health consequences, such as depression, sleep and appetite problems, excessive anxiety and panic, inability to concentrate, and hopelessness. These factors can lead to mental and physical health problems in patients and caregivers. Psychiatric symptoms may develop in patients who do not have any prior psychiatric diseases, and it is possible for patients with existing psychiatric diseases to experience disease exacerbations (5–8).

This study aimed to record the demographic and clinical characteristics of patients diagnosed with wheezing who were followed and treated in the Pediatric Allergy and Immunology Clinic and to make emotional, behavioral, social, and psychiatric evaluations. A further aim was to assess the psychiatric conditions of their mothers and thus investigate the possible effect of the pandemic on follow-up and treatment.

MATERIALS and METHODS

The study was carried out in Ankara City Hospital's Pediatric Allergy and Immunology Clinic between June 1, 2020 (approximately two and a half months after the first case of COVID-19 was reported in Turkey) and September 1, 2020. All Patients between two and five years of age who were administered to our outpatient clinic (diagnosed with a wheezy infant in our clinic and followed up for at least one year) during the study period were included in the study.

The study was approved by the T.R. Ministry of Health and Ankara City Hospital Clinical Research Ethics Committee (decision number: E1-20-879). Written informed consent

was obtained from the parents before the study began. The study was carried out in accordance with the principles of the Declaration of Helsinki.

All participants were evaluated with a study questionnaire consisting of three sections. This questionnaire included a sociodemographic information form prepared by the authors, a clinical evaluation form, and a psychiatric evaluation section consisting of standard scales.

1. ***Sociodemographic Information Form:*** It included sociodemographic characteristics, such as age, gender, personal background, and family history, as well as data related to the history of wheezing (age at first episode, total number of episodes, hospital admission history, and medication information).
2. ***Clinical Evaluation Form:*** This included the Test for Respiratory and Asthma Control in Kids (TRACK) administered to the patients to determine their current level of disease control. This test includes five items, including frequency of symptoms in the last four weeks, night awakenings due to symptoms, activity limitation, frequency of bronchodilator medication in the last three months, and use of oral corticosteroids in the last year. It is designed for children under five years of age. The score for each item is between 0 and 20, and the total score ranges from 0 to 100. Eighty points and above indicates good disease control, while less than 80 points are interpreted as the loss of control. The validity and reliability studies of the Turkish version of the TRACK developed by Murphy et al. (9) was conducted by Büyüktiryaki et al.(10).
3. ***Evaluation of Psychiatric Symptoms:*** The Strengths and Difficulties Questionnaire (SDQ) for patients aged two to four was used for the two- to four-year-old patients, and the SDQ for patients aged five to 17 was used for the five-year-old patients. The Depression Anxiety Stress Scale 21 (DASS-21) and the Brief Resilience Scale (BRS) were administered to the mothers.

The SDQ, which is used to screen mental health problems in children and adolescents, was developed by Robert Goodman in 1997 (11). The validity and reliability studies of the Turkish version were performed by Güvenir et al (12). The SDQ contains 25 questions, some of which question positive behavior characteristics, while others ask about negative behavior characteristics. These questions are grouped under five subheadings: conduct problems, hyperactivity/inattention, emotional symptoms, peer problems, and prosocial behaviors. Each heading is evaluated within itself, and the sum of the first four headings yields the total difficulties score.

The BRS was developed by Smith et al. (13) in 2008 to measure resilience. Adapted to Turkish by Doğan et al., it is a five-point Likert-type scale measurement tool consisting of six items (14). Their findings show that the scale is a valid and reliable measurement tool that can be used in Turkish culture. Receiving high scores from the scale indicates that there is a high predisposition to resilience.

The Depression Anxiety Stress Scale (DASS) developed by Lovibond SH and Lovibond PF in 1995 consists of 42 items (15). Brown et al. (16) published a short form called DASS-21. The 21-item short-form was used in this study. The Turkish validity and reliability study of DASS-21 was performed by Yılmaz et al. (17) in 2017. DASS-21 has seven questions prepared to measure each of the dimensions of depression, anxiety, and stress. It uses a four-point Likert-type scale that is coded as 0 “not suitable for me”, 1 “it suits me a little”, 2 “generally suitable for me”, and 3 “completely suitable for me”. The higher the score, the greater the emotional distress the person is experiencing.

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics version 22.0 statistical software package for Windows (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as the mean and standard deviation for data with normal distribution and as the median and interquartile range (IQR, 25th–75th percentile) for non-normally distributed data. The chi-square test was used to compare nonparametric data; the Mann–Whitney U test was used for comparisons among non-normally distributed continuous variables and independent samples t-test for normally distributed continuous variables. One-way ANOVA was used to compare normally distributed parameters among the TRACT groups (full control, partial control, uncontrolled). Kruskal-Wallis Tests were conducted to compare non-normally distributed parameters among the TRACT groups. While investigating the associations between non-normally distributed variables, the correlation coefficients and their significance were calculated using the Spearman test. A value of $p<0.05$ was considered statistically significant.

RESULTS

Of the 58 patients participating in the study, 34 (58.6%) were boys and 24 (41.4%) were girls. Their ages ranged from 24 to 60 months (median 48.0, IQR = 19). When examined in terms of wheezing history, the patients had at least one (3.4%) and at most ten (10.3%) attacks. When evaluated in terms of hospitalization history, 27 (46.6%) had been hospitalized at least once, and three patients (5.2%) had to be hospitalized in the intensive care unit during an attack. The demographic characteristics and clinical data of wheezing history are summarized in Table I.

When questioned about symptoms during the pandemic period, at least one of the symptoms that could be confused with COVID-19, such as cough and shortness of breath, was seen in 22 patients (37.9%), 37.9% presented to the outpatient clinic, and 29.3% presented to the emergency department. Ten

Table I: Demographic characteristics and clinical data of wheezing history.

Parameter	n (%)
Gender	
Female	24 (41.4)
Male	34 (58.6)
Week of birth	
<37 week	15 (25.9)
37-42 week	39 (67.2)
>42 week	4 (6.9)
Type of birth	
Vaginal delivery	28 (48.3)
C/S	30 (51.7)
Precense of additional disease	12 (20.7)
Precense of additional allergic diseases (atopic dermatitis, allergic rhinitis, food allergy etc…)	12 (20.7)
Precense of familial allergic disease	18 (31)
Precense of familial psychiatric disease	2 (3.4)
Family type	
Nuclear	42 (72.4)
Extended	16 (27.6)
Socioeconomic status	
Low	8 (13.8)
Middle	49 (84.5)
High	1 (1.7)
Garden house	22 (37.9)
House with balcony	50 (86.2)
Place	
Urban area	52 (89.7)
Rural area	6 (10.3)
Job change during the pandemic	15 (25.9)
Income reduction during the pandemic	29 (50)
Clinical data of wheezing history	
Total number of attack	
1-3 attack	36 (62)
4-6 attack	12 (20.6)
≥7 attack	10 (17.2)
Hospitalization history	27 (46.6)
PICU hospitalization	3 (5.2)
Medication used in the last attack	
Only SABA	17 (29.3)
SABA and inhaled corticosteroids	19 (32.8)
Systemic corticosteroids	5 (8.6)

PICU: *Pediatric intensive care unit,* ***SABA:*** *Short acting beta2-agonist*

(17.2%) patients had a COVID-19 Polymerase Chain Reaction (PCR) test during their admission, and three patients' tests were positive. The clinical data of the patients regarding the pandemic period are summarized in Table II.

TRACK was used to determine the current disease control status. The TRACK score was 80 and above in 36 of the patients (62.1%), which was defined as complete control.

Considering the DASS-21 that was administered to the mothers, according to the cut-off point, five mothers (8.6%) had mild-moderate depression, six (10.3%) had mild-moderate anxiety, two (3.4%) had severe anxiety, and two (3.4%) had mild stress symptoms.

Tablo II: Clinical status of patients during the pandemic period.

Parameter		n (%)
Had any symptoms that suggest Covid-19?	yes	22 (37.9)
Had any outpatient clinic application during the pandemic period?	yes	22 (37.9)
Had any emergency service application during the pandemic period?	yes	17 (29.3)
Had any telemedicine interview during the pandemic period?	yes	8 (13.8)
Used SABA during the pandemic period?	yes	8 (13.8)
Used oral corticosteroids during the pandemic period?	yes	4 (6.9)
Used antibiotics during the pandemic period?	yes	26 (44.8)
Any change in the maintenance treatment dose during the pandemic period?	yes	6 (10.3)
Any change in the maintenance treatment dose during the pandemic period?	yes	5 (8.6)
Has your child been tested for COVID-19 during the pandemic period?	yes	10 (17.2)
Have you been tested for COVID-19 during the pandemic period?	yes	7 (12.1)
Have you had contact with an individual diagnosed with COVID-19 during the pandemic period?	yes	4 (6.9)

Comparing the children with wheezing according to the control level determined by the TRACK score, there was no statistically significant difference between the groups in terms of DASS-21 depression, anxiety, and stress scores ($p > 0.05$). No correlation was found between TRACK scores in patients and DASS-21 subscores in mothers.

When the BRS data were examined, 38 mothers (65.5%) had moderate resilience scores, and two (3.4%) had low resilience scores. According to the control levels based on the TRACK score, there was no statistically significant difference between the groups in terms of BRS results. There was no correlation between the mothers' resilience scores and the patients' TRACK scores.

The distribution of the SDQ data applied to evaluate the patients' psychiatric symptoms according to the cut-off points is shown in Figure 1. When the SDQ scores were analyzed according to both TRACK control levels, there was no statistically significant difference in terms of SDQ total difficulties scores. There was no significant correlation between the TRACK score and the SDQ total difficulties score. When the SDQ subgroups were examined, no difference was found according to the TRACK control status. The TRACK score did not correlate with the scores of the SDQ subgroups.

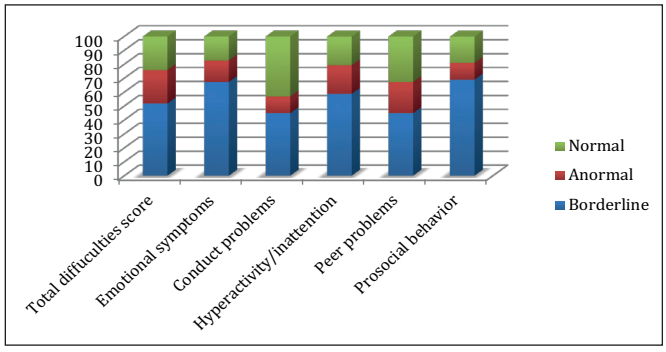

Figure I: Distribution of SDQ total diffuculties score and subgroups by cut-off point.

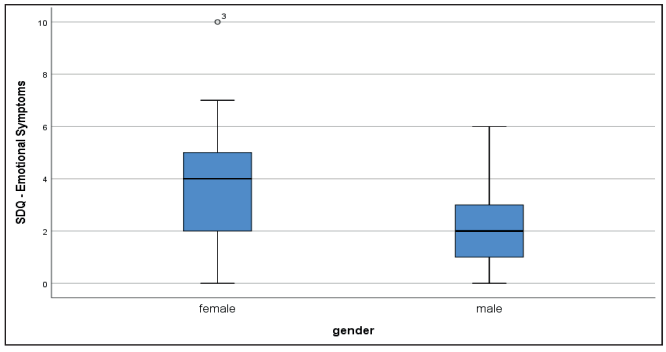

Figure II: The effect of gender on SDQ-emotional symptoms.

Looking at the effect of gender, no difference was observed in the DASS-21 scores of the mothers. Looking at the patients' SDQ data, among the SDQ subgroups in children, emotional symptoms were found to be higher in girls than in boys (p = 0.008) (Figure 2).

When the patients were evaluated in terms of a number of attacks, there was no correlation between DASS-21, BRS, and SDQ scores. Considering the effect of hospitalization history on psychiatric data, there was no significant difference in DASS-21, BRS, and SDQ total and subgroup scores. When the relationship between the patients' symptomatic status and the psychiatric evaluation data was evaluated, there was no statistically significant difference between DASS-21, BRS, and SDQ total and subgroup scores. When evaluated in terms of parameters that could affect psychiatric data, such as mother's educational status, socioeconomic status, and income reduction during the pandemic period, there was no significant difference between the groups. The data on the evaluation of the scales in terms of parameters that may be related are summarized in the Supplemental File.

When the correlation between the scales was examined, a strong positive correlation (r = 0.348, p = 0.007) was observed between DASS-21 depression and SDQ total difficulties scores (Figure 3). There was no correlation between DASS-21 anxiety and DASS-21 stress score and SDQ total difficulties score. There was also no correlation between SDQ and BRS scores. There was a moderate negative correlation between BRS and DASS-21 depression score (r = 0.519, p < 0.001), DASS-21

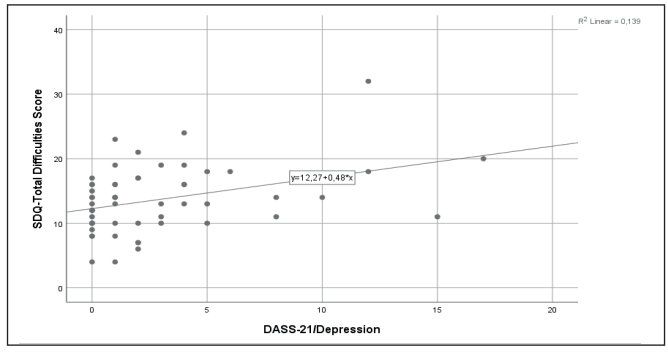

Figure III: Correlation between SDQ Total Difficulties Score and DASS-21/Depression.

anxiety score (r = 0.417, p = 0.001), and DASS-21 stress score (r = 0.428, p = 0.001).

DISCUSSION

Viral respiratory tract infections are the trigger for 85% of wheezing attacks in children. Since SARS-CoV-2 is a respiratory pathogen, it may not be easy to distinguish the symptoms that occur during a wheezing attack associated with COVID-19 from a wheezing attack due to another trigger. Dry cough and shortness of breath are among the most common symptoms during both wheezing episodes and COVID-19 infections.18 It was determined that about 40% of the patients in this study experienced at least one of these symptoms during the pandemic period and presented to the outpatient clinic or emergency department as a result.

There are currently insufficient data to indicate that COVID-19 is a risk factor for respiratory diseases like wheezing attacks or asthma or increased disease severity in asthma patients infected with SARS-CoV-2 (19,20). In this study, three patients were infected with COVID-19 and recovered with mild symptoms without any attacks or hospitalization.

It is known that epidemics harm mental health and psychological well-being and significantly increase psychiatric morbidity in the general population (21). This effect is more pronounced in adults with a history of chronic disease and their caregivers (22). There are fewer studies in the literature evaluating the effect of pandemics on mother-child mental health (23). Malkawi et al.(24) reported that they found mild depression, anxiety, and stress scores (median: 10/4/18, respectively) in mothers in their study that used the DASS-21 to evaluate the mental health of mothers with healthy children aged four to 18 years old. In the same study, it was emphasized that quarantine effects, such as lifestyle changes, the increased time required for child care at home, and domestic violence, maybe the cause of these difficulties and that providing psychological support to mothers should be a priority. In our study, the depression, anxiety, and stress levels of the mothers were evaluated with the same scale, and the median scores were much lower compared to the

study by Malkawi et al. (24) This may be explained by the fact that psychological effects occur as a result of more than one factor. Although mothers of two-to five-year-old patients with frequent hospital admissions and hospitalization history due to respiratory tract disease were included in this study, it was observed that current disease control status, hospitalization history, and the symptomatic status during the pandemic period did not contribute to mental health issues in mothers. This situation may be related to the fact that COVID-19 is less common in the pediatric population, and its course is mostly known to be mild by mothers (25).

Studies are evaluating the effect of the pandemic period on children's mental health from different perspectives, with different scales, and in different geographic locations. In a study investigating the effects of quarantines on mental health, it was reported that post-traumatic stress disorder developed in children at a rate of around 30%.26 In a study involving children aged six to 12 in Brazil, the prevalence of anxiety was found to be higher (19.4%) during the COVID-19 pandemic compared to the pre-pandemic period (27). In a study in Italy in which the effect of quarantines on mother-child mental health was evaluated in healthy children aged two to five and their mothers, sleep disorders, boredom, and difficulty following daily routines were found in children, and impaired sleep quality was observed in mothers. Also, it was emphasized that an increase was observed in emotional symptoms and conduct/hyperactivity/inattention problems compared to before the quarantine period according to the SDQ scale (5). In another study conducted in China in which children aged three to 18 were included, it was reported that psychological and behavioral problems such as distraction, irritability, and fear of asking questions about the pandemic were common (28). In another study involving children aged three to 18 from three different European countries, more behavioral problems in Spain, significant mood changes in Portugal, and lower anxiety, sleep, and nutrition problems in Italy were found compared to the others. It was emphasized that the difference was a result of both individual and familial factors (29). When we looked at the SDQ total and subgroup scores in our study according to the cut-off point, it was observed that our patients experienced emotional, conduct, hyperactivity, peer, and prosocial problems at varying rates (17–43%). It is particularly striking that emotional problems were more common in girls. This finding supports the results of a study that found that internalizing problems such as depression and anxiety were more common in girls (30–32). In our study, a positive relationship was demonstrated between the depression scores of mothers and the SDQ total difficulties scores of their children. The relationship of internalization, externalization and general psychopathology in children with maternal depression is a recurrent finding in many studies (33). Maternal depression is considered an important risk factor for childhood mental illness. Therefore, it would be useful to consider the psychiatric problems of mothers along with their children during the follow-up process of these children.

The strengths of our study are that the study group included preschool-age children with respiratory tract disease who need more maternal attention, and the effect of the pandemic on mother and child mental health was evaluated together. The low number of participants and the absence of a control group consisting of healthy children and their mothers can be seen as limitations, but this is because this study was conducted face-to-face, and admissions to hospitals and pediatric allergy clinics decreased in general during the pandemic period.

In conclusion, during the pandemic period, the necessary precautions were taken in our clinic, the follow-up of the wheezy infant patient group continued, and there were no patients who were infected with COVID-19 due to hospital admission. It was observed that patients who tested positive for COVID-19 during the pandemic period recovered with mild symptoms.

As a result of the evaluation of our patients and their mothers in terms of psychiatric symptoms, the fact that the total difficulties scores of the children of mothers with high depression scores were increased highlights the importance of evaluating maternal and child mental health together. Future studies on a larger scale that take family and individual variables into account are needed to evaluate the mental health of children and their mothers.

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Supplemental file: Evaluation of scales in terms of parameters that may be related.

	DASS-21 Median (min-max)			BRS Mean ±SS (Min-Max)	SDQ					
	Depression	Anxiety	Stress		Total difficulties score Mean (min-max)	Emotional symptoms Median (min-max)	Conduct problems Mean ±SS (Min-Max)	Hyperactivity inattention Mean ±SS (Min-Max)	Peer problems Median (min-max)	Prosocial behavior Mean ±SS (Min-Max)
TRACK										
≥ 80	1 (0-15)	2 (0-16)	1 (0-17)	21.1±0.7 (11-30)	13.2±0.7 (4-32)	2 (0-10)	2.9±0.2 (0-7)	4.8±0.3 (0-10)	3 (0-8)	6.8±0.3 (2-12)
< 80	1 (0-17)	2.5 (0-15)	2 (0-16)	20.4±1.0 (11-30)	14.1±1.1 (4-24)	2.5 (0-6)	3.3±0.3 (1-7)	5.0±0.4 (1-9)	3 (1-8)	5.9±0.4 (2-10)
	p=0.511	p=0.469	p=0.082	p=0.561	p=0.532	p=0.642	p=0.394	p=0.717	p=0.731	p=0.128
Hospitalizaiton history										
Yes	2 (0-17)	2 (0-14)	1(0-10)	20.5±0.5 (16-29)	12.5±0.7(6-24)	2 (0-5)	2.6±0.2 (0-5)	4.9±0.4 (0-9)	3 (0-5)	6.3±0.3(4-9)
No	1 (0-12)	2(0-16)	1(0-17)	21.1±1.0(11-30)	14.5±1.0(4-32)	3 (0-10)	3.4±0.3 (1-7)	4.8±0.3 (1-10)	3 (1-8)	6.4±0.4 (2-12)
	p=0.786	p=0.924	p=0.678	p=0.585	p=0.139	p=0.115	p=0.062	p=0.872	p=0.720	p=0.556
Symtomps during pandemic										
Yes	1 (0-17)	3 (0-15)	2 (0-16)	20.8±1.2 (11-30)	14.6±1.1(4-24)	2.5 (0-6)	3.6±0.3 (1-17)	5.3±0.5 (1-10)	1 (1-8)	6.8±0.5 (2-10)
No	1 (0-15)	1 (0-16)	1 (0-17)	20.8±0.6 (11-30)	12.9±0.7(4-32)	2 (0-10)	2.7±0.2 (0-7)	4.6±0.3 (0-8)	3 (0-8)	6.3±0.3 (2-12)
	p=0.200	p=0.159	p=0.165	p=0.585	p=0.139	p=0.468	p=0.062	p=0.872	p=0.492	p=0.556
Gender										
Famele	2 (0-15)	2.5 (0-16)	1.5 (0-17)	21.2±1.0 (11-30)	14.2±1.2(6-32)	4 (0-10)	2.9±0.3 (0-7)	5.0±0.4 (1-10)	2 (0-8)	6.7±0.4 (2-12)
Male	1 (0-17)	2 (0-5)	1 (0-16)	20.5±0.7 (11-29)	13.1±0.7(4-23)	2 (0-6)	3.1±0.2 (0-7)	4.3±0.3 (0-9)	3 (1-8)	6.3±0.3 (2-10)
	p=0.343	p=0.386	p=0.193	p=0.554	p=0.415	p=0.008*	p=0.614	p=0.799	p=0.513	p=0. 502
Education status of mother										
Elementry	1 (0-8)	2 (0-10)	1 (0-9)	20.1±0.8 (14-30)	13.2±0.7(7-21)	2 (1-7)	3.0±0.2 (0-5)	4.5±0.3 (1-8)	3 (0-8)	6.1±0.3 (3-12)
High school	1 (0-15)	3 (0-14)	1 (0-12)	21.0±0.9 (16-29)	12.9±1.3(4-24)	2 (0-6)	2.8±0.4 (0-7)	4.8±0.5 (0-9)	2 (1-5)	6.7±0.5 (2-10)
University	2.5 (0-17)	3 (0-16)	2 (0-17)	21.8±1.4 (11-30)	14.8±1.5(4-32)	2.5 (0-10)	3.3±0.4 (1-7)	5.6±0.6 (1-10)	3 (1-8)	6.8±0.5 (2-10)
	p=0.548	p=0.582	p=0.551	p=0.512	p=0.523	p=0.903	p=0.750	p=0.270	p=0.986	p=0.553
Income reduction during pandemic										
Yes	1 (0-17)	2 (0-11)	1 (0-11)	20.7±0.8 (14-30)	12.7±0.8(4-24)	2 (0-5)	2.8±0.3 (0-6)	4.7±0.4 (0-10)	3 (0-8)	6.5±0.4 (2-12)
No	1.5 (0-15)	2(0-16)	2 (0-16)	21.0±0.9 (11-30)	14.5±1.0 (4-32)	2.5 (0-10)	3.3±0.2 (1-7)	5.1±0.36 (1-9)	3 (1-8)	6.5±0.3 (2-10)
	p=0.889	p=0.871	p=0.488	p=0.846	p=0.185	p=0.441	p=0.220	p=0.585	p=0.352	p=0.977

p < 0.05*, ***TRACK:* *Test for respiratory and asthma control in kids*, ***DASS-21:*** *Depression anxiety stress scale-21*, ***BRS:*** *Brief Resilience Scale*, ***SDQ:*** *Strengths and difficulties questionnaire*, ***SS****: standart deviation*

Social Workers in Pediatric Intensive Care Units: A Physician Perspective

Çocuk Yoğun Bakım Ünitesinde Sosyal Hizmet Uzmanları: Bir Hekim Bakışıyla

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ABSTRACT

Objective: The role of social workers, who are beginning to be integrated into the entire health system, is now becoming more and more understood. In our study, we aimed to discuss the duties of social workers at PICU, the results of their work in harmony with the physicians, and their importance for the intensive care team.

Material and Methods: Sixtysix children aged between 1 month and 18 years old who were asked for social service consultation between January 2019 and December 2020 at our hospital's PICU were included in the study. The age, diagnosis, sex, marital status (married-divorced), number of days of hospitalization, number of recurrent hospitalization, reason and result of consultation, necessity of psychiatric consultation and frequency of follow-up were retrospectively examined and recorded through the hospital information system. The collected data were analyzed by means of SPSS (version 22.0, SPSS Inc. Chicago, IL, USA).

Results: The median age (months) (min-max) was found to be 172, 50 (6-209), and the median (min-max) duration of hospitalization (days) was found to be 2 (1-76). Family neglect was found to be the most common cause of social work indications (77.3%; n: 51). The number of patients who were given social counseling and referred to a psychiatrist was 25 (37.9%). Family neglect and abuse were detected in 5 (7.6%) patients. Apart from these, it was observed that problems such as drug supply, financial support, ID application, home device supply assistance, care center approvals and child custody were solved in each 1 (1.5%) patient.

Conclusion: The inclusion of social workers in the children's intensive care unit teams can also prevent many social problems that can be neglected otherwise. Physicians are more focused on patient treatment, so we believe that it will be beneficial to question the family and social status of patients together with a social service unit and specialists integrated into children's intensive care units.

Key Words: Child psychiatry, Child abuse, Pediatric intensive care unit, Social worker

ÖZ

Amaç: Tüm sağlık sistemine entegre olmaya başlayan sosyal hizmet uzmanlarının rolü giderek daha iyi anlaşılmaktadır. Çalışmamızda, çocuk yoğun bakım ünitesinde (ÇYBÜ), sosyal hizmet uzmanlarının ÇYBÜ'deki görevlerini, hekim ile uyumlu çalışmasının sonuçlarını ve yoğun bakım ekibi için önemini tartışmayı amaçladık.

Gereç ve Yöntemler: Hastanemiz ÇYBÜ'de 2019 Ocak-2020 Aralık tarihleri arasında 1ay-18 yaş arası çocuk hastalardan, sosyal hizmet konsültasyonu istenmiş 66 hasta çalışmaya dahil edildi. Hastaların yaş, tanı, cinsiyet, aile

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Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. The ethics committee decision of our study was approved by the Balıkesir University ethics committee with the number E-94025189-050.03-15740 on 18/02/2021.

Contribution of the Authors / Yazarların katkısı*: *ATAKUL G: Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study. ***ASLAN K:*** Planning methodology to reach the Conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***DEMIRCAN TULACI O:*** Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***OZHAN P:*** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments. ***CAGLAR A:*** Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar.

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durumu (evli-boşanmış), yatış gün sayısı, tekrarlayan yatış sayısı, konsültasyon nedeni ve sonucu, psikiyatri konsültasyonu gerekliliği ve takip sıklığı retrospektif olarak hastane bilgi sistemi üzerinden incelenerek kaydedildi. Toplanan veriler SPSS (version 22.0, SPSS Inc. Chicago, IL, USA) ile analiz edildi.

Bulgular: Hastaların yaşları (ay) median (min-max); 172.50 (6-209) ve median (min-max) yatış süreleri (gün); 2 (1-76) olarak bulundu. Sosyal hizmet endikasyonları arasında en sık nedenin aile ihmali ihtimalinin değerlendirmesi, suicid girişimleri ile psikiyatrik sorun tespiti açısından değerlendirilmesi (%77.3; n:51) olduğu tespit edildi. Sosyal danışmanlık verilen ve psikiyatri uzmanına yönlendirilen hasta sayısı 25 (%37.9)'du. 5 (%7.6) hastada aile ihmali ve istismar tespit edildi. Bunlar dışında 1 (%1.5)'er hastada, ilaç temini, maddi destek, kimlik başvurusu, ev tipi cihaz temini yardımı, bakım merkezi onamları alınması ve çocuğun vasi sorunu çözümü gibi sorunların çözüldüğü görüldü.

Sonuç: Sosyal hizmet uzmanlarının çocuk yoğun bakım ünitesi ekibine dahil edilmesi, gözden kaçabilecek birçok sosyal problemin de önüne geçmeyi sağlayabilir. Hekimlerin hasta tedavilerine daha çok odaklanması nedeniyle, çocuk yoğun bakım ünitelerine entegre olmuş bir sosyal hizmet birimi ve uzmanları ile beraber hastaların aile ve sosyal durumlarının sorgulanmasının fayda sağlayacağını düşünmekteyiz.

Anahtar Sözcükler: Çocuk psikiyatrisi, Çocuk istismarı, Çocuk yoğun bakım ünitesi, Sosyal hizmet uzmanı

INTRODUCTION

Social workers, are specialists who provide services such as organizing the relations of the patient with their family and environment, resolving personal and family problems after leaving the hospital, and developing skills to cope with their problems with their professional knowledge, skills and discipline in addition to the economic, social, psychological, educational, supportive and developing services to be carried out in order to ensure effective use of medical treatment for outpatient or inpatient examinations (1). Social workers assess, include, intervene, coordinate and advocate on behalf of the most vulnerable populations, while addressing non-medical factors and social needs that affect health with a focus on equality. According to the ethical rules of the National Association of Social Workers (NASW), the primary mission of the social workers is to pay special attention to the needs and empowerment of people who are vulnerable, oppressed and living in poverty, enhance human well-being and help meet the basic human needs of all people. A historical and distinctive feature of social work is that the profession focuses on individual well-being and the well-being of society in a social context. The basis of social work is to pay attention to the environmental forces that create, contribute to and address problems in life (2).

Today, social workers are employed in many hospitals in our country. According to Article 35 of the Inpatient Treatment Institutions Regulation: "1 social worker is employed for every 100 beds". Accordingly, Balıkesir Atatürk city hospital has the right to employ 10 social workers according to the health personnel distribution chart of the Ministry of Health (3). There are approximately 650,000 social workers in the United States, more than half of whom work in healthcare settings (4). The data in Turkey were presented at a symposium held in Manisa in 2015 and these data show that a total of 1007 social workers work actively, 918 in institutions affiliated to the Ministry of Health, 75 in university hospitals, 14 in private hospitals in the field of medical social services, and most social workers are employed in institutions affiliated to the Ministry of Health (5). It can be predicted that this number may have increased with additional appointments since 2015, but this number has not yet been presented in any article.

In Turkey, there is no study reporting the need for a social worker in pediatric intensive care units (PICU) and its effects on pediatric intensive care. In our study, we wanted to show the importance and results of the roles of social workers in intensive care units and their harmonious work with physicians by examining the consultation data referred from the pediatric intensive care units to the social service units.

MATERIALS and METHODS

Our pediatric intensive care unit in Balıkesir Atatürk city hospital has 19 beds and serves patients requiring level 2 and 3 intensive care with different diagnoses. There are currently 8 social workers working actively within our hospital and social workers have been actively assigned in certain departments: 2 are in the child follow-up center, 1 in the community mental health center, 1 in the home health unit, 1 in the palliative care center, 1 in the addiction counseling unit and the other 2 carry out the works and operations in the medical social service unit of the hospital. 66 children aged between 1 month and 18 years old who were asked for social service consultation between January 2019 and December 2020 at our hospital's PICU were included in the study. The age, diagnosis, sex, marital status (married-divorced), number of days of hospitalization, number of recurrent hospitalization, reason and result of consultation, necessity of psychiatric consultation and frequency of follow-up were retrospectively examined and recorded through the hospital information system. The collected data were analyzed by means of SPSS (version 22.0, SPSS Inc. Chicago, IL, USA). The ethics committee decision of our study was approved by the Balıkesir University ethics committee with the number E-94025189-050.03-15740 on 18/02/2021.

RESULTS

In our study, the data of a total of 66 patients were examined. The median age (months) (min-max) was found to be 172, 50 (6-209), and the median (min-max) duration of hospitalization (days) was found to be 2 (1-76). 46 (69.7) of the patients were

Table I: Distribution of diagnoses by age groups.

Diagnosis n	Age Group (ay)			Total n
	0-72 month n (%)	72-144 month n (%)	144-208 month n (%)	
Suicide / intoxication	0	2 (5.1)	37 (94.9)	39
Accidental intoxication	8 (100)	0	0	8
Neurological diseases	8 (88.9)	0	1 (11.1)	9
Sepsis	1 (100)	0	0	1
Diabetic Ketoacidosis	0	0	2 (100)	2
Drowning	0	1 (100)	0	1
Falling from high	2 (100)	0	0	2
Respiratory diseases	1 (50)	0	1 (50)	1
Substance use	1 (50)	0	1 (50)	1
Total (n)	21	3	42	66

Table II: Consultation reasons for patients who are asked to be evaluated by social workers.

Consultation reasons	n (%)
Detection of negligence or psychiatric problems	51 (77.3)
Trouble reaching the family	5 (7.6)
Providing refugee assistance	1 (1.5)
Assessment of care center requirement	2 (3)
Assessment of need for social counseling and socioeconomic support	4 (6.1)
Home appliance supply assistance	1 (1.5)
Home transport assistance	2 (3)
Total	66 (100)

Table III: Consultation results for patients who are asked to be evaluated by social workers.

Consultation results	n (%)
Social notification + referral to psychiatrist	5 (7.6)
Social reporting and prosecution reporting	2 (3)
Clothing and companion assistance	1 (1.5)
Providing access to the family	4 (6.1)
Obtaining consent and permissions for the care center	1 (1.5)
Making an official application to initiate a social review	4 (6.1)
Referral to social counseling and psychiatry specialist	25 (37.9)
Detection of abuse or family neglect	7 (10.6)
Social counseling service only	4 (6.1)
Resolving the custody problem	1 (1.5)
Ensuring the transfer of the patient and his family home	2 (3)
Detection of abuse / family neglect	5 (7.6)
Helping with identity application	1 (1.5)
Socio-economic support assistance	1 (1.5)
Home appliance supply assistance	1 (1.5)
Supplying of quarantine document	1 (1.5)
Medication assistance	1 (1.5)

female and 20 (30.3) were male. 42 (63.6) of the patients who requested consultation were followed up in Level 2 PICU and 24 (36.4) in Level 3 PICU. Considering their attendance to school, it was observed that 21 (31.8%) patients were not at school age, 40 (60.6%) patients were attending school, and 5 (7.6%) patients dropped out of school. When the marital status of the patients' families was questioned, it was learned that 21 (31.8%) families were divorced and 45 (68.2%) families were still married. 61 (92.4%) of our patients who needed social service consultation were Turkish citizens, 2 (3%) were Syrian citizens, 1 (1.5%) was Iranian citizen and 2 (3%) were Afghan citizens. 19 of the patients (28.8%) had recurrent PICU admission. The diagnoses of the patients evaluated by social workers according to their age groups are given in Table I. The reasons for the consultation of the patients who are asked to be evaluated by social workers are given in Table II. The consultation results of patients who are asked to be evaluated by social workers are shown in Table III.

It was seen that 39 (59.1%) of the 66 patients in our study were evaluated by a child psychiatrist, and 13 (33.3%) of them required psychologist follow-up. When the patients were examined in terms of their regular visits to child psychiatry specialist, it was found that 15 (38%) of 39 patients continued their visits regularly. It was observed that 22 (56%) of the patients who were evaluated by child psychiatry started treatment and 1 (0.2%) patient was admitted to the child psychiatry service. The diagnoses of the patients evaluated by the child psychiatrist are given in table IV.

After the study data were collected, the social service department consultations requested for the neonatal unit were

Table IV: Frequency of diagnoses by child psychiatry.

Psychiatric Diagnoses	n (%)
Behavioral Disorder	10 (33.3)
Depression	12 (40)
Adaptation disorder	3 (10)
Anxiety disorder	4 (13.3)
Substance Use Disorder	1 (3.3)
Total	30 (100)

also questioned. There were 10 patients in a year, and it was learned that in 9 of them the family rejected the baby and the social status of 1 family was asked to be examined. The data of these patients were not included in the patients included in the study.

DISCUSSION

Understanding the professional collaboration between health and social workers is crucial as it is a vital part of achieving better patient outcomes, improving patient satisfaction, reducing hospital stays, reducing costs and contributing to fewer and shorter delays in delivery of care (6, 7). In addition to managing the medical treatments applied in intensive care units, palliative care centers, and health centers where oncology patients are monitored, it is possible to make assessments of the patient's non-medical needs and psychosocial status with team solidarity (8, 9). In the studies conducted, the need for social workers to participate in professional teams in the health sector and palliative care is also strongly discussed (10).

Nowadays, the number of intensive care units providing care and treatment of critical patients in the pediatric age group is also increasing. Therefore, the social needs of sick children increase in parallel. The social service unit, which has an increasing role in intensive care units, can solve patient problems in many issues and support the clinical team. In our study, we found that the pediatric intensive care physicians played an important role in achieving a clear result as patient and family oriented with a multidisciplinary approach, including social workers and, where necessary, child psychiatry specialists.

Although it seems that various indications lead to the need for social worker consultation, it is noticeable that the most common indications are suicide attempts and diagnoses of drug poisoning at a young age in order to ensure the detection of problems caused by a family or individual (patient) himself/herself. From this point of view, it is important to ensure the detection of the situation of family neglect. Because physicians give priority to treatment, deepening the medical history should be considered as the contribution of the social worker. In terms of identifying and reporting child neglect and abuse cases of patients in PICU, social workers manage the process and take responsibility for reporting the crime. These reports are of great importance in combating child neglect and abuse, and also ease the workload of intensive care personnel at this point. In addition, patients are consulted with child psychiatry doctors and monitored. Interviews with the family about whether patients had repeated suicide attempts and whether they were undergoing psychiatric follow-up were one of the important contributions of social workers. In some studies conducted in our country, cases of childhood poisoning were examined and it was reported that family education and adolescent or family structures that are considered risky should be examined (11, 12).

The presence of refugee patients in our country leads to the need for more social support. In our study, social workers engaged in communication, information and financial support with the families of refugee patients. In addition, in terms of providing a companion before patient discharge, the determination of the parent who can take care of the child was also performed by the social worker. Their assistance to the family in applying for identification of patients, in case of necessity, accelerates the treatment and follow-up process from the point of view of the patient and the hospital. These aids contributed to the prevention of prolonged hospitalization and the efficient use of beds. But since our study is not specific to this topic, and our provable data is not studied statistically, it remains only at the level of opinion. After that, prospective studies can investigate the effect of social support on hospitalization periods of pediatric patients in pediatric services and PICUs.

Turkey has a heterogeneous structure in a socio-economic and cultural sense. In families with low socioeconomic levels, it is necessary to communicate with charities in order to provide some special needs for the sick child while in hospital. An important issue that we want to draw attention to in our study is that in terms of this economic support, social workers communicate with the necessary institutions for solving problems. Providing patients with access to their homes after discharge and providing medicines that families cannot provide are other important issues that the social workers solve.

When our patients in need of a social worker were divided into age groups, the vast majority were patients over 12 years of age, and this was followed by children between 0-6 years of age. We believe that this frequency increases due to period-specific difficulties such as accelerating cognitive development during adolescence, increasing emotion intensity and impulsive behavior, choosing a profession, building relationships with the opposite sex. The younger age group is an age group open to neglect, which requires more attention for care and is difficult to follow from the point of view of the family. A study published in our country in 2012, in which 33 years of experience with drug intoxication in children was transferred, reported that two

different peaks were observed in drug intoxication in similar age groups, in boys aged 1-5 and in girls aged 13-16 (13). It can be considered that the requirement for a social worker is parallel to the increase in similar age groups due to similar indications.

One of the most important consultant units referred to as a result of social worker and physician evaluation is child psychiatry specialists. As a result of the psychiatric evaluations of the patients evaluated by psychiatry, the most common psychiatric diagnosis was major depressive disorder (40%; n =12). Depressive disorder is followed by behavioral disorder (33.3%; n=10), adaptation disorder (10%; n=3), anxiety disorders (13.3%; n=4) and substance use disorder. Studies conducted in 2013 and 2019 reported that child psychiatry consultations were most frequently requested due to suicide attempt and depressive symptoms (15,16). In our study, it was determined that 15 (38%) of the patients continued their visits regularly. In the studies conducted in Turkey, the rates of regular psychiatric treatment were found between 34% and 70.2% (14,16-18). When compared with these studies, the follow-up rate of our patients can be considered as low. This may be due to the difficulty in accessing the child psychiatrist and / or the low awareness of families about seeking psychiatric treatment. The reason is that our social workers serve different units, including adults, and do not work specifically for the pediatric intensive care unit. In order to prevent re-hospitalization of the patients who are evaluated in the pediatric intensive care unit and to continue their psychiatric visits regularly, we think that it will be beneficial to follow up regularly by a single social service specialist in charge of pediatric intensive care, and to ensure that families and children are followed up periodically. If we look at it from a different perspective, our study also covers the approximately 10-month period of the COVID-19 pandemic. Families and children may not be able to provide regular visits due to reasons such as the intensity of the pandemic in hospitals, changes in the appointment system and the possibility of infection.

Social workers have taken their place among the professions whose importance in the field of health has increased with the increasing importance of the psycho-social dimension of health. But despite the rapid expansion of the scope of services provided in the field of medical social work in Turkey, it is still believed that there are differences between hospitals and provinces in terms of professional staff and practices vary according to people, institutions and provinces. At this point, as well as the lack of regulations of the medical social service unit, the lack of staff and lack of in-service training cause variability in the quality of the service. Many healthcare professionals still do not have enough information about what kind of services the social worker provides. Generally, awareness can develop after a social worker solves a problem that a patient cannot solve about his / her psycho-social situation.

The inclusion of social workers in the children's intensive care unit teams can also prevent many social problems that can be neglected otherwise. Physicians are more focused on patient treatment, so we believe that it will be beneficial to question the family and social status of patients together with a social service unit and specialists integrated into children's intensive care units. Today, physicians and nurses working in pediatric intensive care units frequently take these responsibilities and try to question the family status of their patients, but these may be insufficient.

This study only includes one-year data of one hospital. This issue can be considered as a limitation of our study. As physicians, we estimate that there are many social problems in PICUs throughout Turkey and we believe that this issue should be investigated with multi-center studies. We think that healthcare providers must work in coordination with social workers to solve problems other than medical treatment, and this will increase the quality and effectiveness of service. For this reason, as pediatricians and social workers, we think that in a world where social and family social problems are increasing, there should be a social worker working actively in pediatric intensive care units.

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Endocan Levels in Children with Polycystic Kidney Disease

Polikistik Böbrek Hastalığı Olan Çocukların Endocan Düzeyi

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ABSTRACT

Objective: Autosomal dominant polycystic kidney disease (ADPKD) is a common renal disorder that is characterized by hypertension and renal failure. Recently, it has been emphasized that endocan which is an endothelial dysfunction biomarker, could increase in many renal diseases. High endocan levels have also been reported in hypertensive ADPKD adult patients with renal failure. However, studies are limited on children. In this study, we investigated the serum endocan levels in normotensive ADPKD children with normal renal function.

Material and Methods: The study consisted of 20 ADPKD children without hypertension and renal failure as a patient group, and 20 healthy age- and sex-matched children as a control group. Serum endocan levels were determined by enzyme-linked immunosorbent assay techniques and compared between the two groups.

Results: The mean age of patients was 9.9±4.12 years, and the mean age of the control group was 10.2±3.83 years. There was no significant difference between the two groups in terms of gender, age, and BMI (p=0.751, p=0.813, p=0.781, respectively). The leukocyte (p=0.449), hemoglobin (p=0.337), platelets (p=0.134), serum uric acid (p=0.671) and serum creatinine (p=0.074) levels, eGFR (p=0.459) were not significantly differed between groups. The mean serum endocan level in the PKD group was 345.8±169.5 pg/ml, and in the control group was 448.61±258.2 pg/ml. Serum endocan levels did not change between groups (p=0.159).

Conclusion: Unlike the adult ADPKD patients, this study suggested that serum endocan level was normal in children with ADPKD without hypertension and renal failure.

Key Words: Child, Endocan, Polycystic kidney disease

ÖZ

Amaç: Otozomal dominant polikistik böbrek hastalığı (ODPKB), hipertansiyon ve böbrek yetmezliği ile karakterize yaygın görülen bir böbrek hastalığıdır. Son zamanlarda endotel disfonksiyonu biyobelirteçlerinden olan endocanın birçok böbrek hastalığında artabileceği vurgulanmıştır. Böbrek yetmezliği olan hipertansif ODPKB'li erişkin hastalarda da yüksek endocan seviyeleri bildirilmiştir. Ancak, çocuklar üzerinde yapılan çalışmalar sınırlıdır. Bu çalışmada, normal böbrek fonksiyonu olan normotansif ODPKB'li çocuklarda serum endocan düzeylerini araştırdık.

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Gereç ve Yöntemler: Çalışmaya, hasta grubu olarak hipertansiyonu ve böbrek yetmezliği olmayan 20 ODPBH'li çocuk ve kontrol grubu olarak yaş ve cinsiyet açısından benzer 20 sağlıklı çocuk dahil edildi. Serum endocan seviyeleri, enzime bağlı immünosorbent tahlil teknikleri ile belirlendi ve iki grup arasında karşılaştırıldı.

Bulgular: Hastaların yaş ortalaması 9.9±4.12 yıl, kontrol grubunun yaş ortalaması 10.2±3.83 yıldı. Cinsiyet, yaş ve VKİ açısından iki grup arasında anlamlı fark yoktu (sırasıyla p=0.751, p=0.813, p=0.781). Gruplar arasında Lökosit (p=0.449), hemoglobin (p=0.337), trombosit (p=0.134), serum ürik asit (p=0.671), serum kreatinin (p=0.074) seviyeleri, ve eGFR (p=0.459) düzeyleri açısından anlamlı fark bulunmadı. PKB grubunda ortalama serum endocan düzeyi 345.8±169.5 pg/ml, kontrol grubunda 448.61±258.2 pg/ml'di. Serum endocan seviyeleri gruplar arasında değişmedi (p=0.159).

Sonuç: Erişkin ODPKB hastalarından farklı olarak, bu çalışmada hipertansiyon ve böbrek yetmezliği olmayan ODPKB'li çocuklarda serum endocan düzeyinin normal olduğu saptandı.

Anahtar Sözcükler: Çocuk, Endocan, Polikistik böbrek hastalığı

INTRODUCTION

Polycystic kidney disease (PKD) is an inherited kidney disease that can cause morbidity and mortality in childhood. (1). It is characterized by the increasing formation and expansion of multiple fluid-filled cysts in the parenchyma of the kidneys (2). The progression of cyst enlargement compresses the surrounding kidney areas and leads to fibrosis in renal parenchyma. The growth rate of the renal cysts and decreasing GFR also causes hypertension. Therefore, early diagnosis and optimal treatment of hypertension are essential to retard cyst growth and improvement of cystic disease (3). Many pathologic mechanisms that explain hypertension in PKD include activation of the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system, vascular vasopressin V1 receptors, macrophages, and reduction of nitric oxide production, and also an alteration of intracellular calcium levels (3-5). In addition, endothelial dysfunction which could lead to unbalanced vasoconstriction and ischemia of renal parenchyma is going to propose as an increasingly alternative pathway for renal damage in polycystic kidney disease (6).

Many biomarkers including kidney injury molecule–1 (KIM-1), N-acetyl-β-d-glucosaminidase (NAG), heart-type fatty acid-binding protein (HFABP), macrophage migration inhibitory factor (MIF), neutrophil gelatinase-associated lipocalin (NGAL), monocyte chemotactic protein–1 (MCP-1) have been investigated for understanding PKD progression (7). A new biomarker called endocan has also been investigated in PKD (6).

Endocan is a soluble that is secreted by vascular endothelial cells in various organs, as well as kidneys (8). It plays a key role in cell proliferation, migration, inflammation, neovascularization, and endothelial function (8). Its synthesis from the kidneys and its involvement in endothelial dysfunction suggests that endocan may be a potential early marker in PKD patients (6).

Raptis et al.(6) have reported that serum endocan levels are higher in adult hypertensive polycystic kidney diseases with renal failure compared to the healthy group. However, to our knowledge, there is no study about the endocan levels in PKD children with or without hypertension and renal failure. In this study, we want to investigate the serum endocan level in children with PKD without hypertension and renal failure.

MATERIAL and METHODS

Twenty children with ADPKD and 20 age-sex matched healthy children, ages between 5-17 years, were prospectively analyzed between February 2019 and January 2020 in our Pediatric Nephrology Department. Patients were included in the study if they had normal renal blood pressure and renal function with a documented diagnosis of ADPKD, according to the 'International consensus statement on the diagnosis and management of autosomal dominant polycystic kidney disease in children and young people' as PKD group (9). The child with a positive family history of PKD and one or more kidney cysts was accepted as PKD. Age-sex matched healthy children without any disease were also accepted as the control group.

Children with an acute or chronic inflammatory disease, history of recurrent urinary tract infection, asthma or chronic obstructive lung disease, cardiac disease, anemia, diabetes mellitus, insulin resistance, impaired glucose tolerance, hematologic or solid organ malignancies smoking habit, obesity, use of any medications, hepatic dysfunction, hypertension, and renal failure (estimated filtration rate below 90 mL/min/1.73m^2) were excluded from the study.

Normotension was determined from The American Academy of Pediatrics 'Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents' (10). Hypertension was defined as high in repeated office measurements (auscultatory confirmed blood pressure readings ≥95th percentile at 3 different visits) or ambulatory blood pressure measurements (mean systolic blood pressure and diastolic blood pressure > 95th percentile and systolic blood pressure and DBP diastolic blood pressure >25%) (10).

We used hemogram, CRP, urine analysis and urine culture for the parameters of inflammation status. Demographic data and medical history were collected from the files. Laboratory investigations of hemogram, urea, serum creatinine, uric acid, urine analysis, estimated glomerular filtration rate (eGFR), and also serum endocan level were all investigated. Body mass index (BMI, the ratio of height and weight, expressed as kg/m^2) was used to define obesity. The eGFR (ml/min per 1.73 m^2) was calculated using the original Schwartz equation.

Human Endocan Measurements

Blood samples were obtained after overnight fasting. Samples were allowed to clot for 30 min, centrifuged at 2000x g for 15 min for the separation of serum, and stored at -80°C until analysis.

The concentration of endocan was evaluated using an enzyme linked immunosorbent assay (ELISA) method. We used a commercially available human endocan ELISA kit (Uscn Life Science Inc, Wuhan, PR China). The ELISA process was applied according to the manufacturer's instructions. The absorbance was measured at 450 nm on a spectrophotometer. The intra-assay coefficient of variation was <10% while inter-assay coefficient of variation was <12%. The minimum detectable dose of this kit is typically less than 6.2 pg/ml. Linear measurement range of the assay was 15.6-1000 pg/ml.

The study was approved by the Clinical Research Ethics Committee of Ankara Pediatrics Hematology Oncology Training and Research Hospital (28.05.20219/2019-155).

Statistical analysis

SPSS v.20 was used for statistical analysis. Mann-Whitney U and t-tests were used for independent groups. The relationship between variables was examined by Chi-square analysis. p< 0.05 was considered statistically significant.

RESULTS

Twenty patients with PKD and 20 healthy controls were included in this study. The male/female ratio was 12/8 in the PKD group, and 10/10 in the control group. The mean age of patients with PKD was 9.9±4.12 years, the mean age of the control group was 10.2±3.83 years. The mean BMI of the PKD group was 18.7±2.47 kg/m^2, the mean BMI of the control group was 19.03±4.11 kg/m^2. There was no significant difference between the two groups in terms of gender, age, and BMI (p=0.751, p=0.813, p=0.781, respectively). The characteristics of the PKD and control groups are presented in Table I.

The mean follow-up period of the patients with PKD was 48.4±28.6 months.

The mean leukocyte level of patients with PKD and the control group were 7.6±2 µL, and 7.05±1.4 µL, respectively. The mea hemoglobin level of patients with PKD was 13.1±1.24g/dL, and the mean hemoglobin level of the control group was 13.5±1.23 g/dL. The mean platelets level of patients with PKD was 333.2±72.2 µL, the mean platelets level of the control group was 302.4±53.8 µL. There was no significant difference between groups for the levels of leukocyte (p=0.449), hemoglobin (p=0.337), and platelets (p=0.134).

Table I: The baseline characteristics of the PKD and control groups.

	PKD group (n=20)	Control group (n=20)	p
Age (year)	9.9±4.12	10.2±3.83	0.813
Gender (male/female)	12/8	10/10	0.751
Body mass index	18.7±2.47	19.03±4.11	0.781

Table II: The levels of complete blood count and biochemical parameters.

	PKD group (n=20)	Control group (n=20)	p
WBC (µL)	7.6±2	7.05±1.4	0.449
Hb (g/dL)	13.1±1.24	13.5±1.23	0.337
PLT (µL)	333.2±72.2	302.4±53.8	0.134
Urea (mg/dL)	28.1±7.5	22.7±6.4	0.031
Uric acid (mg/dL)	4.5±1.09	4.3±1.06	0.671
Creatinine (mg/dL)	0.57±0.17	0.63±0.13	0.074
eGFR (mL/min/1.73 m^2)	120.5±12.5	125±23.6	0.459
Blood endocan level (pg/ml)	345.8±169.5	448.6±258.2	0.159

The mean serum creatinine level was 0.57±0.17 mg/dL for patients with PKD, and 0.63±0.13 mg/dL for the control group. The mean serum uric acid level of patients with PKD was 4.5±1.09mg/dL, the mean serum uric acid level of the control group was 4.3±1.06 mg/dL. There was no significant difference between groups for the levels of serum creatinine (p=0.074), and uric acid (p=0.671).

The mean serum urea level for the PKD group was 28.1±7.5 mg/dL, the mean serum urea level for the control group was 22.7±6.4 mg/dL. The mean urea levels of the PKD group were significantly higher than the control group (p=0.031).

The mean eGFR for patients with PKD and the control group were 120.5±12.5 mL/min/1.73 m^2, 125±23.6 mL/min/1.73 m2, respectively. The eGFR (p=0.459) did not significantly differ between groups. The levels of complete blood count and biochemical parameters are presented in Table II.

None of the patients had hematuria or proteinuria in the PKD group.

The mean serum endocan level in the PKD group was 345.8±169.5 pg/ml and in control group was 448.61±258.2 pg/ml. Serum endocan levels did not change between groups (p=0.159). Serum endocan levels of groups are presented in Table II.

DISCUSSION

Polycystic kidney disease is an inherited, monogenetically, cilia-related disorder. The PKD affects an estimated greater than 10 million people around the world and eventually results in renal replacement therapy (RRT) and kidney transplantation (2). Many prognostic factors for disease progression in PKD have

been identified such as the early age of onset, hypertension, total kidney volume, and proteinuria. The identification of new molecular prognostic factors continues due to the growing knowledge of pathological cyst processes. To date, several cellular changes described with cyst formation and disease progression (1,3). Epithelial cell proliferation, fluid secretion, and extracellular matrix deposition are the major factors for cystogenesis. Increased inflammation is related to cyst formation. Many chemokines, cytokines, and growth factors, inflammatory cells contribute to cystogenesis. These molecular changes lead to alteration in the blood circulation of the regional kidney area (1,2).

Furthermore, increased cyst number and sizes induce local hypoxia which eventually results in fibrotic kidneys (2). The relationship between endothelial dysfunction and molecular alterations

suggests that new endothelial biomarkers could predict disease progression in PKD. Recently, a new endothelial biomarker called endocan was studied in various kidney diseases as well as PKD (6).

Endocan is a soluble proteoglycan that is secreted by vascular endothelial cells of many tissues such as lung, tumor endothelium, glandular tissues, germinal centers of lymph nodes, and also kidneys. It is an endothelial activation marker that is involved in inflammation, endothelial dysfunction, and angiogenesis (8).

Previous studies have demonstrated elevated plasma endocan levels in polycystic kidney disease, immunoglobulin A nephropathy, chronic kidney disease, and hypertension (11-14).

Yilmaz et al.(12) reported that serum endocan levels are inversely correlated with eGFR. Additionally, Raptis et al. (6) reported that serum endocan levels in ADPKD patients with impaired renal function were significantly higher compared to normal renal function. Also, they were reported high serum endocan levels in patients with ADPKD and normal renal function compared to healthy controls. From different studies, increased levels of serum endocan was explained by a marker of vascular inflammation which is an important process in the development of CKD (6,12). However, most of these studies includes adult patients, with and without hypertension and renal failure.

It is known that increasing endocan levels are correlated with inflammation and endothelial dysfunction which may play an important role in the pathophysiology of hypertension (13). Balta et al. (13) reported a significant increase in endocan levels in patients with newly diagnosed untreated HT compared with the normotensive group.

In this study, we evaluated the serum endocan levels in ADPKD children with normal renal function and normal blood pressure. We found no significant difference between the PKD and the control groups in terms of serum endocan levels.

Many studies reported that endocan is secreted from many cells as well as tubules and glomeruli (8). Li Recently et. al. (15) detected that endocan is mainly expressed from glomeruli in the kidneys. However, ADPKD is mainly a renal tubular disorder (1). Therefore, normal serum endocan levels of our patients who have normal renal function can be explained by the presence of mainly tubular alteration. In addition, none of our patients had hypertension. The high serum endocan levels in other studies with ADPKD adult patients may be related to the presence of hypertensive patients in their groups. It could be possible that serum endocan levels of our patients are going to be high when hypertension and renal dysfunction develop in their adulthood. However, we didn't include patients with hypertension and impaired renal function as a separated group. This was our limitation. On the other hand, to the best of our knowledge, this was the first study that evaluates serum endocan levels in children with ADPKD without hypertension and renal failure.

But the limitations of this study were that it has a small number of patients, and we did not use national reference for standard blood pressures in the pediatric age group.

CONCLUSION

Serum endocan levels did not change in ADPKD children without hypertension and renal failure. These results could suggest that endocan is mainly expressed from glomeruli, not from tubules, and the presence of hypertension and renal failure could elevate endothelial dysfunction and serum endocan levels in children with ADPKD. The study includes a low number of patients, and results require more prospective studies.

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Surgical Ovary Masses in Children: A Single Center Experience of 11 Years

Çocuklarda Cerrahi Over Kitleleri: 11 Yıllık Deneyim

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ABSTRACT

Objective: The majority of childhood ovarian masses are benign. However, malignant tumors encountered in adulthood may also be seen in childhood. There is still no ovarian tumor management protocol for children. We shared our experiences with ovarian mass cases operated in our clinic.

Material and Methods: Patients aged 0-18 years and had surgery in our hospital between 2010 and 2020 due to ovarian masses were included in the study. The ages of the patients, the maximum diameter and structure of the mass on ultrasonography (USG) and other imaging modalities, symptoms on presentation, tumor markers, operation data, and histopathology results were recorded. The patients were divided into three groups in relation with tumor histopathology, and the demographic data were compared among groups.

Results: In 11-year period, 107 surgical operations were performed on 106 patients due to ovarian masses. The ages of the patients were between 2 days and 17 years, with a mean age of 13.4±14.1 years. Of the masses, 9 (8.4%) were malignant (3 (2.8%) borderline), 44 (41.1%) were benign, and 54 (50.5) were non-neoplastic. Histopathology results of 53 surgical operations performed for neoplastic ovarian masses were germ cell tumor in 31 (29%), epithelial tumor in 19 (17.8%), sex cord stromal tumor in 2 (1.9%), and leiomyoma 1 (0.9%) patient.

Conclusion: Adult protocols should be used when necessary in rare childhood ovarian malignant tumors, and large multi-center patient series should be constituted in order to establish pediatric protocols related to the subject. A multidisciplinary approach is necessary in childhood ovarian masses.

Key Words: Children, Masses, Ovary, Surgery

ÖZ

Amaç: Çocukluk çağı over kitlelerinin çoğunluğu benigndir. Ancak yetişkinlik döneminde görülen malign tümörlerde çocukluk çağında görülebilmektedir. Bu tümörlerel ilgili çocukluk çağına ait bir protokol hala yoktur. Bizde kliniğimizde opere edilen over kitleleri ile ilgi deneyimimizi paylaştık.

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Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. Ethical approval for this study was obtained from the ethics committee of Umraniye Training and Research Hospital (29.04.202-139).

Contribution of the Authors / Yazarların katkısı*: *AKIS YILDIZ Z: Planning methodology to reach the Conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***ARPACIK M:*** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, aking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***KOC B:*** Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in the writing of the whole or important parts of the study. ***TOSUN I:*** Planning methodology to reach the Conclusions, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. ***YALCINKAYA C:*** Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Reviewing the article before submission scientifically besides spelling and grammar. ***ILCE Z:*** Constructing the hypothesis or idea of research and/or article, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar.

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Gereç ve Yöntemler: Hastanemizde 2010 ile 2020 yılları arasında over kitlesi nedeniyle opere edilen 0 ila 18 yaş arası olgular çalışmaya dahil edildi. Hastaların yaşları, ultrasonografi (USG) ve diğer yapılan görüntüleme yöntemlerinde kitlenin maksimum çapı ve yapısı, başvuru semptomları, tümör belirteçleri, operasyon verileri, patoloji sonuçları kaydedildi. Patolojiye göre 3 gruba ayrılarak demografik veriler karşılaştırıldı.

Bulgular: Çalışmanın yapıldığı 11 yıllık süreçte 106 olguya over kitlesi nedeniyle 107 ameliyat yapılmıştır. Olguların yaşları 2 gün ile 17 yaş arasında değişmekle birlikte ortalaması 13.4±14.1'dir. Bu ameliyatlardan 9 (%8.4)'ü malign (3'ü (%2.8) borderline), ve 44 (%41.1)'i benign neoplastik over kitlesi, 54 (50.5)'i nonneoplastik over kitlesiydi. Neoplastik over kitlesi nedeniyle yapılan 53 ameliyatta patoloji sonuçları; olgulardan 31 (%29)'u germ hücreli tümör, 19 (%17.8)'i epitelyal tümörler, 2 (%1.9)'u seks kord stromal tümör, 1 (%0.9) leomiyom olarak değerlendirildi.

Sonuç: Çocukluk çağı over kitlelerinde multidisipliner yaklaşım unutulmamalıdır. Çocukluk çağında az görülen over tümörlerinde gerektiğinde yetişkin protokollerinden yararlanılırken, çok merkezli çalışmalarla seriler oluşturulmalı ve böylece konu ile ilgili çocuk protokolleri oluşturulmalıdır.

Anahtar Sözcükler: Çocuk, Kitleler, Over, Cerrahi

INTRODUCTION

The majority of childhood ovarian masses are benign. The most common ovarian masses are non-neoplastic ones such as simple cysts and torsions (1,2). Neoplastic ovarian masses originate from germ, stromal and epithelial cells. In childhood, most common tumors are germ cell tumors, and comprise 60-85% of all tumors. Epithelial neoplasms are encountered most frequently in adults, on the contrary, these are quite rare in children (3,4).

Although the exact rate of malignancy in the childhood is not known, the risk for a malignant ovarian mass is at least 100 times lower than in postmenopausal women (3,5). Adult ovarian malignancy treatment protocols are clear since ovarian malignancies are frequent in adulthood. However, only case reports and small series have been published concerning childhood ovarian masses, and treatment protocols are not as straightforward as adults.

Although the risk of malignancy is low in childhood ovarian masses, the rate of oophorectomy is high in benign masses. This is mostly due to the fear of malignancy and supposing that the torsioned ovary will not function due to necrosis. Performing oophorectomy in the children increases the risk of both future infertility and the risk of premature menopause. While aiming to protect patients from malignancy, new problems are created by performing oophorectomy in harmless benign masses (5-7).

In our study, demographic, clinical and histopathological characteristics of pediatric cases who had surgery for ovarian masses in Umraniye Training and Research Hospital, a tertiary pediatric hospital with pediatric surgery and gynecology clinics, will be presented, and childhood ovarian malignancies will be discussed in the light of the literature.

MATERIAL and METHODS

The patients between 0 and 18 years of age and diagnosed with an ovarian mass in Umraniye Training and Research Hospital between 2010 and 2020 were retrospectively analyzed using the hospital registry system. Ethical approval for this study was obtained from the ethics committee of Umraniye Training and Research Hospital (29.04.202-139).

The patients who underwent surgical procedures were included in the study. Cases with incomplete medical records, masses other than ovarian masses, surgical procedures performed for sexual development disorders, and the cases that did not have surgery were excluded. The ages of the patients, the maximum diameter and structure of the mass on ultrasonography (USG) and other imaging modalities, symptoms on presentation, tumor markers, operation data, and histopathology results were recorded.

The type of the surgical procedure was recorded as open surgery or laparoscopic surgery. The surgical procedures were grouped as oophorectomy/salpingo-oophorectomy, ovary-sparing surgery and only detorsion. Masses were first divided into two groups as non-neoplastic and neoplastic. Neoplastic masses were again divided into two groups as benign and malignant masses.

In the non-neoplastic group, simple cysts were grouped as hemorrhagic cysts, necrosis due to torsion, and the cases that had surgery for torsion only and detorsioned. Tumors were divided into four main groups as neoplastic germ cell tumors, sex-cord stromal tumors, epithelial tumors and the others. Malignant neoplastic masses and the tumors with low malignancy potential (borderline) were included in the malignant masses group. The cases were divided into three groups in terms of ages, as 0-9, 10-13, and 14-17 year-old groups.

The data were analyzed with IBM SPSS statistics 22 program (IBM SPSS, Turkey). Descriptive statistics were employed to analyze frequency distribution and the means. The $\chi 2$ (Chi-square) and Fisher's exact tests were used to compare two groups. Significance level was set at $p < 0.05$.

RESULTS

A total of 371 patients were diagnosed with ovarian masses in an 11-year period. Of these, 265 patients were followed up

Table I: Childhood ovarian masses that had surgery.

Group	Mass	Count	Percent (%)	Mean age (year)	Right side (n)	Bilateral (n)	Torsion (n)	Oophorectomy (n)
Neoplastic ovary masses								
Germ cell tumor	Mature teratoma	28	28.6	14.5	17	1	8	9
	Immature teratoma	1		14	1	0	0	1
	Dysgerminoma	2		17	1	0	0	2
Sex-cord stromal tumor	Sertoli cell tumor	1	1.9	6	1	0	0	1
	Fibroma	1		17	0	0	0	0
Epithelial tumor	Serous cystadenoma	7	17.1	15.2	4	1	3	0
	Mucinous cystadenoma	2		13.5	2		0	0
	Borderline Serous cystadenoma	2		15.5	1	1	0	1
	Borderline Mucinous cystadenoma	1		17	1	0	0	1
	Serous cystadenocarcinoma	1		15	0	0	0	1
	Mucinous cystadenocarcinoma	1		15	1	0	0	1
Other	Cystadenofibroma	5		15.2	3	0	1	0
	Leiomyoma	1	0.9	15	0	1	0	0
Non-neoplastic ovary masses	Hemorrhagic cyst	25	51.5	14	15	0	8	2
	Simple cyst	10		11.4	7	0	3	0
	Corpus luteal cyst	6		14.5	5	0	1	0
	Newborn	7		0.07	3	1	5	4
	Detorsion	6		12.1	5	0	6	0
Total		107	100	13.4	67	5	35	23

without surgery, and 107 surgeries were performed on 106 patients. Of these masses, 9 (8.4%) were malignant (3 (2.8%) borderline), and 44 (41.1%) were benign neoplastic ovarian masses while 54 (50.5) were non-neoplastic ovarian masses. The histopathology result was not available in 6 (5.6%) cases who had only detorsion. The histopathology results of 53 surgical operations performed for neoplastic ovarian mass were: germ cell tumor in 31 (29%), epithelial tumors in 19 (17.8%), sex cord stromal tumor in 2 (1.9%), and leiomyoma in 1 (0.9%) patient (Table I).

The ages of the patients were between 2 days and 17 years with a mean age of 13.4±14.1 years. The patients under one year of age constituted 6.6% of all cases. There were 12 (11.3%) cases in the 0-9 year-old group, 26 (24.5%) cases in the 10-13 year-old group, and 69 (65%) cases in the 14-17 year-old group. The age groups were compared in terms of ovarian mass histopathology (Figure 1). As the patient's age increased, the number of patients with an ovarian mass also increased. The prevalence of malignant ovarian masses was significantly higher in patients aged 14 years and over ($p < 0.006$).

The surgical technique was laparotomy in 61 patients, laparoscopy in 45 patients and drainage in 1 patient. It was seen that the laparoscopy rate has increased significantly after 2015 ($p < 0.008$). Unilateral oophorectomy or unilateral salpingo-oophorectomy was performed in 21 (19.6%), bilateral salpingo- oophorectomy in 2 (1.8%), ovary conserving surgery in 78 (72.8%), and only detorsion in 6 (5.6%) of the surgical operations. Among 9 patients with malignant or borderline histopathology, 8 (88.8%) had unilateral oophorectomy or salpingo-oophorectomy, 1 had bilateral salpingo-oophorectomy, and only mass excision was performed in a borderline case. Oophorectomy or salpingo-oophorectomy was performed in 15 (15.3%) of 98 non-malignant cases. Of these cases, 4 (4.08%) had necrosis due to torsion in the neonatal period, 8 (8.11%) had masses with torsion and had emergency surgical operations, and 3 (3%) had solid ovarian masses that could not be dissected from the normal ovarian tissue.

The presenting complaint was abdominal pain in 75 (70.1%) patients, 7 (6.5%) patients had problems related to menstruation, 12 (11.2%) patients had complaints other than abdominal pain and menstruation problems (abdominal distension, nausea, vomiting, groin pain), 1 (0.9%) patient who previously had surgery for borderline serous cystadenoma had surgery due to a mass appeared in her follow-up, and in 12 (11.2%) cases the ovarian masses were diagnosed incidentally (Figure 2). While 73 (74.48%) of 98 benign cases presented with abdominal pain, this rate was 2/9 (22.22%) in malignant cases (including borderlines). Cases with benign masses presented with abdominal pain more frequently compared to the malignant cases, the difference being statistically significant ($p < 0.001$).

The mass was located in the right ovary in 66 (62.2%), in the left ovary in 35 (33%), and bilateral ovaries in 5 (4.7%) patients. There was no statistically significant difference between the

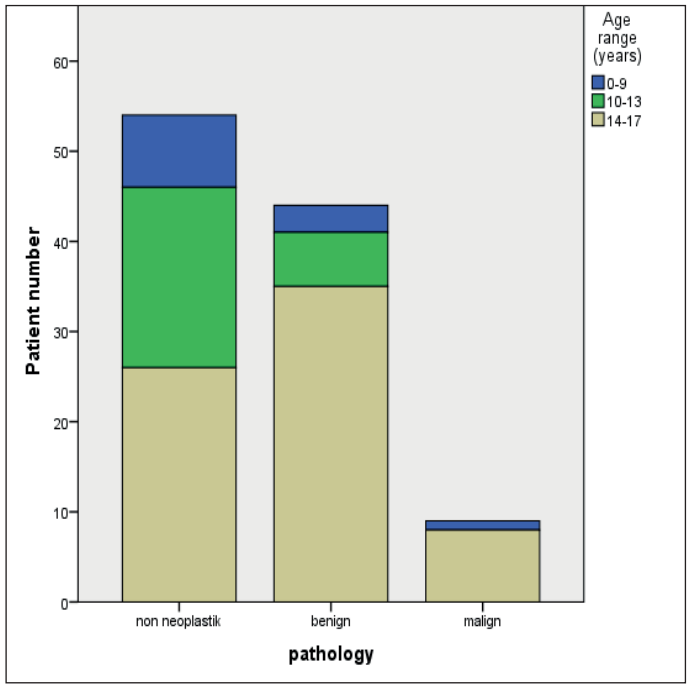

Figure 1: Age distribution in relation with ovarian mass histopathology.

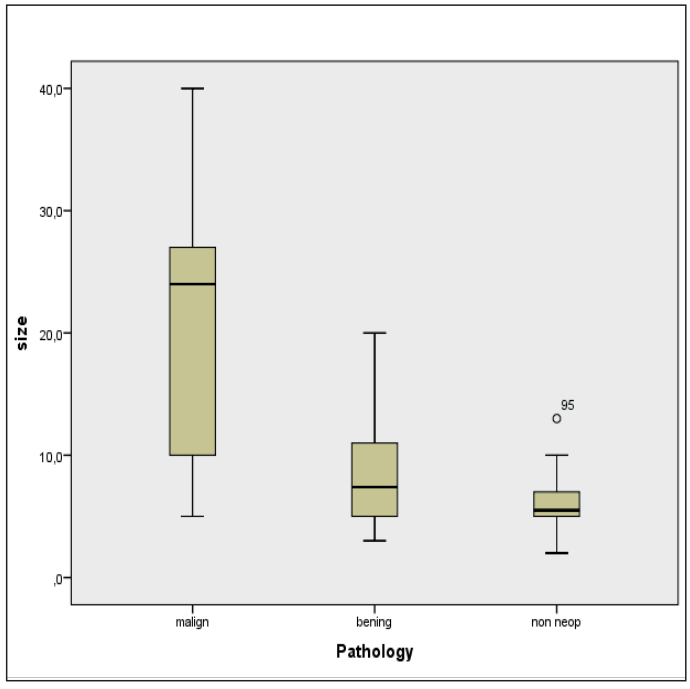

Figure 3: Distribution of the greatest diameter of ovarian masses in relation with their histopathology.

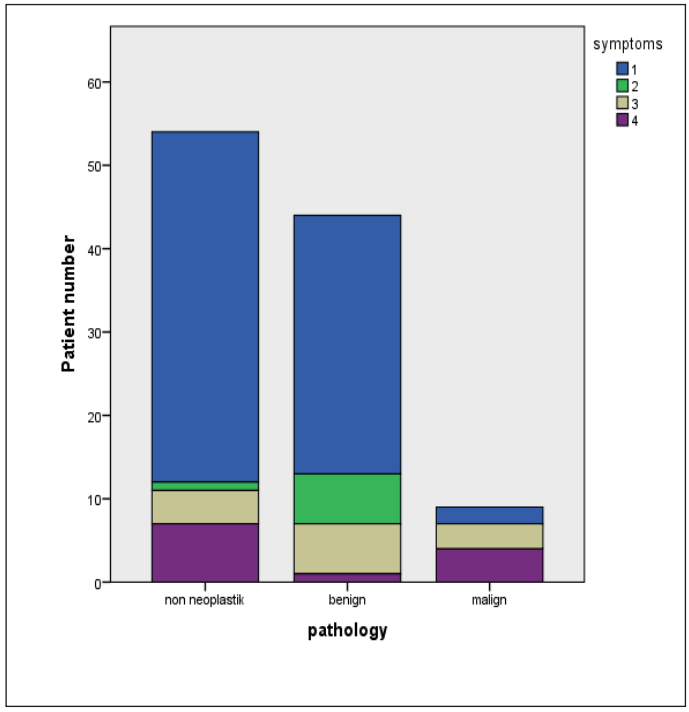

Figure 2: Distribution of the presentation symptoms in relation with the histopathology of the masses (1-abdominal pain, 2-menstrual problems, 3-other 4-incidental).

masses with or without torsion for their localization in right or left ovaries (p <0.816). Likewise, there was no statistically significant difference in the right or left ovarian localization of malignant, benign or non-neoplastic masses (p <0.475).

Preoperative USG was not performed in only 4 cases. In these cases, ovarian cysts were detected incidentally during appendectomy, and cystectomy was performed. On USG, a solid component or complex structure was detected in 40 cases, 10 cases were reported as torsion only, 25 cases were reported as masses with torsion, and 28 cases were reported as simple or hemorrhagic cysts. Nine (25.7%) of the 35 cases considered to have torsion on USG were not evaluated as torsion at surgery. Twenty-four of 32 cases found to have torsion during surgery were also reported as torsion on USG, but 3 of the other 8 (25%) cases were evaluated as solid mass, and 5 as simple cysts. Oophorectomy was performed in 13 (40.6%) of 32 cases with torsion. None of the cases with a malignant or borderline histopathology had torsion.

The largest mean diameter of the mass was found as 20.66 cm in malignant and borderline masses, and 7.35 cm in benign masses (Figure 3). The diameters of malignant masses were statistically significantly greater than benign masses (p <0.001).

Preoperative tumor markers were requested in all cases with neoplastic masses. In non-neoplastic masses, tumor markers were not requested in 18 of 54 patients. At least one of cancer antigen 125 (CA125), beta-human chorionic gonodotropin (BHCG), alpha fetoprotein (AFP), lactate dehydrogenase (LDH), carcinoembryonic antigen (CEA) was high in 22 (24.7%) of 89 cases for whom tumor markers were requested. High levels were found in 7 (77.7%) malignant, 10 (22.7%) benign, and 5 (13.8%) non-neoplastic ovarian masses. Tumor markers were significantly higher in malignant masses (p <0.001). Seventy-

eight (72.89%) cases were operated by pediatric surgeons and 29 (27.10%) cases by gynecologists. The cases operated by gynecology and pediatric surgery were compared for their ages: younger or older than 14 years of age. The gynecology department statistically significantly operated more cases over the age of 14 years ($p < 0.001$).

DISCUSSION

In our hospital, which is a tertiary health center, 78 out of 107 pediatric ovarian masses were operated by pediatric surgery in 11 years, and this corresponds to 7 cases/year. Considering that an average of 2000 children have surgery annually in our clinic, we may say that pediatric surgeons rarely perform surgery on ovarian masses when compared to other surgical operations. In our institution, 1/3 of the total childhood ovarian pathologies were operated by gynecologists. A number of studies in the literature on childhood ovarian masses were published by gynecologists. In particular, ovarian masses of adolescents are treated by gynecologists in many institutions (2,3,7,8). Although pediatric surgeons did not work regularly and actively in our institution between whiles in the 11-year period included in our study, surgical operations of most of the cases were performed by pediatric surgeons.

Publications often include limited number of cases due to the rarity of childhood ovarian masses. These publications mostly included patients over 18 years of age (1,3,8,9). However, the international Committee on the Rights of the Child defines the child as an individual under the age of 18 years (10). In our study, the characteristics of ovarian disorders needing surgery were investigated including only the patients under the age of 18 into the study.

The mean age of our patients was 13.4±14.1 years. Although the patients aged 18 and over were not included in our study, the mean age of our patients was greater than in most of the previous studies (1,7,8,11). The mean ages in the investigations performed in obstetrics and gynecology departments are greater than in our study, on the other hand, the mean ages are smaller in studies conducted in pediatric surgery departments (1,2,7-9,11). This may be due to the fact that gynecologists mostly perform surgery on adolescents, and pediatric surgeons operate infants and younger patients. Our results indicated that the gynecologists performed surgery on adolescents at a statistically significantly higher rate in our hospital. Another reason may be that we do not remove simple ovarian cysts in neonates since the risk of malignancy is very small in patients under 1 year of age (1,3). In our study, we did not encounter any malignant ovarian tumors in patients younger than 1 year of age.

Compared to other studies, the prevalence of malignant ovarian masses in patients ≥ 14 years is higher in our study. This is probably due to the fact that germ cell malignancies and sex cord stromal tumors seen in younger ages are less in number in our series compared to other studies, and epithelial tumors are more (1, 2,9,11).

Similar to previous studies, most of the ovarian pathologies in our study were located in the right ovary. It has been argued that the reason for this is that the ovarian masses on the right side had surgery considering acute appendicitis, while those on the left ovary were usually left undiagnosed. In addition, it has been claimed that the left ovary is protected from torsion due to presence of the sigmoid colon, and therefore ovarian torsions mostly occur in the right ovary (5,8,12,13). However, in our study, either histopathology of the mass or the presence of torsion were not significantly correlated with the side of the ovarian mass.

The most frequent presenting symptom of the patients is abdominal pain. Similar to other studies, 71% of the patients in our study presented with abdominal pain (2,3). In our study, the patients with non-neoplastic or benign masses mostly presented with abdominal pain, while the patients with malignant masses presented with symptoms such as abdominal distension, or were diagnosed incidentally.

Although USG is not as reliable and sensitive in children as in adults, it is the preferred imaging modality for ovarian masses in our clinic, as in other clinics (1). Magnetic resonance (MRI) or Computed Tomography (CT) is requested if the mass contains a solid component, suspicion of malignancy or if torsion cannot be distinguished on USG. MRI or CT imaging was available in addition to USG in all of our patients who had surgery due to malignancy. It has been shown in a number of studies that the risk of malignancy increases as the diameter of the mass increases on USG. It has been widely agreed that the risk for malignancy is higher in large masses (8,11,13). In our study, malignant masses had significantly bigger diameters compared to benign masses.

We request tumor markers in our clinic if there is a neoplastic appearance on USG (presence of a solid component, complicated cyst) or if the diameter of the mass is ≥5 cm. However, tumor markers are less specific in the childhood age compared to the adults (1). Tumor markers were high in only 24.7% of our cases. Hembram et al.(8) found high tumor marker levels in 12% of 58 ovarian masses that had surgery, however their sample size was smaller than our study. In a study conducted in China, high tumor marker levels were found in 73% of the malignant ovarian masses and in 20% of the non-tumorous masses (2). Similarly, in our study, high tumor marker levels were found in 77.7% of the malignant masses and in 13.8% of the non-neoplastic masses.

In a meta-analysis covering 44 publications on childhood ovarian masses between 2000 and 2017, 24 publications analyzed laparoscopy. Malignant masses were included in only one of those publications. In that study, only 2 cases with malignant masses had laparoscopic surgery. Time of surgery, amount of bleeding and hospital stay were found to be lower in laparoscopic surgery. However, there are no sufficient data regarding tumor rupture and spillage into the abdomen when malignant masses are operated laparoscopically (14). In our study, only 1 case with a malignant mass had laparoscopic surgery. There was no tumor rupture or spillage during surgery. Although we wanted to prefer laparoscopic surgery in other malignant masses encountered after 2015, open surgery was preferred due to the fact that the masses were over 30 cm in diameter, they did not leave enough working space in the abdomen, and a large incision would be needed to remove the mass without rupturing it (Figure 1). Other studies have also reported that laparoscopy can be performed safely for benign masses, however open surgery is recommended for malignant masses (1.8).

In publications on adult ovarian masses, it has been argued that laparoscopy could be safely performed in malignant masses (15). In our clinic, the malignancy rate is 8.4%, while the rate of laparoscopy is 42.1%. Although the laparoscopy rate is low in our clinic, the significant increase in this rate after 2015 shows that our experience both with laparoscopy and ovarian masses has increased over time. In previous studies, the rate of laparoscopy has also increased over time (1,3).

Approximately 9-30% of ovarian pathologies present with torsion (6,7,9,12). In our study, this rate is 32%, and higher than in other studies. The treatment of torsioned ovary has changed over time from oophorectomy to ovary sparing surgery. Today, oophorectomy is not recommended even if the ovary is necrotic (16,17). A study conducted in the USA in 2015 reported oophorrectomy rate as 78% on 2041 pediatric ovarian torsion cases (16). Similarly, another study from USA in 2020 reported oophorectomy rate as 22.5%. Recently, it has been argued that the rate of oophorectomy has been decreasing in cases with torsion, but this is still not sufficient (17). In our clinic, the rate of oophorectomy in cases with torsion is at an acceptable level with 40.6%, according to these studies. In our clinic, oophorectomy was performed in 4 cases with intrauterine torsion in order to protect the patient from infection with necrotic ovarian tissue, resembling a parchment paper. Apart from this, oophorectomy has been performed mostly in torsioned mature cystic teratomas. Perhaps, the fact that malignancy risk cannot be excluded since a frozen section is not available in cases with ovarian torsion and a solid mass who had surgery at night, and impossibility to dissect the ovary with impaired circulation from the mass, lead us, pediatric surgeons, to oophorectomy. Although the risk of malignancy in a torsioned ovary in childhood is not known exactly, it was found as 1.8% in a study by Oltmann et al. (18). Apart from this, as in our study, malignancy was not found in torsioned ovary pathologies in a number of studies. These show that worrying for malignancy is unfounded. Lately, it has been recommended that the mass or malignancy should be evaluated with postoperative USG after detorsion if it is not possible to dissect the ovarian tissue from the mass during surgery in cases with a mass and torsioned ovary (16-18).

The rate of oophorectomy in operated ovarian masses varies between 18% and 35% when torsion cases are not analyzed separately in studies (2,3,5,8,9). Oophorectomy or salpingo-oophorectomy was performed in 23 (21.4%) of our cases. This rate is similar to the rates in other studies. However, since we performed only 9 operations for malignancy, this indicates that we performed oophorectomy due to the suspicion of malignancy in benign masses or due to ovarian torsion. Although fertility is preserved in unilateral oophorectomy, this surgery is not harmless. Some studies have reported cognitive impairment and predisposition to Parkinson's disease after unilateral oophorectomy (11). Studies have shown that the rate of ovary sparing surgery is gradually increasing (5).

Ovarian tumors constitute 1% of all tumors in the childhood. The probability of malignancy is between 4% and 20% in patients that had surgery due to ovarian masses (5). In our study, 5.6% of the cases had malignant and 2.8% of them had borderline tumors. Similar to our study, the most common tumors in other studies were germ cell tumors and epithelial tumors in rank order, while sex cord stromal tumors were the least frequently encountered tumors (1,2,14). Although germ cell neoplasms are the most frequently encountered tumors in those studies, their risk of malignancy is lower than the epithelial tumors. The possibility of malignancy is higher in epithelial tumors compared to germ cell tumors especially when borderline and malignant tumors are taken together. In our study, the rate of malignancy is not low in epithelial tumors, and has been found as 4/18 (22.22%). However, it has been claimed that epithelial tumors constitute only 2-5% of malignant ovarian masses in childhood, and they are quite rare in children (19,20). When our cases are analyzed in terms of malignant masses, 4/8 (50%) of our cases had epithelial malignant tumors when 2/6 (33%) borderline masses were included.

Childhood epithelial ovarian cancer is more common at the ages of 15-19 years. Data are very limited on childhood ovarian cancers. That is why adult data are used. In children, mucinous ovarian carcinoma or low-grade serous ovarian carcinoma are seen most frequently, and their prognosis is better than in the adults (21). Treatment should include oophorectomy, removal of tumor-bearing tissues, and staging. Fertility preserving surgery is recommended, but conservative treatment should be avoided in bilateral stage 1, stage 2, and stage 3 cases, and bilateral salpingo-oophorectomy and hysterectomy should be performed (1,15,22). Although fertility sparing surgery is preferred in stage 1 cases, surgical treatment should be

completed by performing unilateral salpingo-oophorectomy and hysterectomy after the reproduction period (23).

We performed unilateral salpingo-oophorectomy in 2 cases followed up due to mucinous cystadenocarcinoma and borderline epithelial tumor, and ovary-sparing surgery was performed in a borderline case. However, our case with serous borderline tumor in which we performed unilateral oophorectomy had recurrence, and diagnosed with serous adenocarcinoma. In this case, oophorectomy of the contralateral ovary and hysterectomy were performed.

A council attended by pediatric surgery, obstetrics, and oncology departments was held for all patients with epithelial malignancies to decide their treatments.

Frozen section should be performed in case of a suspicion for malignancy in ovarian masses. If frozen section indicates an epithelial ovarian cancer; abdominal washing, biopsies of peritoneum and omentum, and intraoperative abdominal exploration should be performed. If frozen section is not available, all those mentioned above should be performed in any case (15,24). We performed frozen section and intraoperative abdominal exploration in all of our malignant cases.

Recurrence is seen in one of three cases with epithelial borderline tumors after fertility-sparing surgery. These cases must be followed up with CA125 levels and radiological imaging. The risks of osteoporosis, and cardiovascular and neurological disorders increase after bilateral salpingo-oophorectomy and hysterectomy in malignant tumors. The patients should be followed up for those disorders. It is very difficult to overcome these complications in children compared to postmenopausal women who have completed their fertility. It is oncologically safe to keep the contralateral ovary and uterus only in unilateral stage 1 cases to prevent these complications, and to ensure fertility. In low-grade carcinomas, patients may also benefit from postoperative chemotherapy. Carboplatin and paclitaxel are mostly recommended in these cases. Although 90% of epithelial ovarian cancers are sporadic, 10% are due to genetic mutations. Genetic consultation should be performed in cases with childhood epithelial ovarian cancers (15,24).

The present study has a number of limitations. First, in a retrospective single-center review of medical records, some details of history and physical examinations may not be rigorously documented. Second, small sample size and the exclusion of ovarian masses that were not operated. These limitations may have led to bias in analyzing the clinical spectrum of ovarian masses in children.

CONCLUSION

When faced with an ovarian mass, it should be remembered that a multidisciplinary approach is needed. Except for cases requiring emergency surgery such as torsion, all necessary examinations and radiological imaging should be performed, and the opinions of the relevant departments should be obtained. We should increase the rate of laparoscopic surgery and ovary conserving surgery, which positively affect the quality of life of patients, and avoid oophorectomy, particularly in ovarian torsion. Adult protocols should be used when necessary for rare childhood ovarian tumors, such as epithelial tumors, and large multi-center patient series should be constituted in order to establish pediatric protocols related to the subject.

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Perioperatif Anksiyetenin Giderilmesinde Görsel Bilgilendirme Teknolojisinin Yeri

Relieving Perioperative Anxiety Utilizing Audiovisual Information Techniques

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ÖZ

Amaç: Çocuk hastaların annelerinde gözlemlenen perioperatif kaygı düzeyini azaltmak amacıyla uygulanabilecek görsel bilgilendirme veya dikkat dağıtma teknikleri giderek yaygınlaşmaktadır. Çalışmamızda farklı iki görsel bilgilendirme tekniğinin annelerin perioperatif kaygı düzeyleri üzerine etkisinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Prospektif, çift kör ve tam randomize yöntemle planlanan çalışmamıza, günübirlik cerrahi tedavi uygulanan 79 olgunun annesi dâhil edilmiştir. Annelere yaşanacak süreçteki aşamaları anlatan, canlandırma (Grup C) ve sözlü tanıtım (Grup T) içerikli iki farklı amatör video izlettirilmiştir. Çalışmaya dâhil olan bütün annelere, ameliyat kararının alındığı gün ve ameliyat günü sabahı video seyrettirilmesini takiben, Durumluk – Sürekli Kaygı Ölçeği (STAI - TX) uygulanmıştır. Sonuçlar ANOVA test SPSS 22.0 kullanılarak analiz edilmiştir.

Bulgular: Randomizasyon sonucunda 31 anne video C, 48 anne video T'yi izlemiştir. Annelerin demografik bulguları ve durum kaygı ölçümleri karşılaştırıldığında aralarında istatistiksel anlamlı fark bulunamamıştır (p>0.05). Video izlemi sonrası Grup T'deki annelerin %54.2'si ile Grup C'dekilerin %38.7'sinde durum kaygılarının azaldığı görülmekle birlikte, gruplar arası değişkenler karşılaştırıldığında istatistiksel anlamlı fark bulunamamıştır (p=0.133). Gruplar arasında "durum kaygı yüzdelik değişimi" karşılaştırıldığında, istatistiksel anlamlı fark bulunamamıştır (p=0.240). "Sürekli kaygı yüzdelik değişimi" karşılaştırıldığında ise, iki grup arasında istatistiksel anlamlı fark bulunmuştur (p=0.029). "Sürekli kaygı yüzdelik değişimleri" açısından tanıtım videosunu izleyen çok çocuklu ve hastane yatış deneyimi olan annelerin, canlandırma videosuna göre kaygılarındaki azalma istatistiksel olarak anlamlı bulunmuştur (p=0.022, p=0.028).

Sonuç: Annelerin ölçülen perioperatif istemsiz kaygı düzeylerinde, canlandırma videosu sonrasında artış, tanıtım videosu sonrasında ise azalma olduğu saptanmıştır.

Anahtar Sözcükler: Anksiyete, Bilgilendirme teknikleri, Günübirlik cerrahi

ABSTRACT

Objective: Use of virtual reality is under investigation in reducing perioperative anxiety by means of either distraction or informative procedures. In this study, we observed the outcome of data transfer by means of two different audiovisual content in relieving parental anxiety.

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Yazarların katkısı / Contribution of the Authors*: *GÜVENÇ BH: Araştırma ve/veya makalenin hipotezini veya fikrini oluşturan, Sonuçlara ulaşmak için planlama/metodoloji belirleme, Araştırma/çalışmanın sorumluluğunu üstlenmek, ilerlemenin seyrini denetlemek. ***BİLGİLİ YD:*** Hasta takibinde sorumluluk almak, ilgili biyolojik malzemelerin toplanması, veri yönetimi ve raporlama, deneylerin yürütülmesi, Sonuçların mantıksal olarak Yorumlanması ve sonuçlandırılması. ***ÖZÇINAR ORHAN S:*** Araştırma ve/veya makalenin hipotezini veya fikrini oluşturan, Sonuçlara ulaşmak için planlama/metodoloji belirleme, Sonuçların mantıksal olarak Yorumlanması ve sonuçlandırılması, Çalışma için gerekli literatür taramasında sorumluluk almak. ***KARAASLAN Y:*** Sonuçlara ulaşmak için planlama/metodoloji belirleme, Hasta takibinde sorumluluk almak, ilgili biyolojik malzemelerin toplanması, veri yönetimi ve raporlama, deneylerin yürütülmesi. ***UZUN K:*** Çalışma için gerekli literatür taramasında sorumluluk almak. ***AKMAN N:*** Hasta takibinde sorumluluk almak, ilgili biyolojik malzemelerin toplanması, veri yönetimi ve raporlama, deneylerin yürütülmesi. ***İŞLER Z:*** Çalışma için gerekli literatür taramasında sorumluluk almak. ***DUMAN E:*** Yazım ve dilbilgisi dışında bilimsel olarak gönderilmeden önce makaleyi gözden geçirme. ***GÜVENÇ N:*** Yazım ve dilbilgisi dışında bilimsel olarak gönderilmeden önce makaleyi gözden geçirme. ***TATLI UÇARCI D:*** Sonuçların mantıksal olarak Yorumlanması ve sonuçlandırılması.

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Material and Methods: We recruited 79 mothers in this prospective, double blind, completely randomized trial. They were subject to two informative videos illustrating all events in a day-case surgery. The two peer oriented videos, one concerning animation (Video C) and other with verbal content (Video T), were designed and filmed by our nursing staff. Mothers completed the same State-Trait Anxiety Inventory (STAI - TX) questionnaires, on admission to hospital and on day of surgery after watching the videos following randomization. The results were analyzed using ANOVA test SPSS 22.0.

Results: Thirty one were randomized to Video C and 48 to Video T. Demographic characteristics and state anxiety levels proved statistical insignificance between two groups (p>0.05). State anxiety levels were decreased by 54.2% for Video T and 38.7% for Video C, however, no statistical significance was present between the groups (p=0.133). There were no significant differences according to change of percentage in "state" anxiety between the groups (p=0.240). There was significant difference in change of percentage in "trait" anxiety (p=0.029). There was significant reduction in change of percentage in "trait" anxiety amongst video Group T; with more than two children (p=0.022) and previous hospital experience (p=0.028).

Conclusion: In our study, involuntary anxiety levels were decreased following video experience with verbal content only.

Key Words: Anxiety, Information techniques, Daycase surgery

GİRİŞ

Ameliyat olması gereken çocukların yaş ve kilosunun düşük olması, yatış yapılacak ve anestezi alacak olmaları, ailenin ekonomik yapısı ve son zamanlarda COVİD-19 gibi birçok nedene bağlı olarak ailelerde kaygı, endişe ve korku benzeri duyguların yaşandığı bilinmektedir. Endişe ve kaygı gibi duyguların genellikle iletişim eksikliği ve bilgisizlikten kaynaklandığı gösterilmiştir. Buna bağlı olarak günümüzde, çeşitli perioperatif psikolojik hazırlık metotlarının giderek yaygınlaştığı dikkati çekmektedir. Yapılan literatür incelemesinde, hastalara uygulanan farklı görsel etkileşim yöntemlerinin, kontrol gruplarına göre ameliyat öncesi kaygı düzeyini azaltmakta daha etkin olduğu vurgulanmaktadır (1,2). Uygulanan yöntemlerde, verilen eğitimin özellikle çocuğa odaklandığı, ebeveynlerin ise sürece dolaylı olarak katıldıkları görülmektedir. Ancak ebeveynler tarafından yaşanabilecek perioperatif kaygı ve stresin dolaylı olarak aktarılma olasılığı göz ardı edilemeyecek düzeydedir. Bu nedenle verilecek olan eğitim, yalnızca çocuklar değil ebeveynler açısından da etkili bir yöntem olarak önem taşımaktadır.

Çalışmamızda, günübirlik cerrahi için servisimize başvuran 0 - 6 yaş hastaların annelerinde, iki farklı görsel işitsel bilgilendirme tekniğinin perioperatif kaygı düzeyleri üzerine etkisi araştırılmıştır.

GEREÇ ve YÖNTEMLER

Çalışmamıza Temmuz 2020 – Mart 2021 tarihleri arasında, elektif koşullarda günübirlik inguinal herni, inmemiş testis, hidrosel ve sünnet ameliyatı olmak üzere Çocuk Cerrahisi Kliniği'mize başvuran, 0-6 yaş arası hastalarımızın anneleri dâhil edilmiştir Prospektif, çift kör ve tam randomize olarak yapılan çalışmamıza, tedavi için başvuran ardışık 123 hastadan 79'unun annesi katılmıştır. Çalışmaya dâhil edilen olguların cinsiyet, kardeş sayısı, aile yapısı, ikamet yeri, sağlık güvencesi, hastane deneyimi ve annenin eğitim durumu parametrelerini içeren demografik veriler kaydedilmiştir. Video izlemeyi kabul etmeyen veya izlemeyi yarıda bırakan, okuma yazması olmayan, Türkçe bilmediğinden dolayı iletişim kurulamayan ve ameliyat sonrasında taburculuğu bir sonraki güne devredilen hasta sahibi 44 anne çalışma dışı bırakılmıştır. Çalışma Zonguldak Bülent Ecevit Üniversitesi, İnsan Araştırmaları Etik Kurulu'nun 05.06.2020/797 numaralı karar ile onaylanmıştır.

Kaygı düzeyi ölçümü

Çalışmamızda, Spielberg ve ark. tarafından anlık ve devam eden kaygı düzeylerini ölçmek için geliştirilmiş olan "Durumluk – Sürekli Kaygı Envanteri" (STAI - TX) kullanılmıştır (3). Bu ölçek, Öner N. ve Le Comte A. tarafından Türk toplumuna göre uyarlanmış olup, geçerlik ve güvenilirlik çalışmaları yapılmıştır (4). STAI - TX; durumluk kaygı ve sürekli kaygı alanlarının her birinde 20 ayrı soruyu kapsayan, her bir soruya cevap olarak dört değişenden oluşan, doğrudan (direct) ve tersine dönmüş (reverse) ifadeler içeren likert tipi bir ölçektir. Doğrudan ifadeler, olumsuz duyguları; tersine dönmüş ifadeler ise olumlu duyguları dile getirmektedir. Durumluk kaygı ölçeğinde dört başlıkta toplanan cevap seçenekleri; (1) Hiç, (2) Biraz, (3) Çok ve (4) Tamamıyla şeklinde tanımlanırken, sürekli kaygı ölçeğinde (1) Hemen hiçbir zaman, (2) Bazen, (3) Çok zaman ve (4) Hemen her zaman şeklinde tanımlanmıştır. Durumluk kaygı ölçeğinde tersine dönmüş on (1, 2, 5, 8, 10, 11, 15, 16, 19 ve 20. maddeler), sürekli kaygı ölçeğinde ise tersine dönmüş yedi (21, 26, 27, 30, 33, 36 ve 39. maddeler) ifade vardır. Puanlama sonrasında 20 ile 80 arasında değişkenlik gösteren bir sayı elde edilir. Bu sayının yükselmesi kaygı düzeyinin arttığına işaret etmektedir.

Hazırlanan Amatör video kayıtları

Bir anne ile kızı tarafından dramatize edilmiş ve hastanın kliniğimize başvurusundan taburcu olmasına dek, ameliyat görüntüsü hariç bütün aşamaları içeren, 16 dk. 31sn. sürelik canlandırma (video C) videosu ile aynı sürecin servis hemşirelerimiz tarafından anlatıldığı, 5 dk. 53 sn. süren sözlü tanıtım (video T) videosu, ekibimiz tarafından amatör olarak hazırlanmıştır.

Randomizasyon süreci

Kliniğimizin rutininde elektif olarak cerrahi tedavi planlanan tüm hastalar, planlanan ameliyat gününden bir gün önce tekrar değerlendirilmekte ve ailelerin ameliyat süreci ile ilgili soruları cevaplanmaktadır. Bu başvuru sırasında, çalışmamıza dâhil

edilen annelere STAI-TX formu doldurtulmuştur. Hastaların ve ebeveynlerinin demografik özellikleri (yaş, cinsiyet, kardeş sayısı, aile yapısı, ikamet yeri, hastane deneyimi ve annenin eğitim durumu) yüz yüze görüşme tekniği ile kaydedilmiştir. Çalışmamıza katılan hastalar ameliyat günü planlanan saatte kliniğimize başvurmuştur. Ardından kör araştırmacı tarafından her anneye, üzerinde Grup C ve Grup T yazan ve dörder adet olmak üzere toplamda sekiz kapalı zarftan biri seçtirilerek, çalışmaya katılacak olan annenin hangi gruba dâhil olacağı belirlenmiştir. Rastgele seçilen video anneye izlettirilmiş ve tekrar STAI-TX formu doldurtulmuştur.

İstatistik değerlendirme

Verilerin istatistiksel analizi SPSS Statics Version 22.0 programında yapılmıştır. Veri dağılımı Shapiro-Wilk testi ile belirlenmiştir. Sürekli veriler mean±standart sapma veya median (minimum – maksimum) olarak, kategorik veriler ise frekans ve yüzde olarak ifade edilmiştir. Sürekli veriler iki grup arasında bağımsız örneklem t testi ve Mann-Whitney U testi ile karşılaştırıldı. Kategorik verilerin gruplar arasında karşılaştırılmasında Yates düzeltmeli ki-kare testi, Fisher Exact ki-kare testi ve Pearson ki-kare testi istatistiksel analizleri kullanılmıştır. p<0.05 istatistiksel olarak anlamlı kabul edilmiştir.

BULGULAR

Tam randomizasyon süreci ile 31 anne Grup C'ye, 48 anne Grup T'ye dâhil olmuştur. Demografik özellikler araştırıldığında her iki grubun homojen dağıldığı görülmüştür (p>0.05) (Tablo I).

Tablo I: Demografik Özelliklerin Gruplar Arasında Dağılımı.

Demografik Özellikler	Grup C n (%)	Grup T n (%)	p
Cinsiyet Kız Erkek	 4 (12.9) 27 (87.1)	 6 (12.5) 42 (87.5)	1.000
Çocuk Sayısı Bir İki ve Üzeri	 10 (32.3) 21 (67.7)	 18 (37.5) 30 (62.5)	0.814
Aile Yapısı Çekirdek Geniş	 19 (61.3) 12 (38.7)	 32 (66.7) 16 (33.3)	0.805
İkamet Yeri Kırsal Kent Merkezi	 9 (29.0) 22 (71.0)	 15 (31.3) 33 (68.8)	1.000
Sağlık Güvencesi Var Yok	 30 (96.8) 1 (3.2)	 46 (95.8) 2 (4.2)	1.000
Yatış Sayısı İlk Yatış İki ve Üzeri	 17 (54.8) 14 (45.2)	 25 (52.1) 23 (47.9)	0.993
Anne Eğitim Durumu İlköğretim Lise+Üniversite	 16 (51.6) 15 (48.4)	 26 (54.2) 22 (45.8)	1.000

Ki-kare testi ile karşılaştırma yapılmıştır. p<0.05 anlamlı kabul edilmiştir.

Tablo II: Durumluk – Sürekli Kaygı Ölçümlerinin Gruplar Arasında Dağılımı.

STAI	GRUP C	GRUP T	p
Durumluk			
Video Öncesi	41.0 ± 8.8	43.3 ± 9.1	0.269*
Video Sonrası	42.5 ± 9.1	41.1 ± 9.6	0.492*
Sürekli			
Video Öncesi	40.3 ± 6.2	45.2 ± 8.9	0.005*
Video Sonrası	41.0 (32–58)	40.0 (28–61)	0.845**

*Değerler mean ± standart sapma veya median (min–max) olarak verilmiştir. p<0.05 anlamlı kabul edilmiştir. *Student's t test, **Mann Whitney – U test.*

Tablo III: Durumluk Kaygı Ölçüm Değişiminin Gruplar Arasında Dağılımı

STAI-Durumluk Kaygı Değişimi	Grup C n (%)	Grup T n (%)	Toplam n (%)	p
Artan	14 (45.2)	20 (41.7)	34 (43.0)	
Azalan	12 (38.7)	26 (54.2)	38 (48.1)	0.133
Değişmeyen	5 (16.1)	2 (4.1)	7 (8.9)	
Toplam	31 (100.0)	48 (100.0)	79 (100.0)	

Ki-kare testi ile karşılaştırma yapılmıştır. p<0.05 anlamlı kabul edilmiştir.

Tablo IV: Durumluk – Sürekli Kaygı Ölçüm Yüzdelik Değişiminin Gruplar Arasında Dağılımı.

STAI Yüzdelik Puan Değişimi	Grup C Mean	Grup T Mean	p
Durumluk	%7.7	-%1.7	0.240
Sürekli	%6.9	-%3.9	0.029

Ki-kare testi ile karşılaştırma yapılmıştır. p<0.05 anlamlı kabul edilmiştir.

Annelerin "STAI - Durum kaygı" ön ve son test sonrası aldıkları puanların ortalamaları gruplar arasında karşılaştırıldığında, istatistiksel olarak anlamlı fark bulunamamıştır (p>0.05). Annelerin "STAI - Sürekli kaygı" ön test ortalama puanları iki grup arasında karşılaştırıldığında, istatistiksel olarak anlamlı fark vardır (p=0.005). Grup T'nin "STAI - Sürekli kaygı" ön test ortalama puanı, Grup C'ninkinden yüksektir (45.2±8.9 vs 40.3± 6.2). Annelerin "STAI - Sürekli kaygı" son test ortalama puanları iki grup arasında karşılaştırıldığında ise istatistiksel olarak anlamlı fark bulunamamıştır (p>0.05) (Tablo II).

Çalışmamızda Grup C'ye dâhil olan annelerin 14'ünün (%45.2) kaygı puanlarının arttığı, Grup T'ye dâhil olan annelerin 26'sının (%54.2) ise azaldığı görülmüştür. Durum kaygı değişim dağılımı incelendiğinde iki grup arasında istatistiksel olarak anlamlı fark bulunamamıştır (p=0.133) (Tablo III).

Gruplar arasında yüzdelik değişim incelendiğinde; "STAI - Durum kaygı" puanlarının Grup C'deki annelerde video sonrasında (%7.7) arttığı, Grup T'deki annelerde ise (%1.7) azaldığı görülmüştür. Ancak gruplar karşılaştırıldığında aralarında istatistiksel olarak anlamlı fark bulunamamıştır (p=0.240). "STAI - Sürekli kaygı" puanlarının

Tablo IV: Durumluk – Sürekli Kaygı Ölçüm Yüzdelik Değişiminin Demografik Farklılıklara Göre Gruplar Arasında Dağılımı.

Demografik Özelliklerin Yüzdelik Puan Değişimleri	Grup C	Grup T	p
Erkek Çocuk Anneleri			
Durumluk	0.0 (-40 – 104.1)	-9.1 (-56.5 – 104.4)	0.344**
Sürekli	0.0 (-22.6 – 53.1)	-6.1 (-52.2 – 70)	0.097**
Tek Çocuklu Anneler			
Durumluk	-2.9 (-17.2 – 100)	-8.9 (-44.7 – 59.4)	0.555**
Sürekli	2 (-11 – 12)	3 (-14 – 35)	0.555**
Çok Çocuklu Anneler			
Durumluk	8.4 ± 33.2	-1.1 ±31.4	0.304*
Sürekli	7.7 (-21.2 – 53.1)	-4.9 (-40 – 70)	0.022**
Çekirdek Aile			
Durumluk	8.9 (-28.3 – 104.4)	-3.8 (-52.2 – 70)	0.185**
Sürekli	0.0 (-22.6 – 53.1)	-17.7 (-33.3 – 57.1)	0.982**
Geniş Aile			
Durumluk	0.0 (-40 – 36.4)	-17.7 (-33.3 – 57.1)	0.982**
Sürekli	8.0 ± 20.2	-4.6 ± 16.4	0.079*
Kırsal Bölge			
Durumluk	0.0 (-40 – 104.4)	-17.1 (-33.3 – 57.1)	0.953**
Sürekli	6.7 (-15.4 – 53.1)	0.0 (-33.3 – 19.6)	0.155**
Merkez			
Durumluk	0.0 (-28.3 – 100)	-4.3 (-56.5 – 59.4)	0.260**
Sürekli	6.4 ± 20.8	-3.1 ± 25.6	0.152*
Sağlık Güvencesi Olanlar			
Durumluk	0.0 (-40 – 100)	-6.4 (-56.5 – 59.4)	0.302**
Sürekli	5.3 ± 19.2	-3.7 ± 22.9	0.078*
İlk Yatış Sayisi			
Durumluk	9.1 (-28.3 – 104.4)	-6.3 (-56.5 – 57.1)	0.115**
Sürekli	7.5 ± 22.4	-1.3 ± 26.2	0.260*
İki ve Üzeri Yatış Sayısı			
Durumluk	-3.5 ± 21.8	-1.6 ± 29.8	0.837*
Sürekli	4.0 (-21.2 – 44.1)	-8.3 (-33.3 – 35.9)	0.028**
İlköğretim Mezunu			
Durumluk	4.4 (-40 – 36.4)	-13.5 (-56.5 – 59.4)	0.756**
Sürekli	9.7 ± 17.5	-1.2 ± 23.9	0.123*
Lise+Üniversite Mezunu			
Durumluk	0.0 (-27 – 104.3)	-2.1 (-44.7 – 41.5)	0.304**
Sürekli	-5 (-21.2 – 53.1)	-8.3 (-40 – 38.1)	0.213**

*Değerler mean ± standart sapma veya median (min–max) olarak verilmiştir. p<0.05 anlamlı kabul edilmiştir. *****Student's t test, ******Mann Whitney – U test*

yüzdelik değişimi incelendiğinde ise Grup C'deki annelerin kaygı puanlarının (%6.9) arttığı, Grup T'deki annelerin ise (%3.9) azaldığı görülmüştür. Bu iki grup arasında karşılaştırma yapıldığında, istatistiksel olarak anlamlı fark bulunmuştur (p=0.029) (Tablo IV).

Çalışmamızdaki iki grubun demografik parametrelerine göre "STAI - Durum kaygı" ve "STAI - Sürekli kaygı" yüzdelik değişimleri Tablo V'te incelenmiştir. Grup T'deki annelerin video sonrasında durum kaygılarının her parametrede azaldığı görülmüştür. Çok çocuklu ve hastane yatış deneyimi olan annelerin "STAI - Sürekli kaygı" yüzdelik değişimleri iki grup arasında karşılaştırıldığında, istatistiksel anlamlı fark bulunmuştur (p=0.022, p=0.028). Diğer parametrelerde iki grup arasında istatistiksel olarak anlamlı fark bulunamamıştır (p>0.05) (Tablo V).

TARTIŞMA

Ameliyata hazırlık aşaması çocuk hastalar ve aileleri için travmatik kabul edilebilecek bir süreçtir (5). Aileler bu süreçte korku, endişe, kızgınlık ve panik gibi duyguları yoğun bir şekilde yaşarlar (5). Ebeveynler açısından, çocuklarının ameliyat olmasının gerekliliği en ağır hissedilen endişe ve stres kaynağı olarak ön plana çıkmaktadır. İçselleştirilmiş olan bu kaygı durumunun cerrahi girişim, anestezi ve ameliyat sonrası iyileşme dönemini olumsuz yönde etkilediği bildirilmiştir (6). Weis ve ark. (7) preoperatif dönemde görsel slaytlar kullanarak yaptıkları bilgilendirme sonrasında, hastaların postoperatif dönemde analjezik tedaviye daha az ihtiyaç duyduklarını ve daha hızlı iyileştiklerini göstermişlerdir. Çeber M. (8) ve Cimilli C. (9) preoperatif dönemde kaygı düzeyi yüksek olan hastalarda postoperatif dönemde, tıbbi komplikasyon gelişme

oranının daha yüksek olduğunu ve hastane yatış süresinin uzadığını göstermişlerdir. Uluslararası literatürde çocuk hastalar ve ebeveynlerinde, perioperatif kaygı düzeylerinin azaltılmasına yönelik birçok çalışma yayınlanmıştır. Bu çalışmalarda hastalara yönelik dikkat dağıtma, el kitapçığı verme, müzik dinletme, oyun oynatma, bilgilendirme ve farmakolojik yöntemler uygulanması gibi değişik metotların denendiği görülmektedir (1,10,11).

Literatürde kullanılan ameliyat öncesi bilgilendirme videolarının kontrol grupları ile karşılaştırıldığında kaygı düzeyini azaltmakta etkili oldukları bildirilmektedir (1,12,13). Hatipoğlu ve ark. (2) çalışmasında, görsel ve işitsel teknikler kullanılarak hazırlanan farklı bilgilendirme metotlarından görsel videonun, çocukların kaygı düzeyleri üzerinde daha etkin olduğu bildirilmiştir. Batuman ve ark. (14) çalışmasında, anestezi polikliniğine gelen hasta ve ailesine, doktorun yapılacak girişimleri oyuncak ayı üzerinden uygulayarak anlattığı canlandırma videosunda, anestezi süreci tanıtılmıştır. Benzer bir süreç Meletti ve ark. (15) tarafından hikayeleştirilerek çocuk kitabı haline getirilmiştir. Sonuçlar değerlendirildiğinde annelerin kolaylıkla empati kurabileceği düşünülerek hazırlanan, hasta rolü yapan bir kız ve annesinin görüntülendiği canlandırma videosunun tanıtım videosu kadar etkili olmadığı görülmüştür. Bu durum, perioperatif sürecin görsel olarak detaylandırılmasının, ön görülenin aksine annelerde kaygıyı arttırabileceğini göstermiştir. Hemşirenin tanıtım yaptığı videonun anneler tarafından akran rol model olarak algılanmasının sonucu etkilediği düşünülmektedir. Literatürde, görsel teknikler kullanılarak hazırlanan video sürelerinin 5-22 dakika arasında değiştiği bildirilmektedir (16). Bizim videolarımız bu süre aralığında olmakla beraber, canlandırma videosu tanıtım videosundan daha uzun sürmektedir. Ameliyat stresi yaşayan annelerin konsantrasyonlarının olumsuz etkilenebileceği öngörüldüğünde, bu farkın video süresinden de kaynaklanabileceği düşünülebilinir.

Yayınlanmış olan çalışmalarda diş hastalıkları, kulak burun boğaz, göz, çocuk cerrahisi ve plastik cerrahi alanında yapılan girişimlerin cinsiyet dağılımı açısından homojen olduğu görülmektedir (17-19). Jin Y. ve ark. (17) strabismus hastalarını içeren çalışmaları ile Hua Y. ve ark. (18) alt ekstremite yarası olan olguları içeren çalışmalarında, kız erkek oranlarının birbirine yakın olduğu bildirilmektedir. Berghmans J. ve ark. (20) ile Karabulut N. ve Arıkan D.'nin (13) çalışmaları örneğinde olduğu gibi, erkek ağırlıklı olgulardan oluşan çalışmalar da mevcuttur. Çalışmamızda ameliyat olan çocukların %12.7'sini kız, %87.3'ünü erkekler oluşturmaktadır. Çalışmaya dâhil olan hastalarımızın sünnet ve inguinal patoloji (inmemiş testis, hidrosel ve inguinal herni) ağırlıklı oluşu bu farklılığı açıklamaktadır. Literatürde de belirtildiği gibi, inguinal herni erkeklerde kızlara göre 5-10 kat daha fazla görülmektedir (13,21). Çalışmamızda kız çocuğu sahibi olan ve sağlık güvencesi olmayan annelerin, gruplara göre dağılımında beş kişiden az olgu içermeleri nedeniyle istatistiki karşılaştırma yapılamamıştır.

Farklı toplumlarda ölçülen kaygı düzeyleri, çeşitli nedenlere bağlı olarak değişebilmektedir. STAI-TX test sonuçları göz önüne alındığında, İngiltere ve Amerika Birleşik Devletleri'ndeki ebeveynlerde, çalışmamızda yer alan annelere göre daha düşük kaygı puanları bildirilmektedir (1,22). Buna karşılık Kanada ve ülkemizdeki ebeveynlerde, benzer kaygı puanları bildirildiği görülmektedir (11,23). İtalya'da yapılan bir çalışmada ebeveynlerin kaygı puanları oldukça yüksek bulunmuştur (24). Ebeveynlerin çocuğa yansıtabilecekleri olumsuz duyguların en aza indirgenmesi amaçlanarak verilecek eğitimin, yaşanılan yere ve sosyokültürel düzeye göre etkinliğinin değişebileceği öngörülmektedir. Çalışmamızda, tanıtım videosu ile daha etkin sonuç alınmasının, toplumumuzun sosyokültürel alışkanlıklarından kaynaklandığını düşünmekteyiz.

Tam randomizasyon sonrası annelerin gruplara homojen şekilde dağılmış ve çift kör olarak tamamlanmış olması çalışmamızın güvenilirliğini arttırmıştır. Sosyokültürel farklılıklardan bağımsız olarak sözlü tanıtım yöntemi ile bilgilendirme yapılması, annelerin durum kaygılarını perioperatif dönemde azaltmıştır. Annelerde perioperatif dönemde oluşabilecek istemsiz kaygının, canlandırma yöntemi ile yapılan bilgilendirme sonucu artabileceği, buna karşılık tanıtım yöntemi ile azalabileceği görülmüştür. Hekim meslektaşlarımızın hizmet verdikleri bölgelerde, sosyokültürel farklılıklara yönelik özelliklere dikkat ederek, perioperatif dönemde oluşabilecek kaygıyı azaltmakta kullanılabilecek en etkili yöntemi saptamaları önem taşımaktadır.

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Surgical Approach to Childhood Breast Masses

Çocukluk Çağı Meme Kitlelerine Cerrahi Yaklaşım

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ABSTRACT

Objective: We aimed to investigate the epidemiological and characteristic features of patients treated for breast masses in our clinic and share our experiences.

Material and Methods: Patient records were reviewed retrospectively. Demographic and clinical data were investigated. The patients were divided into those who were operated on at the first admission (group 1) and those who were operated on after the follow-up (group 2) and compared. The statistical analysis evaluated with SPSS version 21. $p<0.05$ was considered significant.

Results: Forty-eight patients who were operated on for breast mass in 10 years were included in the study. There was no difference between the groups regarding mean age and complaints at presentation (p=0.723, P=0.555, respectively). Ultrasound was performed on all patients. It was observed that the masses were located more frequently in the right breast in Group 1 (58.3%) and the left breast in Group 2 (p=0.386). In addition, it was noticed that the masses were most frequently located in the upper lateral quadrant of the breast in both groups (62.5% and 70.89%, respectively). The longest diameters of the masses were longer in group 1 than in group 2 (51.79±11.11 mm and 35.16±3.74 mm, respectively, $p<0.001$). Radiologically, most of the masses were reported as Breast Imaging Reporting and Data System (BI-RADS 3) in both groups (41.7% and 54.2%, respectively, p=0.444). Fine-needle aspiration biopsy (FNAB) was performed on nine patients in Group 1 and one in Group 2 (p=0.004). According to the FNAB reports, phyllodes tumors were detected in two patients, while the others were reported as fibroadenoma. The most common fibroadenomas were detected in the histopathological evaluations after surgical excision. In addition, a premalignant breast mass was detected in 6.2% of all patients.

Conclusion: We recommend surgical excision in children with large, rapidly growing breast masses or suspected phyllodes tumors.

Key Words: Breast masses, Child, Fibroadenoma, Phyllodes tumor

ÖZ

Amaç: Kliniğimizde meme kitleleri nedeniyle tedavi edilen hastaların epidemiyolojik ve karakteristik özelliklerini araştırmayı ve deneyimlerimizi paylaşmayı amaçladık.

0000-0003-0286-362X : ERTURK A
0000-0003-4720-912X : DEMIR S
0000-0002-5408-2772 : OZTORUN CI
0000-0002-3666-295X : ERTEN EE
0000-0002-7512-3895 : BOSTANCI SA
0000-0001-7168-2123 : GUNEY D
0000-0002-5137-7209 : AZILI MN
0000-0002-0383-4559 : SENEL E

Conflict of Interest / *Çıkar Çatışması*: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Ankara City Hospital, No. 2 Clinical Research Ethics Committee (Date/No: 10.11.2021/ E2-21-1011).

Contribution of the Authors / Yazarların katkısı*: *ERTURK A : Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***DEMIR S:*** Constructing the hypothesis or idea of research and/or article, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study. ***OZTORUN CI*** : Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in necessary literature review for the study. ***ERTEN EE:*** Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in necessary literature review for the study, ***BOSTANCI SA:*** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in the writing of the whole or important parts of the study. ***GUNEY D:*** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments. ***AZILI MN:*** Taking responsibility in logical interpretation and conclusion of the results, SENEL E : Constructing the hypothesis or idea of research and/or article, Taking responsibility in logical interpretation and conclusion of the results.

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Gereç ve Yöntemler: Hasta kayıtları geriye dönük olarak incelendi. Demografik ve klinik veriler araştırıldı. Hastalar ilk başvuruda ameliyat edilenler (Grup 1) ve takip sonrası ameliyat edilenler (Grup 2) olarak ayrılarak karşılaştırıldı. İstatistiksel analiz SPSS 21 sürümü ile değerlendirildi. p<0.05 anlamlı kabul edildi.

Bulgular: Çalışmaya 10 yılda meme kitlesi nedeniyle ameliyat edilen 48 hasta dahil edildi. Ortalama yaş ve başvuru şikayetleri açısından gruplar arasında fark yoktu (sırasıyla p=0.723, p=0.555). Tüm hastalara ultrason yapıldı. Kitlelerin, Grup 1'de sağ memede (%58.3), Grup 2'de sol memede (p=0.386) daha sık yerleşim gösterdiği gözlendi. Ayrıca her iki grupta da kitlelerin en sık meme üst lateral kadranda yerleştiği görüldü (sırasıyla %62.5 ve %70.89). Kitlelerin uzun çapları grup 1'de grup 2'ye göre daha uzundu (sırasıyla 51.79±11.11 mm ve 35.16±3.74 mm, p<0.001). Radyolojik olarak her iki grupta da kitlelerin çoğu Breast Imaging Reporting and Data System (BI-RADS 3) olarak raporlandı (sırasıyla %41.7 ve %54.2, p=0.444). Grup 1'deki 9, Grup 2'deki 1 hastaya ince iğne aspirasyon biyopsisi (İİAB) yapıldı (p=0.004). İİAB 'de iki hastada filloid tümör saptanırken, diğerleri fibroadenom olarak rapor edildi. Cerrahi eksizyon sonrası histopatolojik değerlendirmelerde en sık fibroadenom tespit edildi. Ayrıca tüm hastaların %6.2'sinde premalign meme kitlesi saptandı.

Sonuç: Çocuklarda, büyük boyutta, hızlı büyüyen veya filloid tümör şüphesi olan meme kitlelerinde cerrahi eksizyon öneriyoruz.

Anahtar Sözcükler: Meme kitlesi, Çocuk, Fibroadenom, Filloid Tümör

INTRODUCTION

Although the incidence of breast masses is low in children, it is a significant cause of admittance to pediatric surgery in adolescent girls (1). Commonly, the patients admit after they notice the mass on their own. These masses constitute a wide spectrum of anomalies between inflammatory and tumoral conditions (2).

Most of the masses in children and adolescents are benign and almost all are fibroadenomas. Fibroadenomas are the most common breast conditions in adolescents which grow slowly and tend to regress with increasing age. They commonly appear as 2-3 cm, non-tender mobile masses. They can demonstrate relatively rapid enlargement in adolescents and pregnant individuals as they are responsive to estrogen (3). The incidence among adolescents and young adults is around 2.2% (4). Furthermore, fibroadenomas are the most common breast masses that undergo surgical intervention or biopsy (5).

Although the most common type is called as 'classical type', giant fibroadenomas can also be encountered in adolescents. A fibroadenoma larger than 5-10 cm is usually called as 'giant fibroadenoma'(2). Another breast tumor in children is the phyllodes tumor which is a fibroepithelial tumor that constitutes less than 1% of the breast masses of adolescents (6).

Several algorithms are developed for the management of breast masses in adults but, no standardized pathway exists for the evaluation, management and follow-up of such masses in children. The lack of an algorithm causes diverse clinical practices by different physicians. Therefore, we aimed to share our experience with the breast masses in children.

MATERIALS and METHODS

The study is designated as a retrospective review of the patient charts. The study was approved by Ankara City Hospital, No. 2 Clinical Research Ethics Committee (Date/No: 10.11.2021/ E2-21-1011). The patients younger than 18 years old who underwent a surgical procedure for a breast mass between 2011 and 2021 are enrolled in the study.

Data regarding the patients' age, admitting complaint, family history of breast mass, location of the mass defined by ultrasonography (US), longest diameter of the mass, Breast Imaging Reporting and Data System (BI-RADS) classification, preoperative biopsy, follow up duration, histological results, length of hospital stay, complications, recurrence and mortality were evaluated. Patients were divided into 2 groups; the patients who were operated on at the first admittance were enrolled in Group 1 and the patients who were operated after the follow-up visits were enrolled in Group 2. The demographics, clinical findings and results were evaluated and compared between the groups.

The masses smaller than 3 cm in diameter and that remained stable or shrank during follow-up were not operated and were excluded from the study. Surgical excision was offered at the admittance in patients who had a mass larger than 4 cm (Group 1). The masses between 3 to 4 cm were followed up regularly. During follow-up, surgery was offered if the mass did not shrink after 3 menstrual cycles, enlarged or demonstrated findings suggestive of malignancy on ultrasonography (Group 2).

Statistical analyses were performed by the Statistical Package for Social Sciences (SPSS) software version 21 (SPSS Inc, Chicago, IL, USA). Numerical variables were expressed as mean (±SD) and categorical variables were expressed as (%). Descriptive analyses for numerical variables were performed with the Mann Whitney U test as they were not distributed normally. Comparative analyses of the categorical variables were performed with Pearson's Chi-Square and Fisher's Exact test. A p<0.005 value was considered statistically significant.

RESULTS

The girls who had undergone surgical intervention for breast masses are included in the study (n=48). The mean age of the patients was 15.59±1.52 years in Group 1 and 15.56±1.18 years in Group 2. Both groups were compared in terms of

Table I: Comparison of demographic and clinical data of the groups.

	Group 1	Group 2	p
Age(Years),*	15.59±1.52	15.56±1.18	0.723†
Admittion complaints, n (%)			
Palpable mass	23 (95.8)	22 (91.7)	0.555‡
Mastodynia	1 (4.2)	2 (8.3)	
Follow up duration (month),*	-	3.87±1.65	N/A)
Lenght of stay at hospital (days),*	1.79±0.50	1.45±0.58	0.310 †

** Mean±SD, †Mann-Whitney U test used, ‡Pearson Chi-Square test used*

Table II: Comparison of US findings.

	Group 1	Group 2	p
Longest diameter of the mass (cm),*	51.79±11.11	35.16±3.74	<0.001
Side,†			
Right	14 (58.3)	11 (45.8)	0.386‡
Left	10 (41.7)	13 (54.2)	
Location of the mass,†			
Upper lateral	15 (62.5)	17 (70.8)	
Upper medial	4 (16.7)	-	0.207‖
Lower lateral	4 (16.7)	6 (25)	
Lower medial	1 (4.2)	1 (4.2)	
BI-RADS,†			
BI-RADS-3	10 (41.7)	13 (54.2)	0.444§
BI-RADS-4	5 (20.8)	6 (25)	
Not evaluated	9 (37.5)	5 (20.8)	

**Mean±SD, †n (%), ‡Mann-Whitney U test used, §Pearson Chi-Square test used, ‖Fischer exact test used*

age distribution (p=0.723). The most common complaint in admission was palpable breast mass and both groups were comparable in terms of admission complaints (p=0.555) (Table I). One patient had a family history of breast cancer (her aunt).

All patients underwent US examination at the initial admission. One patient with a mass resembling a phyllodes tumor on US underwent magnetic resonance imaging (MRI). No mammography was performed in any of the cases. No difference was found between the groups in terms of laterality of the lesions as the right breast was involved in 58.3% of patients in Group 1 and 45.8% in Group 2 (p=0.386). The most common involved area was the upper lateral quadrant in both groups (62.5% vs. 70.8% in Groups 1 and 2, respectively). The mean of the longest diameter of the masses measured by the US was significantly higher in Group 1 (51.79±11.11 mm in Group 1 and 35.16±3.74 in Group 2, p<0.001) (Table II).

Most of the masses in Group 1 and Group 2 were found as BI-RADS 3 stage according to the BI-RADS classification on US (41.7% and 54.2%, respectively).Five patients in Group 1 and 6 patients in Group 2 had BI-RADS-4 masses. No significant difference was observed between the groups in terms of BI-RADS stages (p=0.444) (Table II).

Table III: Comparison of histological findings

	Group 1	Group 2	p
Preoperative biopsy (FNAB), n (%)			
Yes	9 (37.5)	1 (4.2)	0.004
No	15 (62.5)	23 (95.8)	
Histological diagnosis, n (%) *			
Fibroadenoma	21 (87.5)	21 (87.5)	
Phyllodes tumor	2 (8.3)	-	
Fibrocystic changes	1 (4.2)	1 (4.2)	0.609†
Tubuler adenoma	-	1 (4.2)	
Juvenile papillomatosis	-	1 (4.2)	

Cells with a value of zero were combined with the closest group for statistical analysis, †Fischer exact test used, **FNAB: Fine needle aspiration biopsy.*

Nine patients in Group 1 and 1 patient in Group 2 underwent FNAB. A significantly higher rate of patients received FNAB in Group 1 (p=0.004). FNAB results were inconclusive for phyllodes tumor in 2 patients (both in Group 1) but all others were compatible with fibroadenomas. The histopathological examination results of the masses of these patients after total excision were compatible with Phyllodes tumor and the surgical margin was negative (Table III).

Fibroadenoma was the most common histological diagnosis (Table III). Two patients in Group 1 had phyllodes tumor and 1 patient in Group 2 had juvenile papillomatosis which was considered as premalignant lesions (6.2%). The length of hospital stay was not different between the groups (p=0.31) (Table I). No complication, recurrence or mortality was observed in any of the patients.

DISCUSSION

Breast masses are challenging conditions in pediatric surgery practice as they are significantly rare but potentially may demonstrate malignant transformation later in life. The main cause of the challenge is the lack of systematic guidelines (7). Due to limited studies and sparsity of the conditions in children, no consensus exists regarding the optimal management in children. Immediate removal or follow-up of the existing mass is an important decision for the surgeon.

Breast masses are common sources of anxiety for the parents and the patients. Together with this anxiety, the management process becomes more complicated when limited personal experience of the attending physicians (radiologist, surgeon) are not compatible. In fact, there are studies suggesting that the most common indication for surgery is the anxiety of the patient and the parents (8).

US is commonly considered as a reliable diagnostic tool for breast masses in children. Rarely computerized tomography (CT) or MRI may be needed to evaluate the extent of the lesions. In children, mammography has almost no role in the evaluation of the breast masses (2, 9). Accordingly, we did not perform any

mammography in any of our patients. In accordance with the current literature, the most common site of the masses was the upper lateral quadrant in our study, too (10, 11).

BI-RADS classification is the most common tool for the evaluation of breast masses in adults and is preferred by most radiologists. However, there are studies that conclude that it is not a reliable tool for the evaluation of breast masses in children (1,8,12). Our results also support this conclusion as all masses with possible malign appearance according to BI-RADS classification in our study were finally diagnosed as fibroadenomas.

Another controversial issue in the management of breast masses in children is the indication of the FNAB. Some authors recommend FNAB for masses ≥3 cm diameter (13,14). On the other hand, some argue that the reliability of FNAB in the differential diagnosis of fibroadenoma/phyllodes tumor is limited and that normal breast tissue can be injured during FNAB attempts (7,15). The most commonly accepted indication for a biopsy is to determine the extent of the surgical resection in patients with presumed phyllodes tumor (7). We also preferred FNAB to decide the extent of the surgical resection in patients with presumed phyllodes tumor.

Although there are studies evaluating the relationship between the dimensions of the masses and the necessity for surgical intervention in children, there is no consensus or guidelines for the optimal management process. Some favor expectant management in masses smaller than 5 cm as most of them are benign (2,14,16). On the other hand, some predict an increased risk for phyllodes tumor in masses 3 cm or over, and recommend surgical removal (1,17-19). Our results are also similar as all patients (n=2) with a final diagnosis of phyllodes were in Group 1.

The most common breast mass confirmed histologically after surgical removal in children was fibroadenoma (1,17). Although most of the breast masses in children were benign, an unignorable 6.2% were malign or premalignant.

CONCLUSION

Surgical excision is recommended in children with a breast mass larger than 4 cm at the initial admission, rapid increase in diameter on follow-up, or when differentiation between phyllodes tumor and fibroadenoma is not possible by US. Additionally, preoperative FNAB can be helpful to decide the extent of the surgery.

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Evaluation of Children with Congenital Lung Malformations Who Were Diagnosed in The Prenatal and Postnatal Period

Prenatal ve Postnatal Dönemde Tanı Alan Konjenital Akciğer Malformasyonu Olan Çocukların Değerlendirilmesi

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ABSTRACT

Objective: We aimed to compare clinical features of children with congenital lung malformations (CLM) who were diagnosed in prenatal and postnatal period.

Material and Methods: Children with CLM followed in our pediatric pulmonology department between 2007-2021 were evaluated in terms of sex, age, complaints at presentation, time of onset of symptoms, age at diagnosis, diagnostic methods, gestational ages, birth weights, parental consanguinity, presence of any operations, age and indications of operations and long-term complications. Children who were diagnosed in prenatal period and those in postnatal period were compared in terms of their clinical features.

Results: The mean age of 37 children with CLM was 6.7±5.8 years, and seventeen (45.9%) of the children were girls. Children who were diagnosed during the prenatal period (n:18) had no complaints, whereas cough and recurrent pneumonia were the most common reasons at admission in others. Median age at diagnosis of children who were postnatally diagnosed (n:19) was 30 days (10-1080). Eighteen (48.6%) children were diagnosed by prenatal ultrasonography, 14 (37.8%) by computed tomography, and five (13.6%) by chest x-ray. During follow-up, malformations of two children regressed spontaneously. Twelve children were operated while others were followed up with their anomalies. Asymptomatic follow-up duration of children who were prenatally diagnosed was significantly different than the children who were diagnosed in the postnatal period (36.5±4.7 vs 24.0±12.7 months) (p:0.004).

Conclusion: Children with CLM who were diagnosed in the prenatal period were found to remain asymptomatic for longer. Prenatal diagnosis enables them to live longer without symptoms with appropriate surgical timing.

Key Words: Child, Respiratory System Abnormalities, Prenatal diagnosis

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ÖZ

Amaç: Çalışmamızda prenatal ve postnatal dönemde tanı alan konjenital akciğer malformasyonu olan hastaların klinik özelliklerini karşılaştırmayı amaçladık.

Gereç ve Yöntemler: 2007-2021 yılları arasında Çocuk Göğüs Hastalıkları Bölümü'nde izlenen konjenital akciğer malformasyonu olan hastalar cinsiyetleri, yaşları, başvuru yakınmaları, ilk semptom zamanı, tanı yaşları, tanı yöntemleri, doğum haftaları, doğum ağırlıkları, ebeveyn akrabalığı, operasyon varlığı, operasyon yaşı ve endikasyonları, uzun dönem komplikasyonları açısından değerlendirildi. Prenatal dönemde tanı alan hastalar ile postnatal dönemde tanı alanlar klinik özellikleri açısından karşılaştırıldı.

Bulgular: Konjenital akciğer malformasyonu nedeniyle izlenen 37 hastanın ortalama yaşları 6.7±5.8 yıldı ve 17'si (%45.9) kızdı. Prenatal dönemde tanı alan hastalar (n:18) yakınması olmadan başvururken diğer hastaların en sık başvuru nedenleri öksürük ve tekrarlayan akciğer enfeksiyonuydu. Postnatal dönemde tanı alan hastaların (n:19) ortanca tanı yaşları 30 (en küçük:10; en büyük:1080) gündü. Hastaların 18'i (%48.6) prenatal ultrasonografi, 14'ü (%37.8) bilgisayarlı tomografi, beşi (%13.6) akciğer grafisi ile tanı aldı. İzlemde iki hastanın malformasyonu kendiliğinden geriledi. Oniki hasta opere olurken diğer hastalar mevcut anomalileri ile takip edilmektedir. Prenatal dönemde tanı alan hastaların asemptomatik izlem süresi, postnatal tanı alan hastalardan istatistiksel olarak anlamlı farklıydı (36.5±4.7 ve 24.0±12.7 ay) (p:0.004).

Sonuç: Çalışmamızda prenatal dönemde tanı alan konjenital akciğer malformasyonu olan hastaların daha uzun süre semptomsuz seyrettiği görülmüştür. Prenatal tanı uygun cerrahi zamanlama ile daha uzun süre semptomsuz yaşamalarını sağlamaktadır.

Anahtar Sözcükler: Çocuk, Konjenital akciğer malformasyonu, Prenatal tanı

INTRODUCTION

Congenital malformations of the lung constitute a heterogeneous, rare disease group that include numerous differences in parenchyma, airway, arterial and venous structures resulting from abnormalities during embryological development, and also have many common features (1). Congenital lung malformations are divided into four main groups as congenital pulmonary airway malformation (CPAM), congenital lobar emphysema (CLE), pulmonary sequestration (PS) and bronchogenic cyst, and the prevalence is estimated to be 4 in 10,000 live births. (2).

Many cases can be diagnosed with congenital lung malformations in the intrauterine period by prenatal ultrasonography. Congenital lung malformations can be diagnosed with respiratory distress in the postnatal period or can be detected incidentally in asymptomatic children (3). Computed tomography (CT), which is the gold standard diagnostic method in the postnatal period, is recommended for patients before the operation (4-6). The treatment of children with symptomatic congenital lung malformations is surgical resection. Management of asymptomatic children is controversial. Uncertainty remains about the elective surgical resection of lesions diagnosed in the prenatal period to prevent complications (mainly infection and malignancy), as well as the timing of surgery, and whether resection is necessary for lesions that regress during pregnancy (7).

Accurate diagnosis of congenital lung malformations in the prenatal period enables the prediction of complications such as respiratory distress, recurrent pneumonia, mass effect in the mediastinum, pneumothorax, high-output heart failure and malignancy, and a safe surgical planning (8). In this study, we aimed to evaluate of children with congenital lung malformation, detect of long-term complications and compare the clinical features of patients with congenital lung malformations who were diagnosed in the pre and postnatal period.

MATERIAL and METHODS

All children followed up with congenital lung malformations in the pediatric pulmonology department between 2007 and 2021 were reviewed. The study was conducted in accordance with the principles of the Declaration of Helsinki 2008 and with the approval of Gazi University ethics committee (08.06.2020-372). This study was a retrospective descriptive study. Since the study was conducted retrospectively, patient consent was not obtained.

Children's diagnosis, sex, gestational age, birth weight, place of birth, parental consanguinity, complaints at admission, age at diagnosis, diagnosis in the pre/postnatal period, diagnostic methods, presence of operation, age and indications of operation, duration of hospitalization after operation, accompanying diseases, follow-up duration, asymptomatic follow-up duration were recorded. Preoperative weight, height, body mass index (BMI), z-scores of weight, height and BMI, post-operative and long-term complications of the operated children were also recorded. Children's current age, weight, height, BMI, z-scores of weight, height and BMI of all patients at the last control, number of pneumonia, chest x-ray findings, the percentages of FEV_1 (forced expiratory volume in the 1st second), FVC (forced vital capacity), FEV_1/FVC and FEF_{25-75} (25-75% of forced expiratory flow) in pulmonary function tests (PFT) of patients who complied were recorded. The PFTs were performed according to the American Thoracic Society-European Respiratory Society ATS-ERS guidelines (9). Growth was assessed by weight and height z-scores in children under two years of age, and BMI z-scores in children over two years of age, as recommended by the World Health Organization. A z-score of <-2 Standard Deviation (SD) was considered as growth retardation (10). Pneumonia was defined as an acute respiratory infection affecting the alveoli of the lungs and the distal bronchial tree (11). Patients who had two pneumonia attacks within a year or had at least three pneumonia attacks during their lifetime and were clinically and radiographically normal between attacks were considered to have recurrent pneumonia (12). The lateral curvature of the spine over 10 degrees

to the right or left, which was detected radiologically in the coronal plane, was evaluated as scoliosis (13). Partial or complete fusion of the anterior or posterior ribs was considered to be rib fusion (14). Pectus excavatum was defined as a congenital chest wall deformity in which several ribs and sternum enlarge abnormally, creating a concave or collapsed appearance in the anterior chest wall (15). Children who were diagnosed in the pre and postnatal period were compared in terms of their clinical characteristics.

IBM SPSS Statistics version 22.0 (IBM, Armonk, NY, USA) was used for the statistical analyses. In the statistical analysis of all data obtained, descriptive data were presented as frequency, percentage, mean, ± standard deviation, median, minimum and maximum. The conformity to normal distribution of numerical data was tested with the Shapiro-Wilk test. In the analysis of continuous variables, t-test was used for independent samples when parametric assumptions were met, Mann-Whitney U test was used when they were not met, chi-square test was used in the analysis of nominal variables, and Fisher exact test was used when the distribution was not suitable for chi-square in the analysis of nominal variables. $p<0.05$ was considered significant for all tests.

RESULTS

Over a thirteen-year period, of the 37 children with congenital lung malformations followed up in the pediatric pulmonology department, 16 (43.2%) had PS, eight (21.6%) had CPAM, seven (18.9%) had CLE, and four (4%) 10.8% had bronchogenic cysts and two (5.5%) had coexistence of CPAM and PS. Seventeen children (45.9%) were female. The mean birth weight of the children was 3056±513 grams and 33 (89.1%) were born at term. Eight children (21.6%) had parental consanguinity. Four children had congenital heart disease, one had asthma and one had lignous conjunctivitis. The clinical features of children with congenital lung malformations are given in Table I. Eighteen (48.6%) children were diagnosed prenatally and 19 (51.4%) in the postnatal period. There was no significant difference between the children who were diagnosed in the pre and postnatal period in terms of sex, gestational age, birth weight, and parental consanguinity ($p>0.050$). The comparison of the children who were diagnosed in the pre and postnatal period is given in Table II.

All of the patients who were diagnosed prenatally were born in a tertiary center and evaluated by the pediatric pulmonology department during the neonatal period. Of the patients diagnosed in the postnatal period, 14 (73.6%) were born in a tertiary center. One (5.5%) of the children who were diagnosed in the prenatal period was premature, one (5.5%) had neonatal pneumonia, one (5.5%) was followed in the neonatal intensive care unit (NICU) for clinical follow-up and none of them received respiratory support. Of the children who were postnatally diagnosed, five (26.3%) were hospitalized for neonatal pneumonia, three (15.7%) for transient tachypnea of the newborn, and one (5.2%) for congenital heart disease. There was no statistically significant difference in terms of hospitalization in the NICU of the children who were diagnosed in the pre and postnatal period (p:0.078). One child received nasal continuous positive airway pressure therapy, and two children received incubator oxygen support. While the children who were diagnosed in the prenatal period had no symptoms at the time of admission, the most common reasons for admission were cough and recurrent pneumonia in the children who were postnatally diagnosed. Eighteen of the children (48.6%) had a history of pneumonia.

Eighteen (48.6%) children were diagnosed by prenatal ultrasonography, 14 (37.8%) by CT, and five (13.6%) by chest x-ray. Prenatal ultrasonography were normal in 14 (73.6%) children who were diagnosed in the postnatal period. Malformations were unilateral in all children. Thirteen (35.1%) children's malformations were in the upper lobe of the right lung, eight (21.6%) were in the lower lobe of the left lung, six (16.2%) were in the upper lobe of the left lung, six (16.2%) were in the lower lobe of the right lung, and four (10.9%) were in the middle lobe of the right lung. Right lower lobe was the most common (60.0%) involvement in CPAM, left upper lobe in CLE (85.7%), and left lower lobe in PS (44.4%). Bronchogenic cysts were located in the right middle lobe in all

Table I: Clinical features of children with congenital lung malformations (n:37).

	n (%)
Congenital lung malformations*	
PS	16 (43.2)
CPAM	8 (21.6)
CLE	7 (18.9)
Bronchogenic cyst	4 (10.8)
CPAM+PS	2 (5.5)
Sex*	
Female	17 (45.9)
Male	20 (54.1)
Current age of children (years)†	6.7±5.8
Age at diagnosis of children who were diagnosed in the postnatal period (days) (median, min-max)†	30 (10-1080)
Duration of follow-up (months)†	48.8±26.4
Parental consanguinity*	8 (21.6)
Born at term*	33 (89.1)
Diagnostic methods*	
Prenatal ultrasonography	18 (48.6)
CT	14 (37.8)
Chest x-ray	5 (13.6)
Age at operation (months) (n:12)†	16.3±14.2
Long term complications (n:11)*	
Recurrent pneumonia	4 (36.4)
Rib fusion	4 (36.4)
Scoliosis	2 (18.1)
Pectus excavatum	1 (9.1)

:** *n(%),* **†:** *mean*±SD, ***CPAM: *Congenital Pulmonary Airway Malformation,* ***PS:*** *Pulmonary Sequestration,* ***CLE:*** *Congenital Lobar Emphysema,* ***CT:*** *Computed Tomography,* ***SD:*** *Standard Deviation*

Table II: Comparison of the children with congenital lung malformations who were diagnosed in the prenatal and postnatal period.

	Prenatal (n:18) n (%)	Postnatal (n:19) n (%)	p
Congenital lung malformations			
PS	8 (44.4)	8 (42.1)	
CPAM	7 (38.8)	1 (5.2)	
CLE	0 (0)	7 (36.8)	
Bronchogenic cyst	2 (11.1)	2 (10.5)	
CPAM+PS	1 (5.7)	1 (5.4)	
Sex			
Female	8 (44.4)	9 (47.3)	0.858[a]
Male	10 (55.6)	10 (52.7)	
Parental consanguinity	3 (16.6)	5 (26.3)	0.476[b]
Born at term	17 (94.4)	16 (84.2)	0.217[a]
History of hospitalization in NICU	3 (16.6)	9 (47.3)	0.078[b]
Birth weight (gram) (mean±SD)	2800±456	2960±329	0.227[d]
Current ages of children (years) (mean±SD)	5.6±4.2	7.3±5.6	0.305[d]
Children below 2 years old (n:23)			
Weight z-score (median, min-max)	+1.0 (- 0.8 - + 1.8)	+0.8 (-2.4 - +1.6)	0.097[c]
Height z-score (median, min-max)	+1.4 (- 0.6 - + 2.3)	+0. 9 (-2.6- +2.2)	0.141[c]
Children above 2 years old (n:14)			
BMI z-score (median, min-max)	+ 0.6 (- 0.8 - + 2.8)	+ 0.9 (-2. - +1.8)	0.089[c]
Duration of follow-up (months) (mean±SD)	47.2±20.4	50.4±32.4	0.723[d]
Duration of asymptomatic follow-up (months) (mean±SD)	36.5±4.7	24.0±12.7	0.004[d*]
Age at operation (months) (mean±SD)	17.1±9.1	12.6±10.2	0.166[d]
Post-operative duration of hospitalization (days) (mean±SD)	6.6±5.4	7.9±6.8	0.525[d]
Long term complications	(n:4)	(n:7)	
Recurrent pneumonia	1 (25.0)	3 (43.0)	
Rib fusion	2 (50.0)	2 (28.5)	
Scoliosis	0 (0)	2 (28.5)	
Pectus excavatum	1 (25.0)	0 (0)	

CPAM: *Congenital Pulmonary Airway Malformation,* ***PS:*** *Pulmonary Sequestration,* ***CLE:*** *Congenital Lobar Emphysema,* ***CT:*** *Computed Tomography,* ***NICU:*** *Newborn Intensive Care Unit,* ***BMI:*** *Body Mass Index,* ***SD:*** *Standard Deviation, [a] Chi-square test,[b] Fisher exact test,[c] Mann Whitney U test,[d] Independent samples t test, * Statistically significant*

patients. The median age at diagnosis of those diagnosed in the postnatal period was 30 days (10-1080 days).

The mean FEV_1 was 65.8±19.0%, FVC was 64.8±17.1%, FEV_1/FVC was 95.2±10.8, FEF_{25-75} was 54.5±28.4% of 5 (13.5%) children who were able to perform PFT. All of these children were operated and two had congenital heart disease, one had asthma.

In the chest x-rays of the children, 43.2% had cyst formation, 27% air trapping, 24.3% interstitial thickening, 21.6% mediastinal shift, 13.5% infiltration and 10.8% atelectasis. Thirty-five patients had thorax CT. In the thorax CT, cysts (100%), mediastinal shift (20%), consolidation (50.0%) were detected in children with CPAM, solid lesion unrelated to the tracheobronchial tree (100%), consolidation (37.5%) and atelectasis (37.5%) in children with PS, air trapping (100%), consolidation (42.9%), mediastinal shift (28.6%) in children with CLE, cyst (100%), and consolidation (50%) in children with bronchogenic cysts.

Twelve children (32.4%) were operated. The mean operation age of the children was 16.3±14.2 months. Malformations (CPAM and bronchogenic cyst) of one child (5.4%) who were diagnosed in the prenatal period regressed spontaneously. Four with CLE were operated, two with CPAM, five with PS, and one with bronchogenic cyst. One child with CPAM, one with PS, and one with bronchogenic cyst who were diagnosed in the prenatal period were operated for recurrent pneumonia, while one with CPAM and one with PS were operated under elective conditions. Four children with CLE and three children with PS who were diagnosed in the postnatal period were operated. While these children were operated for recurrent pneumonia, growth retardation developed in three of them during the follow-up. The pathology of a child who was diagnosed as a bronchogenic cyst in the prenatal period was compatible with CPAM. Four children had elective operation plan, but they were postponed due to the concerns of the families about the coronavirus disease 2019 (COVID-19). Other children are followed up with their existing anomalies asymptomatically.

The mean operation age of the patients who were prenatally diagnosed was 17.1±9.1 months, and was 12.6±10.2 months for the children who were diagnosed in the postnatal period (p:0.166). Chylothorax was observed in one child who was operated for PS, while no early complications were observed in other patients. The

mean duration of hospitalization after the operation for the children who were diagnosed in the prenatal period was 6.6±5.4 days, and 7.9±6.8 days for the children who were postnatally diagnosed (p:0.525).

The mean duration of follow-up of the children was 48.8±26.4 months. In the long-term follow-up of the operated children, recurrent pneumonia was observed in four (36.3%), rib fusion in four (36.3%), scoliosis in two (18.1%), and pectus excavatum in one (9%).

The mean duration of follow-up of the children who were prenatally diagnosed was 47.2±20.4 months, whereas it was 50.4±32.4 months for the children who were diagnosed in the postnatal period (p:0.723). In the follow-up, 18 (48.6%) children had pneumonia, 11 (29.7%) children had only cough. Eight (21.7%) children were asymptomatic. The mean asymptomatic duration of follow-up of the children who were diagnosed in the prenatal period was significantly longer (36.5±4.7 months), than the children who were diagnosed postnatally (24.0±12.7 months) (p:0.004). The mean age of the children at the last control who were prenatally diagnosed was 5.6±4.2 years, and it was 7.3±5.6 years for the children who were diagnosed in the postnatal period (p:0.305). Twenty-three (62.1%) children were aged under two. The median weight z-score of these children was +0.9 (min:-2.4; max:+1.8), and the height z-score was +1.2 (min:-2.6; max:+2.3). The median BMI z-score of children aged over two was +0.7 (min:-2.2; max: +2.8). There was no significant difference between the children diagnosed in the pre and postnatal period in terms of current age, weight, height and BMI z-scores (p>0.050).

DISCUSSION

In our study, all children who were prenatally diagnosed were evaluated in the neonatal period before the symptoms started. The most common reasons for admission in the children who were diagnosed in the postnatal period were cough and recurrent pneumonia. The asymptomatic duration of follow-up of the children who were diagnosed in the prenatal period was longer than the patients who were postnatally diagnosed.

Lesions in CPAM are mostly unilateral and do not dominate the lobes, but they are rarely seen in the middle lobe (16). The left upper lobe is most commonly involved in CLE. Multiple lobe involvement is also rare (17). In PS, involvement is mostly found in the left lower lobe, and in bronchogenic cysts, involvement is found in the lower lobes without any side difference (18,19). In our study, similar to the literature, mostly CPAMs were unilateral, CLEs were in the left upper lobe, and PSs were in the left lower lobe. However, different from the literature, bronchogenic cysts were located in the right middle lobe.

In a study conducted in Japan, approximately 65% of 428 patients with congenital lung malformations were symptomatic before the age of three (20). In a meta-analysis, 505 patients who were diagnosed in the prenatal period and followed up with CPAM and PS were evaluated of whom 16 (3.2%) became symptomatic at a median age of 7 months (21). It has been shown that 13% of 154 patients with congenital lung malformations who were diagnosed in the prenatal period have symptoms at a median age of 2 years, and all patients have symptoms at the age of 6 years (22). In our study, children who were diagnosed in the prenatal period became symptomatic approximately at three years of age, whereas it was at two years of age in those diagnosed postnatally. Prenatal diagnosis of children with CPAM allows elective resection in the asymptomatic period, resulting in shorter hospital stay, lower major complications and less medical cost. Early diagnosis allows monitoring in a tertiary center for prenatal counseling, possible fetal intervention, birth planning, experienced NICU and surgery (23). In our study, the delivery of children who were diagnosed in the prenatal period in appropriate centers, as well as the fact that families were well informed about the disease itself and protective measures from the infections may have caused the children to be symptomatic later.

The optimal timing for surgery of patients with asymptomatic congenital lung malformations has not been established. The main rationale for the advocates of the observation strategy is that surgery can be totally avoided for some patients (24). In a study evaluating 61 patients with congenital lung malformations, 48% of the patients had a median operation age at 108 (interquartile range: 8-828) days, while 52% were followed without surgery. It has been reported that 62% of the patients who were diagnosed in the prenatal period were followed up without surgery (25). While less than 1/3 of the children in our study required surgery, 72.2% of the children who were diagnosed in the prenatal period are managed with an observation strategy. Some congenital lung malformations can regress spontaneously in the prenatal or postnatal period. In a study, the incidence of spontaneous regression of congenital lung malformations detected in the prenatal period was 14% (2). In our study, this rate was approximately 5%. Fetal hydrops and pleural effusion may develop in the prenatal period in patients with congenital lung malformations (26). Due to the differences in the approach to congenital lung malformations, possible spontaneous regression and intrauterine complications, it is important that the malformations are detected in the prenatal period, the families are informed about the process in detail, and the surgery or observation decision is determined together with families.

One of the reasons for those who advocate early resection in patients with asymptomatic congenital lung malformations is that it has a positive effect on compensatory lung growth. It has been reported that resection performed in patients younger than 4 years of age is associated with improvement in the lung functions during follow-up (27). On the contrary, Keijzer et al. (28) evaluated patients who were operated before or after the age of 2 and showed that there was no significant relationship between the age of resection and FVC and FEV_1 values at mean age of 10 years. Naito et al. (29) evaluated the pulmonary function and exercise tests of patients who were operated before or after the age of 2 years in their prospective study, and found that the age of resection was not associated with

any abnormal respiratory function or exercise test parameters. They reported that although their total lung capacity was preserved at the ages of 8 and 23, their FEV_1 was decreased. In our study, the mean age at operation was approximately 16 months. Five children who were able to perform PFT were operated patients and two had congenital heart disease and one had asthma. The low average lung function of these children may be related to their comorbidities.

Prenatal diagnosis of congenital lung malformations is difficult due to overlapping findings between different lesions or the presence of complex, hybrid lesions with combined vascular and bronchopulmonary abnormalities (6). In our study, prenatal ultrasonography was normal in approximately 75% of the children who were diagnosed in the postnatal period. The pathology of the operation material was compatible with CPAM in one of the children who was thought to have a bronchogenic cyst on prenatal ultrasonography. Although the diagnosis of congenital lung malformations with prenatal ultrasonography is difficult, the correct diagnosis warrants to better follow-up of the patients.

The prenatal ultrasonographic features of CLE are not well characterized. Patients with CLE may be diagnosed less frequently in the prenatal period than patients with other congenital lung malformations. It has been reported that 73.1% of patients with congenital lung malformations and 24.5% of patients with CLE were detected by prenatal ultrasonography. CLE may be misdiagnosed as CPAM or PS in the prenatal period (30, 31). CLE detected in the prenatal period may disappear and become evident again in the postnatal period (32). In our study, similarly, children with CLE could not be diagnosed in the prenatal period.

In a study in which 61 children with congenital lung malformations were evaluated, it has been shown that 4% of the patients at the age of 1, 8% at two, 12% at five, 5% at 8 had pneumonia of whom 23% had an attack at least once. Due to recurrent pneumonia, 6% of the patients were operated (25). In our study, approximately 85% of the operated children had recurrent pneumonia and this was the reason for the operation. Approximately 30% of the children who were not operated had a history of pneumonia, but they did not have any complaints in the follow-up and their growth was normal. In the long-term follow-up of 119 patients with congenital lung malformations, the risk of recurrent pneumonia was below 10% and decreased after the second year (33). Close follow-up of children with congenital lung malformations, especially those with pneumonia, and monitoring their growth could lead to operation decision of the children.

In patients who have been operated for congenital lung malformations, cutting of the latissimus dorsi and/or serratus anterior muscle during posterolateral thoracotomy may result in muscular atrophy in the postoperative period and may lead to the development of chest wall and/or spinal deformities. Chest wall deformity was detected in 7% of the operated children 5 years after the operation (34). In a study evaluating 74 patients who underwent surgery, scoliosis and chest wall deformity were found in 37% of the patients. Of them, one patient was operated for scoliosis, while one patient was treated using a corset (35). In our study, in the long-term follow-up of the operated children, rib fusion were observed approximately in 33%, scoliosis in 16%, and pectus excavatum in 8% of the patients. Close follow-up of patients who have been operated for congenital lung malformations in terms of musculoskeletal complications that may occur during follow-up enables noninvasive treatment approaches to be applied.

One of the limitation of our study is its retrospective nature. In addition, because of our center is a tertiary care center, symptomatic patients who were diagnosed in the postnatal period may have been referred to us.

Prenatal diagnosis of congenital lung malformations provides an opportunity to predict the complications that may be caused by the malformation, to monitor the growth and to plan the surgery at the most appropriate time for the patient. It is possible to monitor patients who were diagnosed in the prenatal period without symptoms for a longer period of time. Due to very different clinical features and different treatment approaches, it is important to diagnose children with congenital lung malformations during the prenatal period and decide on the timing of surgery together with the families, and to follow up the operated patients in terms of musculoskeletal complications.

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Nadir Bir Siliopati: Joubert Sendromu

A Rare Ciliopathy: Joubert Syndrome

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ÖZ

Joubert sendromu anormal solunum paterni, hipotoni, ataksi, serebellar vermis hipoplazisi, gelişim geriliği, oküler anomaliler, renal kistler ve hepatik fibrozis ile karakterize otozomal resesif geçişli nadir bir siliopatidir. Kraniyal manyetik rezonans görüntüleme (MRG) bulgularında molar diş görünümü Joubert sendromunun tanısında önemli bir bulgudur. Joubert sendromunun karakteristik klinik ve radyolojik bulgularının farkında olunması erken tanı, uygun danışmanlık ve rehabilitasyona yardımcı olacaktır. Bu yazıda hipotoni ve anormal göz hareketleri ile hastanemize başvuran ve Joubert sendromu tanısı alan bir hasta sunulmuştur.

Anahtar Sözcükler: Joubert sendromu, Molar diş, Siliopati

ABSTRACT

Joubert syndrome is a rare autosomal recessive ciliopathy characterized by abnormal breathing patterns, hypotonia, ataxia, cerebellar vermis hypoplasia, developmental delay, ocular abnormalities, renal cysts and hepatic fibrosis. Molar tooth appearance on cranial magnetic resonance imaging (MRI) is an important finding for the diagnosis of Joubert syndrome. Awareness of the characteristic clinical and radiological findings of the syndrome will allow early diagnosis, appropriate counseling and proper rehabilitation. A patient who admitted to our hospital with hypotonia and abnormal eye movements and was diagnosed with Joubert syndrome is presented.

Key Words: Joubert syndrome, Molar tooth, Ciliopathy

GİRİŞ

Joubert Sendromu (JS); hiperpne veya apne gibi anormal solunum paterni, anormal göz hareketleri, hipotoni, ataksi, gelişme geriliği, serebellum ve beyin sapının nöropatolojik anomalileri ile karakterize nadir otozomal resesif bir sendromdur (1). İlk kez 1969 yılında Marie Joubert tarafından tanımlanmıştır (2). Klasik JS, hipotoni, gelişme geriliği ve molar diş belirtisi olarak adlandırılan patognomonik serebellar ve beyin sapı malformasyonu ile karakterizedir (2). Son zamanlarda JS'nun nöroradyolojik özellikleri ve diğer sistem tutulumlarını tanımlamak için, Joubert Sendromuyla ilişkili bozukluklar terimi (JSRD) kabul görmüştür (2).Bu yazıda Joubert sendromu tanısı alan bir olgu eşliğinde literatür bilgileri gözden geçirilmiştir.

OLGU SUNUMU

Beş aylık kız hasta 6 günlükken fark edilen anormal göz ve baş hareketleri yakınması ile polikliniğimize getirildi. Öyküsünden 29 yaşındaki annenin ikinci gebeliğinden 37. gebelik haftasında normal vajinal yol ile 2380 gram doğduğu, doğum sonrası solunum sıkıntısı nedeniyle 4-5 saat kuvözde takip edildiği,

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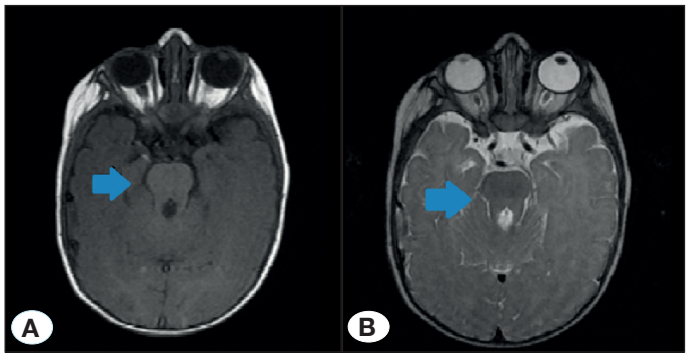

Resim 1: A ve B Aksiyal T1 ve T2 MRG kesitlerinde Joubert Sendromu için tipik molar diş görünümü.

indirekt hiperbilirubinemi nedeniyle bir gün fototerapi aldığı öğrenildi. Anne baba arasında akrabalık yoktu.

Fizik muayenede, baş çevresi 45 cm (50-75 p), vücut ağırlığı 8 kg (3-10 p), boyu 64 cm (10 p)'di. Nörolojik muayenesinde horizontal nistagmus ve aksiyel hipotonisi mevcut olan hastanın diğer sistem muayeneleri normaldi. Gelişimsel değerlendirmede, dil-bilişsel ve hareket işlevlerinde gerilik saptandı. Hastanın hemogram, tam biyokimya, kan gazı değerleri ve metabolik tetkikleri normaldi. Göz muayenesinde takip ve fiksasyonu yoktu, bilateral ekzotropya mevcuttu, göz dibi ise normal olarak değerlendirildi. Abdomen ultrasonografide (USG) böbrek ve karaciğerde anomali tespit edilmedi. Kraniyal Manyetik Rezonans Görüntülemede (MRG) posterior fossada vermis hipoplazisi, molar diş belirtisi olan hastada klinik ve radyolojik bulgularla JS düşünüldü (Resim 1A ve B). Yapılan kromozomal mikrodizin analizi (Infinium™ CytoSNP-850K) normal olarak sonuçlandı. Fizik tedavi ve rehabilitasyon bölümünün önerileri de alınarak hastanın düzenli takibi planlandı.

TARTIŞMA

Otozomal resesif nadir bir hastalık olan JS'nun prevalansı 100.000'de birden daha azdır (1,2). Siliopati olarak da bilinen primer silia disfonksiyonu, anormal genlerden kaynaklanır. Silialar; beyin, böbrekler, retina ve diğer organların işleyişinde önemli bir bileşendir. Siliyogenezdeki bir kusur, çeşitli sinyal yollarının kesintiye uğramasına, JS ve JSRD'nin klinikopatolojik belirtilerine neden olur (2-4). Joubert sendromu radyolojik olarak molar diş belirtisi, hipotoni ve gelişme geriliği ile karakterizedir. Tüm klinik alt tiplerde okülomotor apraksi, nistagmus ve anormal solunum paterni görülebilir (5,6). Ortalama tanı yaşı 33 aydır, bu da farklı klinik fenotiplere sahip sendromun tanısının yenidoğan döneminde zor olduğunu düşündürmektedir (2). Hastalar sıklıkla yaşamın ilk aylarında hipotoni, anormal solunum paterni ve anormal göz hareketleri ile başvururlar (2). Solunum anomalileri Pellegrino ve ark.(8) tarafından vakaların %68'inde ve Kendall ve ark. tarafından vakaların %44'ünde bildirilmiştir (7). Bizim hastamızın öyküsünde de doğum sonrası hipotonik olduğu ve solunum sıkıntısı nedeniyle yenidoğan yoğun bakım ünitesinde kısa süreli takip edildiği öğrenildi.

Joubert Sendromuna yol açan 40'a yakın gen literatürde tanımlanmıştır ve vakaların ancak %50'sinde genetik kusur bulunabilmiştir. NPHP1, AHI1, CEP290, RPGRIP1L, TMEM67, MKS3, ARL13B ve CC2D2A gibi genlerin patogenezde nedensel bir rol oynadığı bilinmektedir (9,10). Hastamıza yapılan mikrodizin analizinde tüm tanımlı genlerin homozigot delesyonları dışlanmıştır. Moleküler tanısının konulması için ileri tetkikler planlanmıştır.

JSRD terimi, merkezi sinir sistemi dışındaki organ tutulumlarını tanımlamak için kullanılmaya başlamıştır (1,11). JSRD orofasiyal dijital, retina, böbrek, okülorenal, karaciğer gibi organların tutulumuna bağlı olarak alt gruplara ayrılır (2). Hastamızda eşlik eden çoklu organ tutulumunun olmaması nedeniyle klasik JS tanısı düşünüldü.

JS'de konjenital hepatik fibroz, yüksek oranda retinal distrofiye eşlik eden polikistik böbrek hastalığı, nefronoftizi, polidaktili ve küçük göğüs kafesi gibi iskelet anomalileri bulunabilir (12). Anormal göz hareketleri, altta yatan okülomotor disfonksiyona bağlı olarak ortaya çıkar ve okülomotor apraksi % 80 oranında en karakteristik ve en sık görülen göz bulgusudur. Nistagmus %72, strabismus %74, pitozis % 43 ve retina dejenerasyonu % 38 oranında bulunan diğer göz bulgularıdır (2, 10). Hastamızda da göz bulgusu olarak horizontal nistagmus mevcuttu.

Temel radyolojik bulgular; vermisin tam veya parsiyel yokluğu, hipoplastik serebeller pedinküller ve buna bağlı 4. ventrikül deformitesidir. Bu bulgular aksiyal MRG'de 'molar diş' görünümüne neden olur (5). Serebeller hemisferler ve serebrum genellikle normaldir. Ancak; %6- 20 oranında korpus kallosum agenezi ve disgenezisine bağlı lateral ventriküllerde hafif derecede genişleme izlenebilir (3,13). Ayrıca konjenital malformasyonlar, hipotalamik hamartom ve nadiren hipofiz bezinin yokluğu eşlik edebilir (3).

Anormal solunum paterni, apnesi olan hastalarda havayolu obstrüksiyonlarını (hipotonik hava yolu, hipertrofik tonsiller) beyin sapı disregülasyonundan ayırt etmek için polisomnogram yapılabilir. Oküler incelemeler görme keskinliği, yarık lamba muayenesi, fundus ve elektroretinogram (retinal distrofi varlığında) değerlendirilmesini içerir. Standart idrar tetkiki ve idrar konsantrasyonu değerlendirilmelidir (3). İnfantların çoğunda kistik böbrek hastalığı ve karaciğer fibrozisi gelişmeyeceğinden takip sürecinde abdomen USG periyodik olarak tekrarlanmalıdır (7).

Tedavi genellikle destekleyicidir ve multidisipliner bir yaklaşım içerir. Anormal solunum paterni olan hastalar apne açısından takip edilmeli ve klinik gerekliliğe göre yenidoğan döneminde kafein gibi uyarıcı ilaçlar, oksijen desteği, ciddi solunum yetmezliği olanlarda mekanik destek ve/veya trakeostomi düşünülebilir. Şiddetli disfajisi olan çocuklarda beslenme için nazogastrik beslenme tüpleri veya gastrostomi tüpü yerleştirilebilir. Nöbet

varlığında antiepileptik ilaçlarla tedavi edilmelidir. Polidaktili için düzeltici cerrahi yapılabilir (7). Bilişsel zorluklar, uygun rehabilitasyon stratejisi ve düzenli takip gerektirir. Prognoz, organ tutulumunun türüne ve yaygınlığına bağlıdır (3).

Klinik heterojenite JS tanısını zorlaştırmaktadır bu nedenle sendroma özgü radyolojik bulgular eşliğinde anormal solunum paterni, hipotonisite, anormal göz hareketleri olan hastalarda akılda tutulmalı ve sonradan ortaya çıkabilecek komplikasyonlar açısından multidisipliner düzenli izlem gerektiği unutulmamalıdır.

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Kawasaki Hastalığının Ender Bir Bulgusu: Safra Kesesi Hidropsu ve Literatürün Gözden Geçirilmesi

A Rare Presentation of Kawasaki Disease: Gall Bladder Hydrops and Review of the Literature

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ÖZ

Kawasaki hastalığı, tedavi edilmemiş olgularda ciddi koroner arter komplikasyonu gelişen, akut, ateşli bir vaskülittir. Akut safra kesesi hidropsu, Kawasaki hastalığı'nın karaciğer, batın tutulumunun minör göstergesi olabilir. Bu olgu sunumunda, kolik tarzında sağ üst kadran ağrısı, ateş, sarılık ile gelen, abdominal ultrasonografisinde taşsız hidropik safra kesesi saptanarak yapılan tetkikler ve fiziksel bakı sonrası Kawasaki hastalığı tanısı konulan, altı yaşında bir erkek hasta sunuldu. Çocuklarda etiyolojisi saptanamayan safra kesesi hidropsuna karın ağrısı ve ateşin eşlik ettiği olgularda, diğer tanı kriterleri saptanmasa da Kawasaki hastalığı ayırıcı tanıda akılda tutulmalıdır.

Anahtar Sözcükler: Hidrops, Kawasaki hastalığı, Safra kesesi

ABSTRACT

Kawasaki disease is an acute febrile vasculitis of childhood in which untreated cases develop severe coronary artery complications. Acute gallbladder hydrops and liver abdominal involvement occur occasionally as minor manifestation of Kawasaki disease. Herein, Kawasaki disease presenting with hydrops of the gallbladder without calculi was reported in a 6-year-old boy. With further examination and laboratory pointed out Kawasaki disease in the patient. Kawasaki disease should be considered in differential diagnosis in children with gallbladder hydrops, abdominal pain and fever of unknown etiology, even if all the diagnostic criteria have not appeared.

Key Words: Hydrops, Kawasaki disease, Gallbladder

GİRİŞ

Kawasaki hastalığı, ilk kez 1967 yılında Japonya'da tanımlanmış, sıklıkla infantları ve küçük çocukları etkileyen, kendini sınırlayan bir multisistem vaskülitidir (1). Hastalık beş yaş altı erkek çocuklarda daha sık (erkek/kız oranı 1.5-1.7'dir) görülür. Etiyolojisi tam olarak anlaşılamadığından tanı koydurucu bir testi bulunmamaktadır. Tanısı, dikkatli öykü ve iyi bir klinik değerlendirmeyle konabilen bir hastalıktır (2). Tedavi edilmeyen hastalarda, komplikasyon olarak koroner arter anomalileri gelişir. Erken tanı ve intravenöz immunglobülin (IVIG) ve aspirin tedavisi ile koroner arter hasarı önemli derecede azalmaktadır (3).

Bu olgu sunumunda, yüksek ateşe eşlik eden karın sağ üst kadran ağrısı ile sarılık yakınması olan ve ultrasonografisinde (US) safra kesesi hidropsu saptanarak Kawasaki hastalığı tanısı konulan altı yaşındaki erkek olgu, atipik kliniği nedeniyle sunulmuştur.

OLGU SUNUMU

Altı yaşında erkek hasta, hastanemize başvurusundan dört gün önce ateş, boğaz ağrısı ve halsizlik yakınması ile dış merkeze başvurmuş. Hastaya, tonsillofarenjit tanısı konularak antibiyotik tedavisi başlanmış. Hastanın ateşinin düşmemesi

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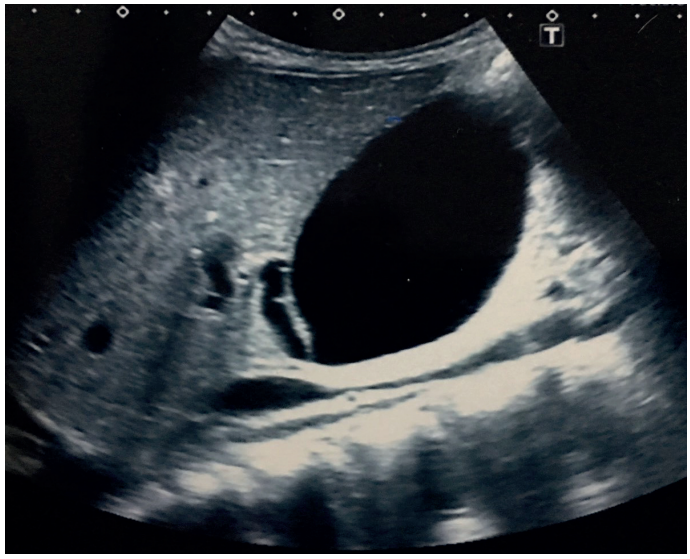
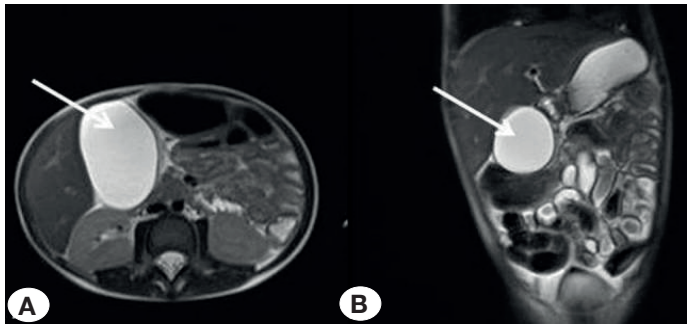


Resim 1: Batın US: Safra kesesi hidropik olup, boyutları 84x69 mm'dir. Duvar düzensizliği olmayıp, duvar kalınlığı (<2 mm) normal.

ve yakınmalarına sağ üst kadran ağrısı ve sarılık eklenmesi nedeniyle başvurduğu üniversitemiz pediatri kliniğinde, orofarenkste hiperemi, tonsiller hipertrofi, kırmızı çilek dili görünümü saptanması sonucu aynı tanıyla Amoksisilin-klavulanik asit başlanmış. Hasta bir gün sonra, yakınmalarının ikinci günü başlayıp devam eden karın ağrısı nedeniyle, çocuk cerrahisi'ne konsülte edildi. Hastanın fizik muayenesinde; bilinç açık, huzursuzdu. Kan basıncı 94/62 mmHg, Aksiller ateş 38.4 °C, batın sağ üst kadranda hassasiyet ve şüpheli kitle saptandı. Laboratuvar tetkiklerinde; aspartat aminotransferaz: 33 U/L (normal: 0-40 U/L), alanin aminotransferaz: 39 U/L (normal: 0-41 U/L), gamaglutamil transpeptidaz: 142 U/L (normal: 10-71 U/L), total bilirubin: 7.38 mg/dL (normal: 0-1.4 mg/dL) direkt bilirubin: 7.07 mg/dL (normal: 0-0.3 mg/dL), hemoglobin: %10.1 g/dL, periferik yaymada %70 nötrofil hâkimiyeti, yüksek CRP; 112 mg/L (normali: 0-8 mg/L) saptandı. ANA, RF, Salmonella, Brusella testleri ve Hepatit markerları negatifti.

Ayakta direkt batın ve PA Akciğer grafisinde bir patoloji saptanmadı. Fizik muayenede sağ üst kadranda hassasiyet ve kitle, laboratuvar tetkiklerinde ise bilirubin yüksekliği saptanması nedeniyle yapılan batın ultrasonografisinde (US); her iki böbrek parankim ekosunda grade I olacak şekilde artış, safra kesesi içerisinde safra çamuruyla uyumlu ekojen seviyelenme ve hidropik görünüm saptandı (Resim 1). US'de safra kesesi hidropsu saptanan hastaya, radyolojik ön tanılar arasında koledok kisti de olduğundan Manyetik Rezonans Kolanjiografi (MRCP) yapıldı. MRCP'de safra kesesi hidropsu dışında intrahepatik ve ekstrahepatik safra yolları normal olarak değerlendirildi (Resim 2A-B). Batın içi ve akciğer bazallerinde serbest sıvı dışında bir patoloji saptanmadı. Hasta yeniden değerlendirildiğinde; mobil, ağrısız servikal lenfadenopati, yakınmalarının başlamasının 3. günü başlayan konjonktival kızarıklık ve anüs etrafı ile kasıklarında eritamatöz döküntü ile soyulmanın yakınmalarına eşlik ettiği saptandı. Bu bulgularla,



Resim 2A-B: Batın MR görüntülemesi; **(A)** Aksiyal ve **(B)** koronal T2 ağırlıklı görüntülerde safra kesesi içerisinde taşa ait görüntü ve safra kanallarında dilatasyon görülmezken genişlemiş-hidropik safra kesesi (oklar) görülmektedir.

hastaya Kawasaki hastalığı tanısı konuldu. Hastada eşlik eden safra kesesi hidropsunun, Kawasaki hastalığının ender bir tutulum şekli olan, batın tutulumunun subakut dönemindeki bulgusu olduğu düşünüldü.

Kawasaki hastalığı tanısı alan hastaya yapılan elektrokardiyografi ve ekokardiyografi, normal olarak değerlendirildi. Hastaya 8. gün IVIG (2 g/kg/gün tek doz) ve aspirin (80 mg/kg/gün, 4 doz) tedavisi başlandı. Tedavi başlandıktan iki gün sonra, ateşi düştü ve karın ağrısı azaldı. Hastanın 9. gün el ve ayaklarında şişlik meydana geldi, 15. gün ise ekstremite şişlikleri geriledikten sonra periungual deskuamasyon (deri döküntüleri) oldu. Hastanın US izlemlerinde 15. güne kadar safra kesesi hidropsunun devam ettiği görüldü. Yakınmaları kalmayan hasta kontrole çağrılarak taburcu edildi.

TARTIŞMA

Kawasaki hastalığının ülkemizdeki insidansı tam bilinmemektedir. Kanra ve ark. (2), altı yıllık çalışmalarında tanı konulmuş dokuz olgu bildirmişlerdir. Kawasaki hastalığın tanısı; ateş (5 günden uzun süren), ekstremite periferinde değişiklikler, eksüdatif olmayan bilateral konjunktival konjesyon, orofarenks mukozasında değişiklikler ve servikal lenfadenopatiden (1,5 cm'den büyük) oluşan beş ana kriterden dördünün olması ile konulur (4). Bu klasik belirtilerin yanında pankreatit, orşit ve safra kesesi hidropsu gibi çocuk cerrahisince izlem ve ayırıcı tanılarının yapılması gereken patolojiler de bu hastalığın başlangıç veya seyri sırasında görülebilmektedir. Batın ve safra kesesi tutulumu göreceli olarak ender komplikasyonlardır. Miyake ve ark. (5) çalışmalarında 310 Kawasaki hastasından yedisinde (%2.3) gastrointestinal tutulum saptamışlardır (6). Kawasaki hastalığındaki batın bulguları çoğunlukla safra kesesi hidropsuna bağlıdır (7). Kawasaki hastalığının gastrointestinal tutulumu ile başlayan klinik, sıklıkla tanı ve tedavide gecikmelere, bu da koroner damar komplikasyonlarının gelişimine neden olabilecek risk faktörüdür (8).

Safra kesesi akut hidropsu; akut kolesistit, konjenital anomali ya da taşa bağlı olmadan safra kesesinin şişmesi olarak tanımlanır.

Hidrops idiopatik olabileceği gibi, leptospiroz, kızıl, Henoch-Schönlein purpurası, total parenteral beslenme, lösemi, nefrotik sendrom ve Kawasaki hastalığında da gözlenebilir. Öyküde, yakın zamanda geçirilen otit, üst solunum yolları enfeksiyonu, sepsis, Ailevi Akdeniz Ateşi, gastroenterit ve viral hepatit de olabilir (1,9). Kawasaki hastalığında görülen safra kesesi hidropsu, ilk olarak 1976 yılında Goldsmith tarafından tanımlanmıştır (10). Kawasaki hastalığına safra kesesi hidropsunun eşlik etme oranı %3-12.7 arasındadır (11). Hidropsun, sistik kanalın aşırı mukus salgısıyla tıkanması sonucu, kesenin boşalamaması ya da inflamasyona ikincil reaktif hipertrofiye lenf düğümlerinin sistik kanalı tıkamasına bağlı olabileceğine dair görüşler vardır (12). Safra kesesi hidropsunun, uzun süren açlık, ateş ve dehidratasyona bağlı safra stazı ve özgül olmayan vaskülit ile de ilişkili olabileceği söylenmektedir (13).

Kawasaki hastalığına bağlı safra kesesi hidropsunun tanısı, karın ağrısı (%100), bulantı kusma (%75), ateş, bazen sarılık ve sağ üst kadran kolik ağrısı (%90) olan hastanın fizik muayenesinde, sağ üst kadranda kitle palpe edilmesi (%55) ve US bulguları ile konur (11,14). Batın US'de, safra yolları normal, taşsız veya konjenital malformasyonsuz, sonalüsent görünümlü ve küresel konfigürasyonlu şişkin bir safra kesesi saptanır.

Safra kesesi hidropsu gelişen hastalarda, ender de olsa safra kesesi perforasyonu olasılığı hastalığın cerrahi olarak izleminin gerekliliğini gösterir. Sun ve ark. (15) 1980-2015 yılları arasındaki literatür taramasında, safra kesesi tutulumu olan 130 Kawasaki olgusu saptanmıştır. Bir olguda safra kesesi perforasyonu olmuş, üç hastada kolesistektomi yapılmış, bir hastada da sepsise bağlı ölüm görülmüştür.

Bizim olgumuzda olduğu gibi, çocuklarda safra kesesi hidropsu, benign ve kendini sınırlayan özellik taşıdığından, uygun olan ilk aşamada konservatif yaklaşımdır. Kawasaki ile ilişkili safra kesesi hidropsunun gerilemesi ortalama 15 gün içerisinde olsa da, 60 günü bulabilmektedir (11,14). Safra kesesi hidropsunun uzun sürede gerilemesine, vaskülite karşı yetersiz bağışıklık yanıtının neden olabileceği ileri sürülmektedir (11). Hastamız, safra kesesi perforasyonu olasılığına karşı, batın muayene bulguları ve US'lerle izlendi. Hastamızın safra kesesi ilk belirtilerden yaklaşık 12 gün sonra normale dönmeye başladığı görüldü.

Kawasaki hastalığında çoklu sistem tutulumu olduğundan, dikkatli öykü ve fizik incelemeyle saptanan subakut dönemdeki bulgular tanıyı destekleyebilir. Hastamızda, safra kesesi hidropsuna eşlik eden vücuttaki döküntüler, lenfadenopati, konjunktival bulgular ve çilek dil ile tanı konulmuştur.

SONUÇ

Kawasaki hastalığının önemli kardiyolojik komplikasyonlarının önlenebilmesi için, akut dönemde tanı konularak, IVIG ve yüksek doz aspirin tedavisinin başlanması önemlidir. Safra kesesi hidropsunun eşlik ettiği bulgularla tanısı konularak, komplikasyonsuz tedavi edilen ve safra kesesi hidropsu kendiliğinden düzelen olgu sunularak, safra kesesi hidropsu saptanan olguların ayırıcı tanısında Kawasaki hastalığının önemine dikkat çekilmesi amaçlanmıştır. Tüm tanı kriterleri ortaya çıkmamış olsa bile, safra kesesi hidropsu, karın ağrısı ve etiyolojisi bilinmeyen ateş eşlik eden çocuklarda ayırıcı tanıda Kawasaki hastalığı düşünülmelidir.

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Neurological Manifestations of Multisystem Inflammatory Syndrome in Children

Çocuklarda Multisistem İnflamatuvar Sendromun Nörolojik Bulguları

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ABSTRACT

Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19 first reported from South East London has a wide spectrum of neurological signs and symptoms including headache, impaired consciousness, aseptic meningitis, encephalitis, seizure, ataxia, and stroke. It is important to diagnose these patients as soon as possible and treat them with a multidisciplinary ap-proach. A few studies have reported post-discharge follow-up data in MIS-C patients with neurological symptoms most of whom showed neurological improvement. Long-term follow-up of MIS-C patients is required to determine possible neurological sequelae.

Key Words: COVID-19, MIS-C, Neurological manifestations

ÖZ

İlk olarak Londra'nın güneydoğusunda bildirilen çocuklarda COVİD-19 ile ilişkili multisistem inflamatuvar sendromun (MIS-C) nörolojik bulguları baş ağrısı, bilinç değişikliği, aseptik menenjit, ensefalit, nöbet, ataksi ve inme gibi geniş bir nörolojik belirti ve semptom yelpazesine sahiptir. Bu hastalara mümkün olan en kısa sürede tanı koymak ve multidisipliner bir yaklaşımla tedavi etmek önemlidir. Nörolojik semptomları olan ve çoğu nörolojik açıdan düzelme gösteren MIS-C hastalarında taburculuk sonrası takip ile ilgili az sayıda çalışma vardır. MIS-C'ye bağlı gelişmesi olası nörolojik sekelleri belirlemek için uzun vadeli takip gerekmektedir.

Anahtar Kelimeler: COVİD-19, MIS-C, Nörolojik bulgular

INTRODUCTION

The novel coronavirus, Corona Virus Disease 2019 (COVID-19), which was identified after a recent outbreak in Wuhan, China, in December 2019, is currently a global pandemic (1). Typical clinical presentations include fever, cough, dyspnea, anosmia, and myalgia (1,2). Angiotensin-converting enzyme 2 (ACE2) receptor, which is the entry point for COVID-19 is present in human organs including lung parenchyma, gastrointestinal tract, nasal mucosa, human airway epithelia, lymphoid tissues, vascular endothelium, smooth muscle cells, glial cells and neurons which also makes the brain a possible target of COVID-19. Another cell membrane protein transmembrane serine protease 2 (TMPRSS2) expressed in some glial cells of animal models is also a target necessary for SARS-CoV-2 invasion. However, the degree of expression is unclear for both proteins (1- 4).

Neurological manifestations of COVID-19 such as change in mental status, encephalitis, hypoguesia are being reported with each passing day (5,6). The rate of neurological findings varies between 7.7-57.4% in different studies (7,8). However, neurological involvement in children with COVID-19 appears to be limited or under reported (9). Children seemed to be only mildly symptomatic with the infection in most cases until Riphagen et al. (10) had reported 8 previously healthy children from South East London with hyperinflammatory shock, a syndrome exhibiting features similar to atypical Kawasaki disease. These children had no significant respiratory issues and were mostly negative for SARS-CoV-2 but exposed to SARS-CoV-2 subjects. Thereafter similar presentations were reported from other areas as well (10-13). The Royal College of Paediatrics and Child Health (RCPCH) referred to this acute condition as pediatric multisystem inflammatory syndrome temporally associated with COVID-19 (PIMS-TS) (14). Later on

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Table I: Case definitions for MIS-C from Centers for Disease Control and Prevention and the World Health Organization.

Centers for Disease Control and Prevention	World Health Organization
An individual aged <21 y presenting with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac,kidney, respiratory, hematologic, gastrointestinal, dermatologic, or neurological) Fever>38.0°C for ≥24 h or report of subjective fever lasting ≥24 h Laboratory evidence including, but not limited to≥1 of the following: an elevated CRP level, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase, or IL-6; elevated neutrophils; reduced lymphocytes; and low albumin **AND** No alternative plausible diagnoses **AND** Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 wk prior to the onset of symptoms ***Additional comments*** Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection	Children and adolescents 0–19 years of age with fever ≥3 days. **AND** ***two of the following:*** 1. Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet) 2. Hypotension or shock 3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiography findings or elevated Troponin/NT-proBNP) 4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers) 5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain) **AND** Elevated markers of inflammation such as ESR, CRP or procalcitonin **AND** No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes **AND** Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19

CRP: *C-reactive protein,* ***ESR:*** *erythrocyte sedimentation rate,* ***IL:*** *interleukin,* ***LDH:*** *lactate dehydrogenase,* ***NT-proBNP:*** *N-terminal pro-B-type natriuretic peptide,* ***PT:*** *prothrombin time,* ***PTT:*** *partial thromboplastin time,* ***RT-PCR:*** *reverse transcription-polymerase chain reaction.*

the illness was labelled multisystem inflammatory syndrome in children (MIS-C) by the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) based on 6 principle elements: pediatric age, persistence of fever, presence of laboratory markers of inflammation, manifestation of signs or symptoms of organ dysfunction, lacking an alternative diagnosis, and a temporal relation to COVID-19 infection or exposure (12,14-16). The defining features are presented in table I.

MIS-C is thought to occur in genetically susceptible individuals with hyperinflammatory response after SARS-CoV-2 infection (17). Children with delayed type I and type III interferon responses after COVID-19 infection may have a higher risk of developing cytokine storm and MIS-C (18). In a large series of MIS-C patients from the United States, a total of 570 children who met the case definition of CDC were reported. The illness in 490 (86.0%) patients involved ≥ 4 organ systems and most of the neurological symptoms developed in these patients. Headache was the most common neurological symptom (19).

Neurological manifestations reported in patients with MIS-C are headache, impaired consciousness, aseptic meningitis, encephalitis, seizure, ataxia and stroke (9,20). According to a systematic review of eight studies, the incidence of neurological symptoms in children with MIS-C was 25-50% (9). Kaushik et al. (21) reported neurological symptoms in 12-58% of affected children. Similar neurological findings were reported in studies by Whittaker et al. (22). and Chiotos et al. (23). Among children diagnosed with MIS-C in New York neurological symptoms including headache, altered mental status, and encephalopathy were seen in 31-47% (4). Another study in the United States found that only 5% of MIS-C patients suffered from severe neurological complications such as seizure, coma, encephalitis, demyelinating disorders, and aseptic meningitis (24). The reported patients with laboratory findings, neuroimaging and/or neurophysiologic evaluation, immunotherapy and outcome in addition to neurological symptoms are shown in table II.

Treatment regimen includes antiviral therapy (if PCR positive for SARS-CoV-2), immunotherapy, inotropic support, anticoagulation and plasma therapy. Vital signs, hydration, electrolytes and metabolic status should be monitored. Steroids, intravenous immunoglobulin (IVIG), infliximab (anti-tumour necrosis factor drug), tocilizumab (IL-6 antagonist) and anakinra (IL-1 receptor antagonist) are the treatment choices (4,32).

MIS-C has a wide spectrum of neurological signs and symptoms ranging from myalgia to encephalopathy. Patients with MIS-C

Table II: Neurological symptoms, laboratory and imaging findings, immunotherapy and outcome of the patients.

First Author/ number of patients	Neurological symptoms	Laboratory parameters	Neuroimaging	Neurophysiologic evaluation	Immunotherapy/Outcome
Abel[25]/1	Somnolence, hypotonia, weakness	High CRP, ferritin, IL-6, NT-proBNP; low platelet count	Restricted diffusion in the bilateral lateral thalamic nuclei	-	Intravenous methylprednisolone, intravenous immunoglobulin, anakinra / Mild residual weakness
Abdel-Mannan[26]/4	Headache, encephalopathy, ataxia, meningism, dysarthria, dysphagia, muscle weakness, hyporeflexia	High CRP, D-dimer, LDH, ferritin	Restricted diffusion (n=3) and signal changes of the genu and the splenium of the corpus collosum (n=4)	Mild myopathic or neuropathic changes (n=3)	Intravenous methylprednisolone (n=2), dexamethasone (n=2), intravenous immunoglobulin (n=2), anakinra (n=2), and rituximab (n =1) / Fully recovered (n=2), wheelchair bound(n=2)
Chiotos/3	Headache/dizziness (n = 1), lethargy/ altered mental state (n = 2)	Low lymphocyte%, albumin; high CRP, D-dimer, PCT, LDH, BNP, troponin	Diffuse cerebral edema (n=1)	-	Intravenous methylprednisolone (n=3), intravenous immunoglobulin (n=3) / Discharged home
Dugue [27]/1	Brief episodes of sustained upward gaze, bilateral leg stiffening	High PCT; low leukocyte	Normal	-	-/Fully recovered
Oualha[28]/1	Right-sided weakness, altered conciousness	High CRP	Sphenoidal sinusitis with cavernous sinus thrombosis	-	Not mentioned/Died
Regev[29] /1	Headache, nuchal rigidity, muscle weakness, and clonus	High CRP, D-dimer, NT-proBNP, troponin; mild elevation INR; low C3, C4 factors; normal fibrinogen	Diffuse brain hemosiderosis	-	Intravenous methylprednisolone, intravenous immunoglobulin /Normal apart from general muscle weakness.
Shenker[30]/1	Trismus, loss of smell and taste, difficulty swallowing, altered mental status, status epilepticus	High CRP, CK, BNP, D-dimer, ESR, ferritin, fibrinogen, IL-6, LDH, PCT	Normal	-	Intravenous immunoglobulin, remdesivir, anakinra / Mental status resolved, seizures continued despite antiepileptic drugs
Verkuil[31]/1	Headache, myalgia, eye movement restriction	High CRP, fibrinogen; normal INR	Eversion of the right optic disc, flattening of the posterior right globe; widened right and left optic nerve sheath diameters, flattened upper border of the pituitary gland, narrowing of the transverse sinuses	-	Intravenous methylprednisolone, intravenous immunoglobulin / Fully recovered

BNP: *Brain natriuretic peptide,* ***CK:*** *Creatine kinase,* ***CRP:*** *C-reactive protein,* ***ESR:*** *Erythrocyte sedimentation rate,* ***IL:*** *Interleukin,* ***INR:*** *International normalized ratio,* ***LDH:*** *Lactate dehydrogenase,* ***NT-proBNP:*** *N-terminal pro B-type natriuretic peptide,* ***PCT:*** *Procalcitonin,* ***PT:*** *Prothrombin time,* ***PTT:*** *Partial thromboplastin time,* ***RT-PCR:*** *reverse transcription-polymerase chain reaction*

should be treated with a multi-disciplinary approach. A few studies have reported post-discharge follow-up data in MIS-C patients with neurological symptoms most of whom showed neurological improvement. Long-term follow-up of MIS-C patients is required to determine possible neurological sequelae.

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