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Book section: Suh KN, Keystone JS. Malaria and babesiosis. Gorbach SL, Barlett JG, Blacklow NR, editors. Infectious Diseases. Philadelphia: Lippincott Williams; 2004.p.2290–308.

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Final publication: The final corrected version will appear in an issue of the journal and added to the journal website. To ensure rapid publication, we ask authors to provide your publication approval during the proofreading process as quickly as possible, and return corrections within 48 hours of receiving the proof.

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- Journal policies detailed in this guide have been followed.

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CONTENTS

EDITORIAL

Dear colleagues,

I am pleased to inform you that Zeynep Kamil Medical Bulletin, first published in 1982, has begun a new life this year as Zeynep Kamil Medical Journal. I would like to thank everyone who contributed to the valuable history of this journal and to share our excitement for the future. It is our goal to further elevate the stature of the journal in national and international research indexes of obstetrics and gynecology, pediatrics, and pediatric surgery. As one of our initial steps toward this objective, we have updated our publishing policies, website layout, and the article submission terms and application system.

Significant changes have been made to the Scientific and Technological Research Council of Turkey (TÜBİTAK) TR index system to demonstrate journal compliance with transparency practices. These include reviewing and clearly declaring publication policies. We are committed to these principles and have created an editorial policy section on our website.

You can access the journal's new website at www.zeynepkamilmedj.com to learn more about our plans and practices, and the new article submission system is available at http://jag.journalagent.com/zkmj/.

It is our greatest wish that readers will continue to support and strengthen Zeynep Kamil Medical Journal with publications of your work. We look forward to working and growing together.

With my very best wishes,

Dr. Semra KAYATAŞ ESER
Editor-in-chief

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ORIGINAL RESEARCH

CASE REPORT

REVIEW ARTICLE

Zeynep Kamil Med J 2021;52(1):1–9
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ORIGINAL ARTICLE

Comparing the first trimester and second trimester fifty grams oral glucose tolerance test values in gestational diabetes mellitus

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ABSTRACT

Objective: The present study aimed to assess the results of pregnant women who have been applied a 50 g oral glucose tolerance test (OGTT) in the first and second trimesters and investigate this method's role in the diagnosis of gestational diabetes mellitus (GDM) and risk factors associated with this disease.

Material and Methods: This retrospective study was performed on 153 pregnant women who were admitted to our hospital's antenatal clinics between March 2011 and August 2011. Fifty grams OGTT was applied to the same pregnant women both in the 1st trimester (between 8th and 14th weeks) and second trimester (between 24th and 28th weeks); values of the test results were then compared. A 100 g OGTT diagnostic test was performed on those with a 50 g OGTT value of ≥140 mg/dl in both trimesters. The study patients were divided into two groups as non-GDM and GDM based on venous plasma glucose values measured 1 h after 50 g of oral glucose load given. The non-GDM group consisted of those with plasma glucose levels <140 mg/dl and plasma glucose levels between 140 mg/dl and 200mg/dl, GDM group plasma glucose levels ≥200 mg/dl. First trimester and second-trimester OGTT values and possible risk factors for GDM (age, gravida, parity, number of abortions, smoking, a previous GDM history, etc.) were compared between non-GDM and GDM groups.

Results: GDM, diagnosed in 4.5% (7) in the first trimester (between 8th and 14th weeks) and 6.5% (10) second trimester, was detected in 11% (17) of 153 pregnant women in the present study. GDM, diagnosed in 41.2% (7 patients) in the first trimester and 58.8% (10 patients) second trimester, was found with a higher rate in pregnant women over 30 years (p=0.000 <0.05). The mean fasting blood glucose (FBG) level was 96 mg/dl in the GDM group and 83 mg/dl in the non-GDM group, with a statistically significant difference, which existed (p<0.05). The mean 50 g OGTT value was 170 mg/dl in pregnant women diagnosed with GDM in the first trimester, and it was 140 mg/dl in those diagnosed in the second trimester, with this difference was considered statistically different (p<0.05). Age, parity, a family history of DM, FBG, a previous GDM history, gravida, a previous macrosomia history, and a previous history of preeclampsia were determined as risk factors that significantly increase the risk of GDM (p<0.05). The half of patients was diagnosed with GDM in the early period of pregnancy. In the present study, 41.2% of cases were diagnosed in the first trimester and 58.8% in the

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second trimester. In general, the patients diagnosed in the first trimester were those being under risk in terms of GDM. According to the present study, it is recommended that the pregnant women should be scanned for GDM in the early period.

Conclusion: With screening tests to be applied to risky groups in early pregnancy, a significant number of cases with GDM recently be detected on time. Thereby, maternal and fetal morbidity and mortality rates might be considerably reduced thanks to providing proper treatments and regular monitoring. Furthermore, for obtaining specific data concerning the factors with potential influence on the risk of GDM, further studies on this topic need to be performed.

Keywords: Early screening, gestational diabetes mellitus, oral glucose tolerance test.

INTRODUCTION

Gestational diabetes mellitus (GDM), defined as diabetes diagnosed during pregnancy, can lead to negative fetal and maternal consequences such as macrosomia, shoulder dystocia, operative delivery, birth injuries, preeclampsia, hemorrhage, and preterm delivery, with raising concerns about this potential impact.[1,2] It has also been found that GDM increases the risk of diabetes that may occur in the post-pregnancy period by 7 times.[2] Most importantly, complications can be reduced thanks to the appropriate treatments given on time to pregnant women diagnosed with GDM with screening and diagnostic tests during pregnancy.[3]

A two-digit (100 g oral glucose tolerance test [OGTT] after 50 g OGTT) or single-digit (75 g OGTT) screening/diagnostic test can be made during pregnancy. Today, in many centers, the two-step screening test continues to be used in diagnostic workup.[4]

American Association of Obstetrics and Gynecology (ACOG) has recommended screening all pregnant women diagnosed with GDM, usually in the second trimester or early third trimester, between 24 and 28 weeks.[5,6] The increased frequency of undiagnosed Type 2 diabetes during pregnancy has led to pregnant women's screening recommendations, investigating risk factors at the first visit.[6] The International Association of Diabetes in Pregnancy Study Group (IADPSG) has informed that early screening should be determined by that region's conditions and abnormal glucose metabolism. In addition, the ACOG has recommended early screening to undiagnosed Type 2 diabetes groups with relevant risk factors.[7]

The American Diabetes Association (ADA) and the ACOG have evaluated people with body mass index (BMI) of ≥25 kg/m², GDM in a previous pregnancy, HbA1c higher than 5.7% (39 mmol/mol), impaired glucose tolerance, high fasting blood glucose (FBG) levels in the previous tests, any first degree relatives with diabetes, and those in high-risk ethnic group (Latin, Asian, African-American), and those with cardiovascular disease, hypertension, HDL of <35 mg dl, triglyceride of >250 mg dl, polycystic ovary syndrome, physical inactivation, history of giving birth to a macrosomia baby (>4000 g), and those over 40 years old as being in risk class. If any of these risk factors are present, they recommend an OGTT in early pregnancy.[8,9] Re-screening is also recommended between 24 and 28 weeks to the early screening test negative pregnant women.[7–9] It has been shown that the risk of a congenital anomaly due to hyperglycemia and the risk of diabetic complications (nephropathy and retinopathy) in early pregnancy increases. Therefore, if diabetes can be caught early and given appropriate treatment on time, the risk of complications due to this disease can be significantly reduced in pregnant women.[10,11]

Our study aimed to determine the appropriate trimester for gestational diabetes screening, elucidate risk factors, and minimize maternal and fetal morbidity and mortality by recognizing diabetic cases at an earlier stage with an administration of a 50 g glucose screening test in the first and second trimesters.

MATERIAL AND METHODS

This study was performed on 153 pregnant women who were admitted to the antenatal clinics of the Turkish Republic Ministry of Health Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital between March 2011 and August 2011. The role of making GDM diagnosis in the early stages of pregnancy was investigated retrospectively by comparing 50 g OGTT, administered to the same pregnant women both in the first trimester (between 8th and 14th weeks) and the second trimester (between 24th and 28th weeks), values. Pregnant women with a single live pregnancy between 8th and 14th weeks and who had regular follow-up were included in the study. Those with chronic or systemic disease, anomalies detected in their current pregnancy, multiple pregnancies, and pregestational diabetes were excluded from the study. The necessary ethical approval was obtained from our hospital's local ethics committee (decision number: 11).

Pregnancy week was calculated based on the last menstrual period and old and current ultrasonography findings. Pregnant women's anamnesis information at the time of first application was recorded to compare risk factors for GDM, identified in similar studies by the literature scanning. Age, gravida, parity, number of abortions, smoking, a previous GDM history, a family history of DM, a previous history of preeclampsia, a large baby birth history, a previous MFD (dead fetus) history, and a fetal anomaly history were all noted. The pregnant women's BMI was calculated by questioning their height and weight.

Our study's threshold values in OGTT were based on those proposed by Carpenter and Causton (Table 1).

Table 1: The values proposed by Carpenter and Causton

Plasma glucose (mg/dl) (h)	50 g screening test	100 g diagnostic test
Hunger	–	≥95
1st	≥140	≥180
2nd	–	≥155
3rd	–	≥140

50 g OGTT was applied to all pregnant women between 8th and 14th weeks included in the study. The study patients were divided into two groups as non-GDM and GDM based on venous plasma glucose values measured 1 h after 50 g of oral glucose load given to the patient after dissolving in 250 cc water, hungry or full, made at any time of the day. Non-GDM consisted of those with plasma glucose levels <140 mg/dl (considered normoglycemia) and plasma glucose levels between 140 and 200 mg/dl (considered abnormal glucose tolerance [AGT]), GDM group plasma glucose levels ≥200 mg/dl (considered GDM).

A 3 h 100 g OGTT was performed on those with AGT after 8 h of fasting and a proper diet. First, FBG was measured, then venous plasma glucose levels were measured at the 1st h, 2nd h, and 3rd h after 100 g of glucose dissolved in 250 cc of water were given to patients, followed by they diagnosed as GDM when they had at least two high values. Besides, in those with a single high value, 100 g OGTT was repeated in the second trimester of pregnancy (24th–28th weeks); those with at least two high values were diagnosed with GDM, a single high value was diagnosed with AGT. 50 g OGTT was repeated in the second trimester (24th–28th weeks) in the non-GDM group when the first trimester 50 g OGTT detected plasma glucose levels <140 mg/d; values of <140 mg/dl considered normal again. In contrast, we performed an additional 100 g OGTT on pregnant women with values of ≥140 mg/dl and <200 mg/dl, then managed them according to the above-mentioned diagnostic criteria; ultimately, we made a diagnosis of GDM in those with blood glucose level ≥200 mg/dl. HbA1c value was measured at the time of diagnosis in all pregnant women diagnosed with GDM and AGT. Eventually; results were analyzed and compared between the groups.

Statistical Analysis

In descriptive statistics of the data, mean, standard deviation, frequency, and ratio values were used. The data distribution was tested with Kolmogorov–Smirnov, and variables were analyzed using Kruskal–Wallis, Mann–Whitney U-test, and independent sample t-test. We performed the Chi-square test to analyze proportional data, the Fischer test when Chi-square conditions were not met. Logistic regression analysis was utilized to investigate the influence levels of variables. Statistical analysis of obtained data was performed using the SPSS 20.0 package program (IBM, Armonk, NY, USA).

RESULTS

In 22 of 153 pregnant women who were applied 50 g OGTT in the first trimester, a plasma glucose level >140 mg/dl was found. While 22 pregnant women were performed 100 g OGTT, 7 were diagnosed with GDM. The first and second trimesters 100 g OGTT values of the remaining 15 pregnant were as follows: Seven were within normal limits, five were diagnosed with GDM by repeating 100 g OGTT in the second trimester, and three with AGT by repeating 100 g OGTT in the second trimester, with a single high value. About 4.5% (7) of all pregnant women were diagnosed with GDM in the first trimester (Table 2).

In the second trimester, pregnant women, 21 of whom had abnormal test results (>140 mg/dl), were with a second trimester gestational week mean of 25.4. Of these 21 pregnant women who were 100 g OGTT applied, five were diagnosed with GDM, six had a single high value and were diagnosed as AGT, and ten had normal values (normoglycemia). About 6.5% (10) of a total of 153 pregnant women were diagnosed with GDM in the second trimester.

GDM, diagnosed in 4.5% (7) in the first trimester and 6.5% (10) in the second trimester, was detected in 11% (17) of the pregnant women in the study. About 5.8% (9) of 153 pregnant women were diagnosed with AGT. The first trimester and second-trimester OGTT screening and diagnostic test results between the study groups are presented in Table 2.

GDM, diagnosed in 41.2% in the first trimester and 58.8% second trimester, was found with a higher rate in pregnant women over 30 years (p=0.000 <0.05). There was no significant difference in terms of height, weight, BMI values, smoking rates, and 1st measurement weeks between group's non-GDM and GDM (p>0.05) (Table 3). Table 3 shows the comparison of risk factors between the study groups.

In GDM group, a previous GDM history (p=0.000 <0.05), a family history of DM (p=0.019 <0.05), a previous history of preeclampsia (p=0.001 <0.05), and FBG value (p=0.002 <0.05) were found with a significantly higher rate than non-GDM group (Table 4).

Table 2: First trimester and second-trimester OGTT screening and diagnostic test results between the study groups

	GDM group		Non-GDM group
	n	%	n
First trimester 50/100 g OGTT screening results	7	41.2	146
The first trimester high 50 g OGTT, normal 100 g OGTT, or AGT. Second trimester 100 g OGTT results	5	29.4	10
Second trimester 50/100 g OGTT screening results	5	29.4	126

OGTT: Oral glucose tolerance test; GDM: Gestational diabetes mellitus; AGT: Abnormal glucose tolerance.

Table 3: Comparison of risk factors between the Groups 1 (GDM absent) and 2 (GDM present) in pregnant women

	Non-GDM group			GDM group			p
	Mean±SD	n	%	Mean±SD	n	%	
Age	27.9±5.2			33.0±5.5			0.001
Age							
≤30		97	71.3		4	23.5	
30		39	28.7		13	76.5	0.000
Height	1.6±0.1			1.6±0.1			0.681
Weight	64.0±11.3			65.9±11.2			0.325
BMI	24.7±4.2			26.0±4.1			0.150
Smoking		15	11		1	6.3	1.000
First measurement week	11.1±2.2			12.1±1.4			0.082

Mann–Whitney U-test/t-test/Chi-square test (fisher test); GDM: Gestational diabetes mellitus; SD: Standard deviation; BMI: Body mass index.

Table 4: Comparison of a previous GDM history, a family history of DM, a previous history of preeclampsia, and FBG value between the study groups

	Non-GDM group			GDM group			p
	Mean±SD	n	%	Mean±SD	n	%	
A previous GDM history		2	1.5		8	47.1	0.000
A family history of DM		48	35.3		11	64.7	0.019
A previous history of preeclampsia		2	1.5		4	23.5	0.001
Fasting blood glucose value (mg/dl)	84.7±9.1			96.2±16.0			

Mann–Whitney U-test/ Chi-square test (fisher test); DM: Diabetes mellitus; FBG: Fasting blood glucose; SD: Standard deviation; GDM: Gestational diabetes mellitus.

It was observed that the number of pregnancies (gravida) and births (parity) was higher in the GDM group than in the non-GDM group. Furthermore, the GDM group tended to have a significantly higher birth rate of large babies (>4000 g) in the previous pregnancies than the non-GDM group (p=0.003 <0.05). The presence and number of abortions, a previous MDF history (dead fetus), and a fetal anomaly history did not significantly differ between groups (Table 5). Comparing the rates of gravida, parity, a large baby birth history, number of abortions, a previous MDF history (dead fetus), and a fetal anomaly history between the study groups are shown in Table 5.

We also compared pregnant women diagnosed with GDM and AGT to those with normoglycemia for the relevant variables, whose results were given below as the following. The mean age, the total number of pregnancies (gravida), number of abortions, number of births (parity), and a previous GDM history in pregnant women with GDM tended to be higher (p<0.05) than both those with normoglycemia and AGT. In those with GDM, the mean parity, a previous history of preeclampsia, a large baby birth history, a family history of DM, and the mean FBG were significantly higher (p<0.05) than those with normoglycemia. None of the variables made a significant difference between the normoglycemic and AGT patients (Table 6). Table 6 presents the analysis of risk factors among pregnant women with GDM, AGT, and normoglycemia.

Taken the effects of risk factors on GDM evaluated with univariate analysis, being over the age of 30 raised the risk of GDM in patients approximately 8 times. While having a family history of DM increased GDM risk in pregnant women by 3.3 times, an FBG level above 87.5 mg/dl increased approximately 5 times. A previous GDM history emerged as the factor that increased the risk the most and increased GDM risk by about 59 times. Again, a previous history of preeclampsia, one of the crucial diseases complicating pregnancy, also increased the risk of GDM approximately 20 times. A large baby birth history, a more typical result in pregnant women diagnosed with GDM, increased the GDM risk 13.6 times. In addition to these findings, while the gravida number being three and over raised the risk of GDM in pregnant women 6 times, this risk rose approximately 18 times in pregnant women, being multiparous (Table 7). Comparing the effects of risk factors on GDM with univariate analysis is demonstrated in Table 7.

Table 5: Comparing the rates of gravida, parity, a large baby birth history, number of abortions, a previous MDF (dead fetus) history, and a fetal anomaly history between the study groups

	Non-GDM group			GDM group			p
	Mean±SD	n	%	Mean±SD	n	%	
Number of pregnancies (gravida)	2.0±1.1			3.3±1.4			0.000
Gravida							
≤2		98	72.1		5	29.4	0.000
>3		38	27.9		9	70	
Number of births (parity)	1.5±0.6			1.9±0.8			0.019
Number of abortions	1.3±0.7			1.5±0.8			0.593
A large baby birth history		3	2.2		4	23.5	0.003
A previous MDF history (dead fetus)		3	2.2		2	11.8	0.095
A fetal anomaly history		2	1.5		1	5.9	0.299

Mann–Whitney U-test/Chi-square test (fisher test); GDM: Gestational diabetes mellitus; SD: Standard deviation.

Table 6: Analysis of risk factors among pregnant women with GDM, AGT, and normoglycemia

	Pregnant women with normoglycemia			Pregnant women with AGT			Pregnant women with GDM		
	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	n	%
Age	27.9±5.2*			27.9±5.2*			33.0±5.5		
Age									
≤30		91	71.7*		6	66.7*		4	23.5
>30		36	28.3		3	33.3		13	76.5
Height	1.6±0.1			1.6±0.0			1.6±0.1		
Weight	63.5±10.6			70.7±17.6			65.9±11.2		
BMI	24.5±3.9			27.7±6.9			26.0±4.1		
Gravida									
≤2		91	71.7*		7	77.8*		5	29.4
>3		36	28.3		2	22.2		12	70.6
Parity	1.5±0.6*			1.4±0.5			1.9±0.8		
Number of abortions	1.3±0.7				0	0	1.5±0.8		
A previous GDM history		2	1.6*		0	0.0*		8	47.1
A previous history of preeclampsia		2	1.6*		0	0.0		4	23.5
A large baby birth history		3	2.4*		0	0.0		4	23.5
A previous MDF (dead fetus) history		3	2.4*		0	0.0		2	11.8
A fetal anomaly history		2	1.6		0	0.0		1	5.9
Smoking		13	10.2		2	22.2		1	5.9
A family history of DM		45	35.4*		3	33.3		11	64.7
FBG (mg/dl)	84.3±9.2*			89.7±7.2			96.2±16.0		

*: Compared to GDM p<0.05. Kruskal–Wallis (Mann–Whitney U-test) Chi-square test (fisher test); GDM: Gestational diabetes mellitus; BMI: Body mass index; AGT: Abnormal glucose tolerance; SD: Standard deviation; DM: Diabetes mellitus; FBS: Fasting blood glucose.

Table 7: Comparing the effects of risk factors on GDM with univariate analysis

Univariate analysis	OR	%95 Confidence interval		p
		Lowest	Highest	
Age (>30/≤30)	8.083	2.482	26.324	0.001
A family history of DM	3.361	1.170	9.654	0.024
FBG (>87,5/≤87,5 mg/dl)	4.935	1.528	15.935	0.08
Gravida (>3/≤2)	6.189	2.043	18.752	0.001
Parity	18.000	2.322	139.564	0.006
A previous GDM history	59.556	10.988	322.790	0.000
A previous history of preeclampsia	20.615	3.441	123.515	0.001
A large baby birth history	13.641	2.750	67.675	0.001

Logistic regression, FBG: Fasting blood glucose; GDM: Gestational diabetes mellitus; OR: Odd ratios; DM: Diabetes mellitus.

Table 8: Comparing risk factors among pregnant women diagnosed with GDM by performing 50 g OGTT in the first trimester and second trimester

GDM	First trimester			Second trimester			p
	Mean±SD	n	%	Mean±SD	n	%	
Age	33.6±5.9			32.6±5.5			0.601
Height	1.6±0.1			1.6±0.1			0.669
Weight	68.1±14.5			64.3±8.7			0.601
BMI	27.4±5.1			25±3.2			0.315
Gravida	3.3±1.3			3.3±1.5			0.962
Parity	2.0±0.6			1.9±0.9			0.635
Abortion	1.3±0.6			1.7±1.2			1.000
A previous GDM history		3	42.9		5	50.0	1.000
A previous history of preeclampsia		2	28.6		2	20.0	1.000
A large baby birth history		1	14.3		3	30.0	0.603
A previous MDF (dead fetus) history		1	14.3		1	10.0	1.000
A fetal anomaly history		1	14.3		0	0.0	0.412
Smoking		0	0.0		1	10.0	1.000
A family history of DM		6	85.7		5	50.0	0.304
First measurement week	11.9±1.2			12.2±1.5			0.417
FBG (mg/dl)	105.9±18.7			89.5±10.2			0.109
First 50 g OGTT	170.3±11.9			139.9±25.9			0.014
HbA1c	6.3±0.6			6.0±0.3			0.364

Mann–Whitney U-test/Chi-square test (fisher test). FBG: Fasting blood glucose; GDM: Gestational diabetes mellitus; DM: Diabetes mellitus; BMI: Body mass index.

50 g OGTT values of pregnant women diagnosed with GDM in the first trimester appeared to be significantly higher than those in the second trimester. No other variable values and distributions showed significant differences between pregnant women diagnosed with GDM in the first trimester and second trimester. Comparing risk factors among pregnant women diagnosed with GDM by performing 50 g OGTT in the first trimester and second trimester are given in Table 8.

DISCUSSION

Seventeen (11%) of 153 pregnant women in our study were diagnosed with GDM; this rate has been reported about 7%, very variable, in the literature.[8] Our plausible conjecture on this result is that we associated this high GDM diagnosis with our study center being the reference hospital.

The IADPSG has informed that early screening should be determined according to that region's conditions and abnormal glucose metabolism. However, the ADA and ACOG have recommended it to the group with risk factors for undiagnosed Type 2 diabetes.[7] It has also been advocated to screen pregnant women with negative screening tests in early pregnancy again between 24th and 28th weeks.[7–9] In our study, 41.2% of GDM cases[7] were diagnosed in the first trimester and 58.8% (10) in the second trimester. In pregnancy, the optimal time interval for screening for GDM is still a controversial issue. As a general hypothesis, insulin sensitivity decreases with advancing gestational age, and insulin resistance increases in cells. Due to this mechanism that develops due to pregnancy's physiological and hormonal changes, advancing pregnancy weeks have been considered more suitable weeks for diagnosing GDM. Therefore, at 24th–28th weeks of gestation, the glucose screening test has been widely preferred for use.[12]

GDM prevalence in the first trimester varies between 1% and 22%.[13] Yeral et al.,[14] in their study, using FBG, 50 g glucose two-step screening test, and 75 g glucose screening test, investigated the rates of GDM detection in the first trimester. It was determined as 5% in FBG, 6% in 50 g double-step screening test, and 10% in the 75 g screening test, respectively. In our study, 4,5% of the pregnant women were diagnosed with GDM with a double-step 50 g OGTT performed in the first trimester. Dashora et al.[15] aimed to diagnose GDM in the early weeks by applying 75 g OGTT at 2-month intervals until the 28th week to 564 pregnant women in a high-risk group for GDM. Besides, in 88% of pregnant women diagnosed with GDM, a GDM diagnosis was made with this method before the 28th weeks.

We used the 50 g double-step OGTT test in our trial and made a GDM diagnosis in the first trimester in 41.5% of those diagnosed with GDM. In the study published by Palatnik et al.,[16] evaluating 19 thousand pregnant women, perinatal outcomes were evaluated in pregnant women diagnosed with GDM with screening and diagnostic tests at different gestational weeks. In pregnant women who had screening tests in five different groups, including those at 24th–26th weeks, 27th, 28th, 29th, and at weeks over 30, it was stated that GDM diagnosis was made more frequently as the gestational week progresses. Approximately 30% of pregnant women with GDM diagnosis consisted of the group diagnosed at 30th weeks and over; however, no significant difference was found between those diagnosed and treated in earlier weeks and those diagnosed and treated in latter weeks regarding perinatal outcomes. Despite these results, it was striking that pregnant women diagnosed with GDM and treated at an earlier week tended to experience significantly less gestational hypertension and preeclampsia than those who were not. Our research did not assess pregnant women's perinatal outcomes; although the number of cases was small, we could diagnose about 41% of pregnant women in the early gestational weeks. American Disease Prevention Committee (USPSTF) published their suggestions in 2014 that treatment started right after early diagnosis can prevent maternal and fetal complications.[7] Considering that 4.5% of our study patients and 41.5% of pregnant women diagnosed with GDM had a GDM diagnosis made in the first trimester, our paper further contributes to the literature by revealing that a significant proportion of GDM diagnoses can be established with screening, especially in a risky group.

It is of high interest to note in the present study that 50 g first trimester OGTT values of GDM patients differed significantly between those who were diagnosed in the first and second trimesters (p=0.014). Whereas the mean 50 g OGTT value was 170 mg/dl in those diagnosed in the first trimester, it was 140 mg/dl in those diagnosed in the second trimester.

Sesmilo et al.,[17] in their studies elucidating the role of the first-trimester FBG levels in GDM diagnosis and investigating its effects on maternal and perinatal outcomes, reported that when the FBG level rose above 88 mg/dl, the risk of GDM increased 2.5 times. It was also found that pregnant women with a blood glucose level of more than 88 mg/dl were more likely to have a large baby (>4000 g) birth than those with between 79 and 87 mg/dl. In support of these results, as mentioned above, the HAPO study investigating the negative effects of hyperglycemia on pregnancy suggested that when FBG values were above 95 mg/dl, fetal macrosomia risk increased 4–6 times.[18] Our study revealed that, in the GDM group, the mean FBG level was 96 mg/dl, while this rate was statistically significantly lower in the non-GDM group than the GDM group. Again, looking at a large baby birth history, it was observed at 23% in the GDM group and 2% in the non-GDM group. In this sense, having a large baby birth history increased the risk of GDM in pregnant women up to 13 times. In many previous studies, FBG value has been significantly higher in patients with GDM than in those without it. Thus, blood glucose levels must be quickly controlled in the early period to prevent the increase of maternal and fetal complications. Our study also supports that FBG limit values should be taken under control early and withdrawn below 90–95 mg/dl, similar to other studies.

One of the biochemical values auxiliary to diagnosing GDM in the first trimester is HBA1c. Some authors argue that complications due to GDM can be prevented with the initiation of treatment according to the HBA1c values checked in the early period and that GDM can be cured earlier. With defining the values between 5.7% and 6.4% as prediabetes, Osmundson et al.,[19] in their study evaluating 5700 pregnant women, determined the value of 6.5% HBA1c as the limit value in the diagnosis of GDM. Besides, they emphasized that patients' HBA1c values were in the prediabetic range, 29% of pregnant women who were applied OGTT were diagnosed with GDM, and in those with HBA1c values lower than 5.4%, this diagnosis rate was identified as 14%. Similarly, in another study conducted in Australia, in those with normal 75 g OGTT values but HBA1c values higher than 5.9%, GDM development rates were established to be higher in later gestational weeks, and perinatal outcomes were also shown to be negatively affected.[20] In our trial, while the mean of HBA1c value in pregnant women diagnosed with GDM in the first trimester was 6.3%, it was detected as 6% in those diagnosed in the second trimester, concluding no statistically significant difference existed. We could not compare HBA1c values among the patients with and without GDM because HBA1c values of those without GDM were not

among our data. However, in line with literature data, we noticed a mean value of 6% and above in GDM.

This research, additionally, aims to show the effect of risk factors on GDM and elucidate the role of early screening in those with risk factors. In the current study, as the next step, a previous GDM history was found at a rate of 47% in the GDM group and 1.5% in the non-GDM group ($p<0.05$). Schwartz et al.,[21] too, in their meta-analysis posted, reported the recurrence rate in those with a previous GDM history as 48%, similar to our data.

The ACOG and the ADA have also recommended early screening by evaluating pregnant women with a previous GDM history as a risky group; these suggestions are compatible with our data and support our study's findings.[8]

Another result we put forward is that a previous history of preeclampsia significantly increases the risk of GDM approximately 20 times ($p=0.001$), with being seen in the GDM group as 23.5%, while in the non-GDM group as 1.5%. In a study by Lee et al.[22] in 2017, in pregnant women with preeclampsia in previous pregnancies, the GDM detection rate in subsequent pregnancies was higher, similar to our study.

When we look at the gravida-parity rates in the GDM group, we found gravida and parity rates to be higher than those in the non-GDM group, similar to the literature.[23]

In the present study, while a family history of diabetes mellitus was detected in 64.7% of pregnant women in the GDM group, this rate was 35.3% in those in the non-GDM group ($p=0.019$). Similarly, the research conducted by Kim et al.[24] on 4500 women showed that the presence of a diabetes history in any first-degree relative increased the risk of GDM by 3–7 times.

As a result, about half of the pregnant women with GDM have been diagnosed in the first trimester, with the ideal time remains a controversial issue in screening for GDM. If pregnant women, especially in the risk group, could be diagnosed by performing OGTT in the early period, we strongly consider that fetal and maternal morbidity and mortality would be prevented. This article, therefore, provides some critical knowledge and insights into the literature on GDM screening in early pregnancy and an overview of the published scientific evidence within this crucial research field. However, due to its retrospective nature and a relatively small number of cases, it is clear that our study results should be interpreted with caution and enlightened with further and more extensive, prospective clinical studies, shedding light on this topic.

Statement

Ethics Committee Approval: The Zeynep Kamil Women and Children Diseases Training and Research Hospital Research Ethics Committee granted approval for this study (date: 20.07.2012, number: 11).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – HT, EK; Design – HT; Supervision – EK, EÇ; Resource – EK, EÇ, HT; Materials – EK, EÇ, HT; Data Collection and/or Processing – HT, ZB, SE; Literature Search – HT, ZB, SE; Writing – HT, ZB; Critical Reviews – EK, EÇ.

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ORIGINAL ARTICLE

The value of measurement of vaginal fluid creatinine and beta-human chorionic gonadotropin in the diagnosis of premature rupture of membranes

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ABSTRACT

Objective: The purpose of the present study is to evaluate β-human chorionic gonadotropin (β-hCG) and creatinine levels in the vaginal fluid regarding to diagnosis of premature rupture of membranes (PROM).

Material and Methods: This study was conducted on 150 pregnant women in the third trimester (28–40 weeks). The patients were grouped as: (1) PPROM group (75 cases) and (2) intact membranes as control group (75 cases). Three milliliters of sterile normal saline were inserted into the posterior fornix of the vagina and then vaginal fluid was aspirated. Creatinine and β-hCG levels in the vaginal fluid were measured β-hCG and creatinine levels were compared between the two groups.

Results: The mean vaginal fluid level in Groups 1 and 2 was 0.60±0.72 (0.37) and 0.22±0.11 (0.2) for creatinine and β-hCG which was positive in 411.69±605.65 (146) and 12.71±24.63 (3.9), respectively. There was a statistically significant difference regarding to mean creatinine and β-hCG levels between two groups ($p<0.001$). Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were all 66.67%, 96%, 94.3%, 74.3%, and 81.3% for creatinine and 94.6%, 82.6%, 84.52%, 93.94%, and 88.67% for β-hCG in detecting PROM with a cutoff value of 0.21 mg/dl for creatinine and 16 mIU/ml for β-hCG.

Conclusion: Measuring of β-hCG level in vaginal fluid is accurate, cheap, and simple methods in the diagnosis of PROM. Furthermore, measuring of creatinine level is a simple and accurate method with a lower sensitivity and accuracy than for β-hCG.

Keywords: Creatinine, premature rupture of membranes, β-human chorionic gonadotropin.

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INTRODUCTION

Premature rupture of membranes (PROM) is rupture of the fetal membranes before the onset of labor and disruption of amniotic membrane integrity. If the disruption in the membranes occurs before 37 weeks of gestation, it is defined as preterm PROM (PPROM). PROM is seen in 10% of all pregnancies and 80% of the cases occur in term pregnancy.[1] PPROM accounts for 3–5% of all pregnancies and is the most common cause of preterm birth.[2] Fetal membranes are more resistant to rupture in early pregnancy. As the gestational age progresses, the membranes begin to weaken and uterine contractions, fetal movements, and increased uterine tension facilitates the rupture of the membranes.[3] In addition, the decrease in the amount of collagen in the membranes near-term increases the risk of rupture. The most important complication of PPROM is preterm birth and related prematurity.[4] Due to the possible complications, it is important to make an accurate diagnosis of PROM. Misdiagnosis of membrane rupture also causes incorrect interventions such as labor induction and prolonged hospital stay. At present, there is no non-invasive, gold standard diagnostic method for the diagnosis of PROM. Direct monitoring of fluid discharge from the cervical os confirms PROM.[5] While the transition of nitrazine paper placed in the vaginal posterior fornix from yellow to dark blue can detect the presence of amniotic fluid in the vagina, many factors such as vaginitis, blood, and semen increase the false positivity rate of the test.[6] Detection of fetal fibronectin in cervicovaginal secretions has been interpreted as a harbinger of labor even in the absence of membrane rupture, with extremely high specificity, but low sensitivity.[7] Another diagnostic method is the detection of insulin-like growth factor (insulin-like growth factor binding protein-1 [IGFBP-1]), which binds to protein-1 and placental alpha microglobulin-1 protein (PAMG1) in cervicovaginal fluids.[8,9] Detection of the PAMG1 in cervicovaginal fluids has high sensitivity and specificity, but the test is not accessible in most centers and is an expensive test. Therefore, alternative tests have been developed and many molecules in the cervicovaginal fluid have been studied.[10]

β-human chorionic gonadotropin (hCG) is found in maternal blood and urine, as well as amniotic fluid.[11] Creatinine is a substance that is excreted by the kidneys. Since most of the amniotic fluid consists of fetal urine, studies have been conducted to investigate the place of creatinine in vaginal washing fluid in the diagnosis of PROM.[12]

In this study, we aimed to determine the place and reliability of β-hCG and creatinine values in the cervicovaginal fluid in the diagnosis of PROM.

MATERIAL AND METHODS

This study was carried out in the delivery room and obstetrics emergency outpatient clinic of Zeynep Kamil Obstetrics and Gynecology Training and Research Hospital. The ethics committee approval was obtained from the Zeynep Kamil Obstetrics and Gynecology Training and Research Hospital in 2014. The study was defined to have a cross-sectional design. Between May 2014 and November 2014, a total of 150 cases who had been admitted to the emergency delivery room with suspected membrane rupture and hospitalized with confirmed diagnosis of membrane rupture with speculum examination or PAMG-1 test, and cases in the same age group who had been admitted to the emergency delivery room for other reasons and had no vaginal bleeding and vaginal infection, and who had not had intercourse for 3 days, with confirmation of no membrane rupture, were included in the study.

Patients were divided into two groups: 75 patients with confirmed membrane rupture and 75 patients without membrane rupture.

During the routine vaginal examination of the patients, 3 cc sterile saline was injected into the posterior fornix with a speculum and aspirated with the same injector and sent to the biochemistry laboratory for β-hCG and creatinine evaluation. The β-hCG and creatinine values obtained in both groups were compared.

Statistical Analysis

When evaluating the findings obtained in the study, the IBM SPSS Statistics 15 (SPSS IBM, Turkey) program was used for the statistical analysis. While evaluating the study data, besides the descriptive statistical methods (mean, standard deviation, and frequency), for comparison of the quantitative data, the Student's t-test was used for comparison of the normally distributed parameters between two groups, and the Mann–Whitney U-test was used for comparison of parameters that were not normally distributed between two groups. The Chi-square test was used to compare the qualitative data. The diagnostic accuracy of each test was evaluated with the true- and false-positive rates (sensitivity and [1-specificity]) using the receiver operating characteristic (ROC) curve analysis. In addition, the area under the ROC curve (AUC) with a 95% confidence interval (CI) was calculated for each test. The most suitable cutoff points were selected based on the ROC curve analysis. Diagnostic screening tests were used to calculate the sensitivity and specificity. Significance was evaluated at $p<0.05$.

RESULTS

The study was conducted between May 2014 and November 2014 with a total of 150 female cases, with ages ranging from 16 to 42 years. The mean age of the cases was 27.95±6.06 years. The number of pregnancies of the cases ranged from 1 to 8, with a mean value of 2.34±1.52, and with a median value of two pregnancies. The duration of gestation varied between 198 days and 280 days, with a mean value of 258.39±22.01 days and a median of 262 days. The cervical openings of the cases varied between 1 cm and 7 cm, with a mean value of 1.81±1.31 cm and a median of 1 cm. The amniotic fluid index ranged from 20 mm to 260 mm, with a mean value of 101.16±35.74 mm and a median of 100 mm. The β-HCG levels of the cases ranged from 1.2 mIU/ml to 3350 mIU/ml, with a mean value of 212.20±471.74 mIU/ml and a median of 29.6 mIU/ml. The creatinine levels of the cases ranged from 0.2 mg/dl to 4.66 mg/dl, with a mean value of 0.41±0.55 mg/dl and a median of 0.2 mg/dl. While it was PROM (+) in 75 (50%) of the cases, it was PROM (–) in 75 (50%) of the cases.

While 70 of the cases (46.7%) had no history of previous birth, 50 (33.3%) had a history of normal spontaneous birth and 30 (20%) had a history of cesarean section. While 70 (46.7%) of the cases were nulliparous, 80 (53.3%) of them were multiparous (Table 1).

Table 1: Evaluations related to PROM

	PROM (+)			PROM (–)			p
	Mean±SD (Median)	n	%	Mean±SD (Median)	n	%	
[1]Age	27.34±5.94			28.56±6.17			**0.222**
[2]Number of pregnancy	2.29±1.59 (2)			2.39±1.46 (2)			**0.428**
[2]Pregnancy duration	260.7±21.33 (265)			255.81±22.51 (259)			**0.078**
[2]Cervical opening	2.29±1.54 (2)			1.32±0.79 (1)			**0.001***
[2]Amniotic fluid index	93.32±37.13 (100)			109.00±32.69 (110)			**0.004***
[3]Previous birth							**0.001***
Normal spontaneous delivery		32	42.7		18	24	
C/S		6	8		24	32	
No births		37	49.3		33	44	
[3]Parity							**0.513**
Nulliparous		37	49.3		33	44	
Multiparous		38	50.7		42	56	

PROM: Premature rupture of membranes; SD: Standard deviation; 1: Student's t-test; 2: Mann–Whitney U-test; 3: Chi-square test; *: P<0.01.

Table 2: Evaluation of β-HCG and creatinine according to PROM

	PROM (+) Mean±SD (Median)	PROM (–) Mean±SD (Median)	p
β-hCG	411.69±605.65 (146)	12.71±24.63 (3.9)	**0.001***
Creatinine	0.60±0.72 (0.37)	0.22±0.11 (0.2)	**0.001***

Mann–Whitney U-test; PROM: Premature rupture of membranes; SD: Standard deviation; β-hCG: β-human chorionic gonadotropin; *: P<0.01.

There was no statistically significant difference between the PROM (+) cases and the PROM (–) cases in terms of mean age, number of pregnancies, and duration of gestation (p>0.05). The cervical opening rates of the cases with PROM (+) were found to be statistically significantly higher than the cases with PROM (–) (p: 0001; p<0.01). The amniotic fluid index level of the cases with PROM (+) was found to be statistically significantly lower than cases with PROM (–) (p: 0.004; p<0.01).

There was a statistically significant difference between the previous delivery types of cases with PROM (+) and cases with PROM (–) (p: 0.001; p<0.01). In cases with PROM (+), the rate of normal spontaneous delivery of the previous delivery type was significantly higher than the cases with PROM (–), and in cases with PROM (–), the rate of previous delivery being C/S was significantly higher than cases with PROM (+). There was no statistically significant difference between the parity distributions of the cases with PROM (+) and the cases with PROM (–) (p>0.05) (Table 1).

The β-hCG level of the cases with PROM (+) was found to be statistically significantly higher than the cases with PROM (–) (p: 0001; p<0.01). The creatinine level of the cases with PROM (+) was found to be statistically significantly higher than the cases with PROM (–) (p: 0001; p<0.01) (Table 2).

In determining the cutoff point for β-hCG, diagnostic screening tests and sensitivity and specificity calculations were made for different points at regular intervals and the ROC curve was drawn. The area under the curve value was 0.963 (AUC: 0.963; 95% CI: 0.936–0.989) (Fig. 1). The cutoff values for β-hCG were calculated separately. When the cutoff value for β-hCG was taken as 16 mIu/ml, the sensitivity and specificity were determined as 94.67% and 82.67%, and the accuracy rate as 88.67% (Table 3).

In determining the cutoff point for creatinine, diagnostic screening tests and sensitivity and specificity calculations were made for different points at regular intervals and the ROC curve was drawn. The area under the curve value was 0.813 (AUC: 0.813; 95% CI: 0.741–0.885) (Fig. 2). The cutoff point determined for creatinine in PROM diagnosis was 0.21. The sensitivity of this value was 66.67% and the specificity was 96% (Table 4).

DISCUSSION

PPROM is one of the most common causes of fetal morbidity and mortality. For this reason, it is important to make a correct diagnosis in PPROM, to prevent possible complications, and to reduce the length of stay in the hospital in case of a wrong diagnosis. Fluid drainage from the cervical os is observed in the speculum examination in the majority of patients admitted to the hospital with the complaint of vaginal discharge. The remaining patient group, that is, patients with no fluid discharge at the time of examination, constitutes the main difficulty in the diagnosis of PROM. Similar methods such as nitrazine (pH) test and the fern test, which have been used frequently in the diagnosis of PROM until today,

Table 3: Cut-off point detection for β-human chorionic gonadotropin

Value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
4	100.00	50.67	66.96	100.00	75.33
5	100.00	56.00	69.44	100.00	78.00
6	100.00	61.33	72.12	100.00	80.67
7	98.67	61.33	71.84	97.87	80.00
8	98.67	64.00	73.27	97.96	81.33
9	96.00	65.33	73.47	94.23	80.67
12	96.00	69.33	75.79	94.55	82.67
13	96.00	73.33	78.26	94.83	84.67
14	94.67	76.00	79.78	93.44	85.33
15	94.67	77.33	80.68	93.55	86.00
16	94.67	82.67	84.52	93.94	88.67
21	93.33	84.00	85.37	92.65	88.67
22	92.00	85.33	86.25	91.43	88.67

Table 4: Cut-off point detection for creatinine

Value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
0.21	66.67	96.00	94.34	74.23	81.33
0.22	61.33	96.00	93.88	71.29	78.67
0.25	60.00	96.00	93.75	70.59	78.00
0.28	57.33	96.00	93.48	69.23	76.67
0.3	53.33	97.33	95.24	67.59	75.33
0.35	52.00	97.33	95.12	66.97	74.67
0.4	46.67	97.33	94.59	64.60	72.00

do not have sufficient reliability and there is still no non-invasive gold standard method, and this has led to the search for new tests IGFBP-1, alpha-fetoprotein, prolactin, fibronectin, β-hCG, and PAMG1. Although the sensitivity and specificity of the PAMG1 test are high, the difficulty for accessibility and its high cost limit its use. In addition to these tests, the presence of urea, creatinine, AST, and ALT, which have been proven to be present in amniotic fluid and in vaginal washing fluid, has been attempted to be used in the diagnosis of PROM.

In the second and third trimesters, most of the amniotic fluid consists of fetal urine. Creatinine filtered from fetal kidneys passes into amniotic fluid through urine. β-hCG is also a substance produced by trophoblastic tissue, found in different concentrations in maternal blood, urine, and amniotic fluid, and is easy to detect.[13] The

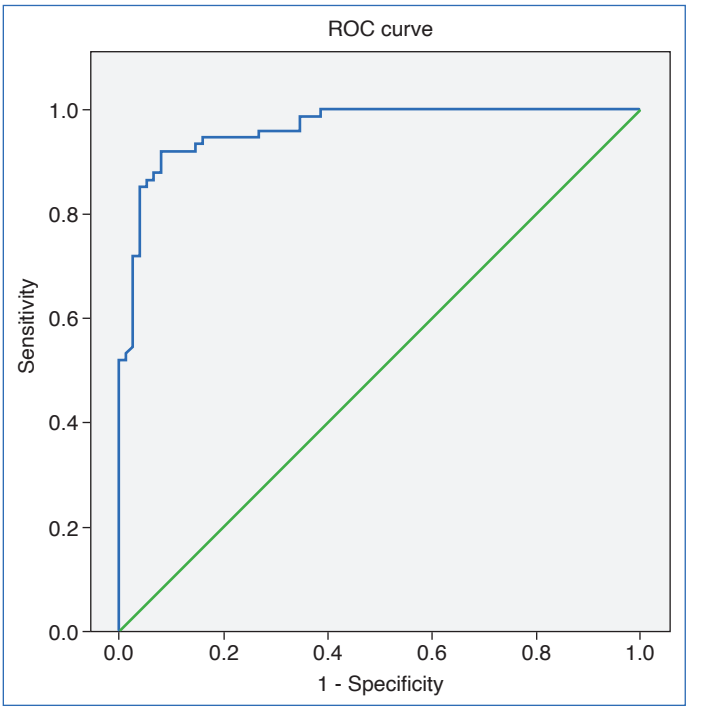

Figure 1: Receiver operating characteristic curve for β-human chorionic gonadotropin.

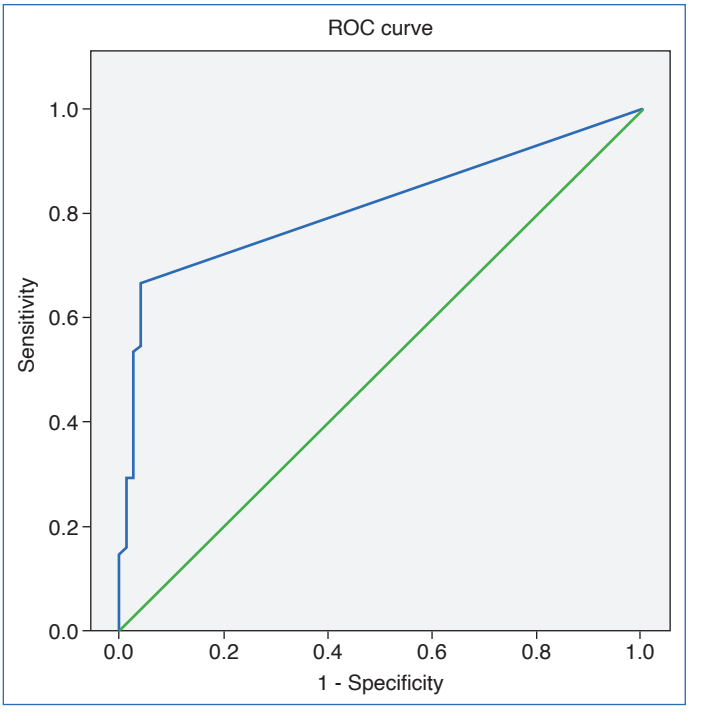

Figure 2: Receiver operating characteristic curve for creatine.

presence of these two substances in low concentrations in vaginal secretions and the increase in the concentration in the vagina after amniotic drainage in PROM means that the use of these substances may be appropriate in the diagnosis of PROM. In our study, we investigated the place of β-hCG and creatinine values in vaginal

washing fluid in the diagnosis of PROM. In our study, we found that β-hCG values and creatinine values in the vaginal washing fluid in the PROM group were statistically significantly higher than the non-PROM group (p<0.001).

In the study conducted by Ghasemi et al.[10] in 2016, it was found that prolactin and β-hCG in vaginal washing fluid had higher sensitivity than urea and creatinine in the diagnosis of PROM. In this study, despite the high sensitivity and specificity of the PAMG1 test, the accessibility and cost were shown as disadvantages. It has been emphasized that β-hCG can be used in the diagnosis of PROM in suspicious cases.

In the study conducted by Cooper et al.,[14] when the beta-hCG cutoff value in the vaginal washing fluid was determined as 50 mIU/mL for the diagnosis of PROM, the sensitivity, specificity, and negative and positive predictive values (PPVs) were found to be 96%, 79%, 95%, and 84%, respectively. In this study, it was found that β-hCG can be used in the diagnosis of PROM.

In the study conducted by Zanjani et al.,[13] when the creatinine cutoff value in the vaginal washing fluid was determined as 0.5 mg/dl for the diagnosis of PROM, the sensitivity, specificity, and negative and PPVs were found to be 96.7%, 100%, 100%, and 96.8%, respectively. In this study, it was found that creatinine could be used in the diagnosis of PROM.

In the study conducted by Ahmed Mohamed et al.,[15] β-hCG, creatinine, and urea were examined in vaginal washing fluid for the diagnosis of endoscopic mucosal resection (EMR). The cutoff values for β-hCG and creatinine were determined as 20 mIU/ml and 0.31 mg/dl. The sensitivity, specificity, and negative and PPVs for β-hCG were determined as 83%, 100%, 100%, and 85.6%, respectively. The sensitivity, specificity, and negative and PPVs for creatinine were determined as 100%, 100%, 100%, and 100%, respectively. In this study, it was found that β-hCG and creatinine could be used in the diagnosis of PROM.

In the study conducted by Tığlı et al.,[16] β-hCG, creatinine, and urea were examined in the vaginal washing fluid for the diagnosis of PROM, and the cutoff values for β-hCG and creatinine were taken as 50 mIU/ml and 0.30 mg/dl. The sensitivity, specificity, and negative and PPVs for β-hCG were determined as 85.3%, 93.3%, 92.7%, and 86.4%, respectively. The sensitivity, specificity, and negative and PPVs for creatinine were determined as 46.6%, 94.6%, 83.7%, and 63.9%, respectively. In this study, it was found that β-hCG was superior to other parameters in the diagnosis of PROM.

A study published in 2019 found that the use of creatinine in the vaginal washing fluid could be used with 94.4% sensitivity and 93.3% specificity. In this study, it was stated that although the PAMG1 test was the gold standard in today's conditions, its high cost and having difficulty in transportation led to the search for new tests.[17]

In our study, when we determined the β-hCG cutoff value in the vaginal washing fluid as 16 mIU/dL, the sensitivity, specificity, PPV, negative predictive value (NPV), and the accuracy rate were found as 94.67%, 82.67%, 84.62%, 93.94%, and 88.67%, respectively. When we determined the cutoff value of creatinine in the vaginal washing fluid as 0.21 mg/dL, we found the sensitivity, specificity, PPV and NPV, and the accuracy rate as 66.67%, 96%, 94.34%, 74.23%, and 81.33%, respectively.

As a result, we determined that the β-hCG value in the vaginal washing fluid could be used in the diagnosis of PROM. Although creatinine can also be used for diagnosis, it has a lower sensitivity and accuracy rate than β-hCG.

When we set the cutoff value for β-hCG as 16 mIU/dL, we obtained similar results to other EMR diagnostic tests, in accordance with the literature.[13–19] Compared to these tests, the fact that β-HCG measurement in vaginal fluid is cheaper, availability, and easy applicability indicates that this test can be used as an alternative to other expensive tests for the diagnosis.

Statement

Ethics Committee Approval: The Zeynep Kamil Obstetrics and Gynecology Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 23.05.2014, number: 85).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – ZB; Design – ZB, GÜ; Supervision – GÜ, MK; Resource – ZB, KS; Materials – ZB, GŞ; Data Collection and/or Processing – ZB, MK; Analysis and/or Interpretation – GŞ, KS; Literature Search – ZB, GÜ; Writing – ZB, KS; Critical Reviews – ZB, MK.

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

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ORIGINAL ARTICLE

Prenatal diagnosis and management of hypoplastic left heart syndrome: Single center results

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ABSTRACT

Objective: Hypoplastic left heart syndrome (HLHS) is the most common reason for neonatal deaths among congenital heart defects. Numerous studies showed that prenatal diagnosis improves prognosis. We aimed to review the prenatal assessment of associated extracardiac anomalies, postnatal outcomes, and surgical management in cases of HLHS that were detected in our center.

Material and Methods: The records of patients diagnosed with HLHS evaluated between March 2017 and April 2020. A detailed anatomy scan was performed, and karyotype analysis was recommended to all patients. Due to poor perinatal prognosis, termination of pregnancy (TOP) was offered an option to families. Serial ultrasonographic examinations every 2–4 weeks. Postnatal echocardiography was performed, and the prenatal diagnosis was confirmed in all offspring. Surgical outcomes were recorded.

Results: Sixteen patients were recruited in our study. The mean gestational age at diagnosis was 20.2±5.1 weeks. About 68.7% of cases were defined as classical type HLHS, and the remaining 31.3% were determined as variant type HLHS. TOP was performed in 9 (56.7%) patients. The mean follow-up interval was 16.4±4.7 months. Urge septostomy was performed in 2 (28.5%) cases after birth due to foramen ovale restriction. Three (42.8%) cases died before the first operation. Norwood procedure was performed in 4 (57.1%) cases. Two cases died after this operation. Glenn shunt and Fontan procedure were performed in the remaining two offspring. The total survival rate was 28.5%.

Conclusion: HLHS has high perinatal morbidity and mortality. Prenatal diagnosis allows the family for the fate of pregnancy and planned delivery in a tertiary center.

Keywords: Echocardiography, heart, mortality, prenatal.

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INTRODUCTION

Hypoplastic left heart syndrome (HLHS) is a complex cardiac anomaly that causes systemic perfusion failure by the left ventricle. Anatomically, various pathologies may lead to HLHS. Due to atresia of the mitral valve and aortic valve, the left ventricular cavity may completely absent, or the hypoplastic development of the aortic and mitral valve may allow the evolution of a small left ventricular cavity. Ascending aorta and aortic arch hypoplasia or aortic coarctation are associated with HLHS.[1]

HLHS has a frequency of 2–3/10,000 live births and constitutes 3–4% of all cardiac anomalies.[2,3] It is 50% more frequently in male babies than girls.[4] Although it is a rare cardiac anomaly, HLHS solely is responsible for 40–50% of cardiac deaths.[5] Non-cardiac anomalies are associated with 5–30% of cases, and the most common anomalies are the central nervous system, gastrointestinal system, and renal system malformations. Chromosomal anomalies are detected in 5–10% of cases, and trisomy 13–18 and monosomy X (Turner syndrome) are most common aneuploidies.[6] Rarely, it may be associated with microdeletion syndromes such as Williams-Beuren syndrome (7q11.23 deletion) and DiGeorge syndrome (22q11.1 deletion).

However, HLHS constitutes a small group of all cardiac anomalies; it is one of the most common cardiac anomalies in the prenatal period. Unlike conotruncal anomalies, an abnormal four-chamber view of the fetal heart seems to be the main factor facilitating the diagnosis. The most common finding in prenatal ultrasonography is the absence of the left ventricle in four-chamber view or the presence of a hypoplastic, hypocontractile, and hyperechogenic left ventricle. Numerous studies indicated that prenatal diagnosis had improved neonatal outcomes.[7]

In this study, we aimed to evaluate the prenatal findings and postnatal outcomes of the cases diagnosed prenatally with HLHS in our clinic.

MATERIAL AND METHODS

Our study was carried out in the Perinatology Department of Van Training and Research Hospital between March 2017 and April 2020. Diagnosis of HLHS was achieved in those findings: (1) In the apical four-chamber view of the heart, the left ventricle is absent, or there was a small and hyperechogenic left ventricle with reduced contractility. (2) The apex of the heart was formed by the right ventricle. (3) No transition from the mitral valve to the left ventricle in color Doppler evaluation. (4) The foramen ovale flap was placed by opening from right to left instead of from left to right (Fig. 1). Furthermore, the absence of the aorta in the three-vessel trachea plan and the aortic arch filling with a reverse flow from the ductal arch in the color Doppler examination confirmed the diagnosis (Fig. 2). Cases with no visible left ventricle in the apical four-chamber examination were defined as classical type HLHS. In contrast, cases with a hyperechogenic and hypocontractile left ventricle were determined as variant type HLHS due to stenosis of the aortic and mitral valve. In all cases, prenatal diagnosis was confirmed with a consensus of perinatologist and pediatric cardiology specialist. After the diagnosis, a detailed fetal anatomic evaluation was performed in all cases to rule out extracardiac anomalies, and karyotype analysis was recommended. Due to poor neonatal prognosis, the option of termination of pregnancy (TOP) was offered to families in all cases. Serial follow-up was performed every 2–4 weeks in cases wishing to continue the pregnancy. All women were delivered in tertiary care centers. Echocardiography was performed in all cases after birth, and the diagnosis of HLHS was confirmed. Long-term surgical procedures and survival rates of the cases were recorded. Statistical analysis was performed using SPSS version 24 (Statistical Package for the Social Sciences, IL, USA). Results were expressed as mean and standard deviation.

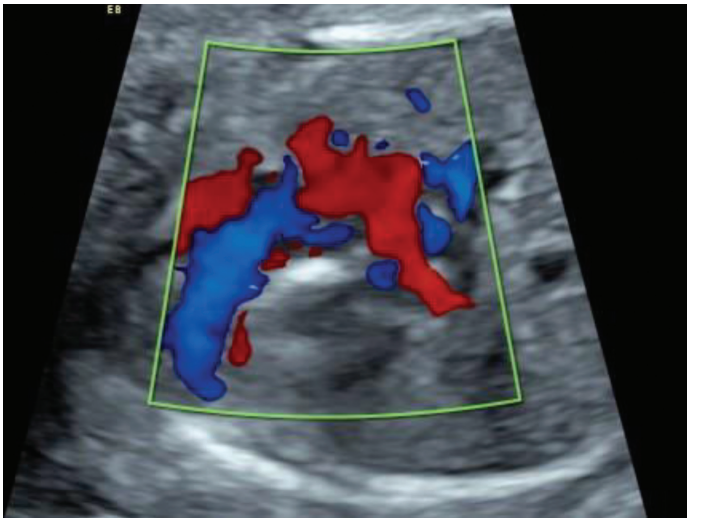

Figure 1: There is no filling of the left ventricle in color Doppler examination and left ventricle hypoplasia is observed in 26 weeks of gestation.

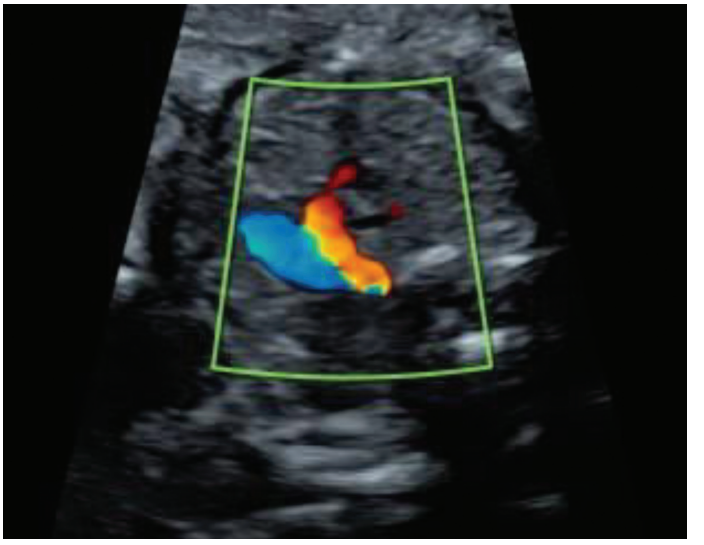

Figure 2: Reverse flow in the aortic arch in three-vessel trachea view in a 19-week fetus.

RESULTS

We recruited 16 cases during the study period. Mean maternal age was 25.6±5.2 years, and mean gestational age at diagnosis was 20.2±5.1 weeks. About 68.7% of fetuses were defined as classi-

Table 1: Prenatal features of 16 cases

Variable	n=16 (%)
Maternal age (years)	25.6±5.2
Gestational age at diagnosis (weeks)	20.2±5.1
HLHS type	
Classical	11 (68.7)
Variant type	5 (31.3)
Nuchal translucency (mm)	3.2±1.1
Karyotype analysis	8 (50)
Extracardiac anomaly	2 (12.5)
Foramen ovale restriction	2 (12.5)
TOP	9 (56.2)

TOP: Termination of pregnancy.

Table 2: Outcome of seven cases who survived in neonatal period

Variable	n=17 (%)
Gestational age at birth (weeks)	37.4±2.1
Birth weight (grams)	2530±355
Route of delivery	
Vaginal	2 (28.5)
Cesarean	5 (71.4)
Sex	
Male	4 (57.1)
Female	3 (42.9)
Foramen ovale restriction	2 (28.5)
Follow-up period (months)	16.4±4.7
NICU stay (day)	86±23
Neonatal death	3 (42.8)
Norwood procedure	4 (57.1)
Glenn shunt	2 (28.5)
Fontan procedure	2 (28.5)
Overall survival	2 (28.5)

NICU: Neonatal intensive care unit.

cal type HLHS and 31.3% as variant type HLHS. The mean nuchal translucency measurement of cases was 3.2±1.1 mm in the first trimester. Karyotype analysis was performed in 8 (50%) cases, and normal karyotype was found in all patients. An extracardiac anomaly was observed in 2 cases (12.5%), including 1 case with unilateral renal agenesis and 1 case with unilateral pes equinovarus. Foramen ovale restriction was revealed in the prenatal period in (31.3%) of the fetuses. TOP was performed in 9 (56.7%) cases. The mean gestational age at birth was 37.4±2.1. The mean birth weight was 2530±355 g of 7 (43.7%) cases born alive. Two (28.5%) cases were delivered vaginally, and 5 (71.5%) cases were delivered by cesarean section. Four (57.1%) cases were female, and 3 (42.9%) cases were male. The mean follow-up period was 16.4±4.7 months, and the mean length of stay in the neonatal intensive care unit was 86±23 days. Foramen ovale restriction was detected in 2 (28.5%) cases after birth, and emergency septostomy was performed in those babies. Three (42.8%) cases died before the first operation. Two of these three cases required emergency septostomy after delivery due to prenatal foramen ovale restriction. Norwood procedure was performed in four babies. Two cases died after this operation. One of those two patients died on the 1st post-operative day, and the other died 5 days after the Norwood procedure. Glenn shunt and Fontan procedure were performed in the remaining two cases. Overall survival calculated as 28.5%. Prenatal features and outcome of cases were demonstrated in Table 1 and Table 2.

DISCUSSION

Recently, progressions on ultrasonography technology and amelioration in physicians skills and experience have improved prenatal diagnosis of fetal anomalies. While cardiac anomalies are detected in 5–8/1000 of all fetuses, some cardiac anomalies remain undiagnosed in the prenatal period. Morris et al.[8] studied 3.4 million birth records in Texas between 1997 and 2007 years and had found the prenatal diagnosis rate 39% for in 558 isolated HLHS babies. Between 2002 and 2012 years, van Velzen et al.[9] had investigated the results of the standard anomaly scanning program in the Netherlands and found the rate 59.6% in prenatal diagnosis for cardiac anomalies. HLHS is the most diagnosed anomaly, and 94% of all fetuses with HLHS were diagnosed correctly.

Getting a prenatal diagnosis of HLHS helps provide the family with detailed counseling regarding postnatal results and treatment methods. Because HLHS treatment can comprise multiple operations and mortality rates are high, some families choose TOP. In their study, Liu et al.,[10] including 381 patients diagnosed with a single ventricle, showed that percentage of 16 families selected TOP. The most crucial factor that affects the TOP decision is being diagnosed before 20 pregnancy weeks. Beroukhim et al.[11] showed 32% TOP rate for the study, including 312 fetuses with a single ventricle. In our study, 9 of 16 cases selected TOP (56.2%). High TOP rates in our study can be explained by the fact that HLHS operation carries out only in limited centers in our country, and mortality rates are still high compared to developed countries.

Delivery of HLHS diagnosed fetuses must be done in tertiary centers experienced in this field. Morris et al.[8] have found 21% perinatal mortality. The baby delivery center was <10 min distance to the cardiac surgery center, 25.1% perinatal mortality with distance 10–90 min, and 39.6% with distance more than 90 min, respectively. Thakur et al.[12] published a meta-analysis that included 228 prenatal, 381 postnatal diagnosed patients and showed that neonatal death rates among babies were 11% and 17% for prenatally and postnatally diagnosed babies. Otherwise, pre-operative acidosis, inotropic agent need, and mortality rate after Stage-1 surgery were found significantly to be lower in the prenatally diagnosed group. Our study delivery

of all cases prenatally diagnosed has been ensured to carry out in tertiary centers under elective conditions.

About 30% of babies with HLHS are accompanied by genetic or/and extracardiac anomalies. Genetic disorders such as Trisomy 18, Turner syndrome, and DiGeorge (22q11.21-2 deletion) and Jacobson syndrome (11 q deletion) are related to HLHS. Hinton et al.[13,14] showed an association between chromosomal mutations 10q22 and 6q23 with HLHS, and they have found that HLHS risk for subsequent pregnancy was 8.1%. We also suggested karyotype analyze in all cases, and results were found normal for all eight patients.

Newborns diagnosed with HLHS are asymptomatic if there is no restriction of foramen ovale during the prenatal period, but 24–48 h after delivery, ductus arteriosus shuts down, and systemic hypoperfusion, hypotension, and metabolic acidosis occur. If urgent medical care cannot be given, death will be inevitable. HLHS has the most complicated surgery treatment among all cardiac anomalies, and incompatible with life if it remains untreated. However, in recent years, survival rates have increased in parallel with amelioration in surgical techniques and improved intensive care units. HLHS treatment includes the stepwise surgical procedure. The first operation is the Norwood procedure that is done 2 or 3 weeks after birth. The two-way Glenn shunt is made after 2–6 months after delivery. The last stage is the Fontan operation and is held when the patient is between 2 and 5 years old. After HLHS surgical treatment, survival rates between 3 and 6 years old are 60–70%.[15,16] High mortality surgical intervention is Norwood operation, and if this operation is successful, the long-term survival rate can reach 90%.[17] A study investigating 26-year birth statistics in Atlanta between 1979 and 1984 has found 0% neonatal survival rate of HLHS patients. However, between 1999 and 2005 years, this rate was 45%.[18] In our study, the long-term survival rate was 28.5%. This ratio is below the rates of developed countries.

Among the patients operated because of single ventricle physiology, long-term studies revealed a high risk of neurodevelopmental retardation. In the single ventricle reconstruction trial study, where 321 children underwent the stepwise surgical treatment in the case of HLHS, the primary surveillance time was 14.3±1.1 months. Mean Bayley score and psychomotor development score in operated patients were found significantly low than the same in the healthy control group.[19] Mahle et al.[20] revealed considerably lower neurodevelopmental test scores in over 8-year-old children who underwent HLHS operation than in the control group.

In parallel with the improvements in fetal surgical techniques, prenatal treatment methods have been tried invariant type HLHS cases. In a few specialized centers, eligible cases with critical aortic stenosis and sufficient left ventricle volume undergo fetal treatment procedures. In their 100 case series between 2000 and 2013 years in fetuses who underwent fetal surgery, Freud et al.[21] showed fetal aortic valvuloplasty bettering the newborn long-term consequences.

CONCLUSION

HSKS is rare, but the most common cause of death due to cardiac anomalies in the neonatal period. Diagnosis in the prenatal period enables delivery to be performed at a tertiary center and improves long-term results.

Statement

Peer-review: Externally peer-reviewed.

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ORIGINAL ARTICLE

Validity and reliability of the Turkish version of the Birth Experiences Questionnaire

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ABSTRACT

Objective: The aim of this study was to examine the validity and reliability of the Turkish version of the Birth Experiences Questionnaire.

Material and Methods: This methodological study was carried out with 110 couple who were admitted to a in Istanbul between January and December 2019. This research is a methodological study. This study was conducted with 110 couple who gave birth in a public hospital in Istanbul between January and December 2019. The data of the study were obtained using Personal Information Form and Turkish version of Birth Experiences Questionnaire. Birth Experiences Questionnaire measurements were tested with validity and reliability analyzes. For this purpose, validity analysis of data; scope validity index, exploratory factor analysis, confirmatory factor analysis (CFA), reliability analysis; Pearson moment product correlation and Cronbach Alpha reliability coefficient tests were used. In the evaluation of data, t-test, correlation analysis, Cronbach α analysis, and CFA were used.

Results: It is a 10-item self-rating scale. To assess the consistency of the questionnaire overtime, test-retest measurement was performed with an interval of 1 day. As a result, no difference was found between the mean scores ($p>0.05$). In the analysis conducted for the internal consistency in the reliability study of the Birth Experiences Questionnaire, the Cronbach alpha reliability coefficient all scales was determined for all scales as $\propto=0.78$ for mothers and $\propto=0.86$ for fathers.

Conclusion: In this study, it was shown that the Turkish version of the scale was valid and reliable.

Keywords: Birth experiences, childbirth, reliability, validity.

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INTRODUCTION

Even though thousands of births have occurred around the world daily, majority of people define the birth as the hardest and the most significant experiences of their lifespan in birth psychology studies.[1,2] During that period, due to mental health issues experienced by the parents, negative impacts might occur on emotional commitment with the baby as well as ruining family relations that lead to emotional, cognitive, and behavioral problems in the children in long-term period.[1,3–5] Negative birth perception was reported to trigger psychiatric diseases.[6,7] It is rather crucial for couples to assess their birth experiences as positive since the birth is a factor increasing psychological vulnerability and sustain their psychological wellness.

Positive birth experience is defined as the occurrence of the birth with certain outcomes targeting healthy mother/baby and satisfaction of individual needs.[8] Since a positive birth experience lets parents get stronger, self-realization, self-esteem, and enhancing connection with their babies, it eases the adaptation to role of parenting. A negative birth experience, on the other hand, is defined as an experience including unfulfilled expectations, feeling of failure, and disappointment.[2,4,9]

Although negative birth experiences effecting mental health at postpartum period are investigated with mothers, fathers also are reported to experience psychological problems at postpartum period.[10,11] Positive birth experience of fathers might contribute their participation to the family at postpartum period. For instance, the fathers considering the birth experience risky or frightening or feeling not providing sufficient support during the birth period are reported to experience certain problems in the adaptation of the role of becoming father.[12]

It is rather important to assess birth experience to gain awareness about mental health of the couples, establish early diagnosis by the physician, prevent serious mental diseases in the future, and determine the infrastructure of the treatment when needed. Even though a number of studies exist in our country investigating mother satisfaction at postpartum period[13] and birth experience,[5,7,14,15] not any studies occurred to examine the birth experience including the fathers in their samples and the assessments with mothers were conducted with instruments including more questions. In studies assessing the psychosocial dimensions of birth experience, the measurement instrument should be brief, clear, standardized, and reliable. The current study might be predicted to close a significant gap in our country. The current study was conducted to present Turkish version of the Birth Experiences Questionnaire developed by Saxbe et al.[1] (2018) including 9 items to assess birth experiences.

MATERIAL AND METHODS

The present methodological study was carried out in a maternity and children's hospital Istanbul province with primipara women admitting to the hospital to deliver birth and their spouses between the dates January 2019 and December 2019. Those women and their spouses selected through improbable random sampling method, understanding and communicating in Turkish, not having any physical and psychological problems to participate in the study, and being volunteer were included in the study. Those women diagnosed as risky pregnancy, developing any medical complication in the mother or baby, and taking cesarean delivery were excluded from the study. The data were collected through face-to-face interviews. The sample size was planned as 10 times more than items[16,17] so that the study was completed with 110 couples. Test-retest measurement was completed in one day intervals with 40 couples to assess stability of the questionnaire overtime. The permission was obtained from Ethic Committee of Health Sciences Faculty of Marmara University (10.09.2018–179). Moreover, the couples included in the study were explained the aim, method, and their contributions to get their verbal permission and they were also informed about they could withdraw from the study whenever they wished.

The data were collected using information form and the Birth Experiences Questionnaire.

Introductory Information Form

It consisted of items including week of the pregnancy, any health problems during pregnancy and delivery method, as well as age, education, and occupation of the participants.

The Birth Experiences Questionnaire

The questionnaire developed by Saxbe et al.[1] (2018) is used in the assessment of birth experience. The permission was obtained from Saxbe for the Turkish validity and reliability study of the questionnaire. It is a 20 itemed self-assessment questionnaire; 10 items for mother and 10 items for spouses. It was developed specifically for birth experience and scanning purposes and assesses the psychological dimension of the birth. The original questionnaire was developed with newly delivered mothers and spouses and confirmed accordingly. Cronbach's alpha value for original questionnaire was 0.81 for mothers and 0.80 for fathers. It includes the items related with birth experience. It assesses the stress, fear, and worries of couples during the period of pregnancy. The Birth Experiences Questionnaire is the shortest, simplest, and the most practical one among the current scales. It is rather suitable for the primary assessment of the birth both for mothers and fathers. It is recommended to implement the questionnaire in the hospital just 1 or 2 days after the birth.[1] Higher scores mean negative birth experience.

Data were analyzed using SPSS version 21 (SPSS Inc., Chicago, IL, USA) and SPSS Amos (Analysis of Moment Structures) version 23. Test-retest methodology was used to assess the consistency overtime, and Pearson's correlation coefficient was calculated. For evaluating the internal consistency and item-total correlation coefficients, Pearson's moment correlation coefficient was used. Cronbach's alpha reliability coefficient was performed to find the coefficient of internal consistency. The Lawshe technique was used to examine the opinions of experts on content validity. Further, an exploratory factory analysis and a confirmatory factor analysis (CFA) were used to assess construct validity.

Findings

The mean age of the mothers in the study was 23.28±6.36 (min: 19 and max: 31) and fathers' 26.54±2.89 (min: 21 and max: 38); mothers had educated 8.30±1.38 (min: 8 and max: 16) years and fathers 8.51±1.63 (min: 8 and max: 16) years. The majority of the mothers

Table 1: Item-subdimension total score correlations of subdimensions of the Birth Experiences Questionnaire

Subdimensions and items	Item-subdimension total score correlation coefficient		Item-total correlation coefficient		Cronbach alpha
	r	p	r	p	∝
Mother (n=110)					
Stress					
Item 1	0.88	0.000	0.42	0.000	
Item 2	0.85	0.000	0.33	0.000	
Item 3	0.73	0.000	0.44	0.000	0.87
Item 4	0.73	0.000	0.44	0.000	
Item 5	0.73	0.000	0.44	0.000	
Fear					
Item 6	0.94	0.000	0.50	0.000	0.89
Item 7	0.95	0.000	0.47	0.000	
Support					
Item 8	0.92	0.000	0.52	0.000	0.84
Item 9	0.93	0.000	0.39	0.000	
Father (n=110)					
Stress					
Item 1	0.77	0.000	0.51	0.000	
Item 2	0.71	0.000	0.38	0.000	
Item 3	0.60	0.000	0.74	0.000	0.80
Item 4	0.83	0.000	0.53	0.000	
Item 5	0.78	0.000	0.49	0.000	
Fear					
Item 6	0.95	0.000	0.52	0.000	0.89
Item 7	0.95	0.000	0.60	0.000	
Support					
Item 8	0.94	0.000	0.72	0.000	0.87
Item 9	0.94	0.000	0.75	0.000	

(98.2%) were determined to be housewife and fathers were workers (97.3%). The mean gestational week of the participants is 38.21±0.83 (min: 36 and max: 41). About 80.9% of the participants reported not experienced any problems in their pregnancy and 94.5% of them stated that they delivered birth through normal spontaneous vaginal labor.

Linguistic Equivalence, Content Validity Analysis

To evaluate the content validity of the instrument, the original version of the Birth Experiences Questionnaire was translated into Turkish version by a psychiatric nurse and lecturer, a obstetrics and gynecology nurse and lecturer, and an English instructor. The researchers reviewed the translated scale and collaborated in generating a Turkish form of text. A Turkish teacher then evaluated the text for linguistic suitability and comprehensiveness. In the next stage, the Turkish version of the scale was blindly translated back into English by two individuals, namely, a lecturer who had completed the doctorate study and lived abroad, and an individual who was studying and living abroad. The scale was then retranslated into Turkish by a lecturer. By this version, it was checked out whether it had changed the meaning of the original scale or not. Then, the final form of the scale was obtained.

Content Analysis

After the linguistic equivalence of the scale was tested, the Turkish version was submitted to 11 experts for the analysis of content validity. The experts were asked to score each item on a scale between 1 and 5 (1 point: Inappropriate; 2 points: Slightly appropriate; 3 points: I'm undecided; 4 points: Appropriate; and 5 points: Very appropriate). The differences in experts' opinions were examined using the Lawshe technique, and the data obtained from the experts were an-

Table 2: Comparison and correlations of the Birth Experiences Questionnaire and its subdimensions' test-retest mean scores

Questionnaire and subdimensions	First administration Mean±SD	Second administration Mean±SD	t	p	r	p
Mother BEQ (Total)	32.47±3.53	33.42±7.42	-0.930	0.358	0.494	0.001
1. Stress	18.32±2.31	18.27±2.47	0.404	0.688	0.949	0.000
2. Fear	8.90±1.56	8.90±1.27	0.000	1.000	0.896	0.000
3. Support	5.25±1.61	6.25±6.94	1.000	0.323	0.484	0.002
Father BEQ (Total)	40.42±2.62	40.70±2.23	-1.086	0.284	0.794	0.000
1. Stress	22.77±2.21	23.02±2.13	-1.220	0.230	0.823	0.000
2. Fear	12.40±1.82	12.37±1.33	0.190	0.850	0.907	0.000
3. Support	5.25±1.61	5.20±1.45	-0.628	0.534	0.951	0.000

SD: Standard deviation; BEQ: Birth Experiences Questionnaire; t: Paired samples t-test; r: Pearson correlation test.

alyzed using the content validity index (CVI). Ultimately, the CVI for the items was found to be 92%. Once the evaluations of the experts were obtained, the agreed on final scale was administered to 20 participants outside of this sample in a pilot study.

Item Analysis

When total score correlations of the 18 items were examined for the reliability testing of the Birth Experiences Questionnaire, the reliability coefficient was found to vary between 0.33 and 0.52 for mothers and 0.38 and 0.75 for fathers. It was found that there was a positive and statistically significant correlation between the item scores and the overall scale score ($p<0.000$) (Table 1). It was shown by investigating the item-subscale total score correlations of each subscale of the Birth Experiences Questionnaire that the reliability coefficients (Pearson's correlation) for the 5 items in the "stress" subscale for mothers were in the range of r=0.33–0.44 and it was r=0.38–0.74 for fathers. Meanwhile, for the 2 items in the "Fear" subscale, the reliability coefficients ranged from r=0.47 to 0.50 for mothers and r=0.52 to 0.60 for fathers. Further, the reliability coefficients for the 2 items in the "Support" subscale were between r=0.39 and 0.52 for mothers and r=0.72 and 0.75 for fathers. This shows that the correlation coefficients of all items have positive and statistically significant correlations ($p<0.001$) (Table 1). As in the original scale, item analysis was not performed for 10th item.

The Internal Consistency Reliability Coefficient

As a result of the reliability studies of Birth Experiences Questionnaire, Cronbach's alpha internal consistency coefficient of the questionnaire was found $\propto$=0.78 for mothers and $\propto$=0.86 for fathers in overall questionnaire.

Test and Retest

For testing the consistency overtime of the Turkish version of the Birth Experiences Questionnaire, 110 women with their spouses got the first evaluation after 2 h of the delivery and they reinvited to the post-maternity clinic after 24 h to get a second respond. Couples were interviewed separately. To avoid a possible bias, couples were interviewed by different health-care professionals they never met before. Test-retest measurements performed in 1 day intervals were assessed through Pearson product-moment correlation coefficient and t-test. When the correlation between the scores of the first and second administration of the Birth Experiences Questionnaire was examined using Pearson's correlation analyses, it was found that the reliability coefficients for the difference between the two measurements of the scale ranged between 0.48 and 0.95. This demonstrates a positive, strong, statistically significant correlation ($p<0.001$) (Table 2). When the mean scores of the participants at the two different time periods were compared using the dependent groups t-test, a statistically significant difference was not found between the mean scores ($p>0.05$) (Table 2).

Construct validity

Three-dimensional CFA was performed for mothers and fathers to ensure construct validity. As the result of CFA for mothers, fit indices were as follows: Chi-square=17.492 (p=0.000), degree of freedom=24 (X^2=17.492; df=24, X^2/df=0.729), root-mean-square error of approximation (RMSEA)=0.071 ($p<0.05$), standardized root-mean-square residual (SRMR=0.036, comparative fit index [CFI]=0.98, non-normed fit index (NNFI)=0.69, goodness-of-fit index [GFI]=0.96, and adjusted goodness-of-fit index (AGFI)=0.93. The factor loads for all items were found to 0.69 in the CFA. The diagram for the CFA is shown in Figure 1. As in the scale developed by Saxbe et al.,[1] 10th item was not subjected CFA.

As the result of three-dimensional CFA for fathers, fit indices were as follows: Chi-square=27.078 (p=0.000), degree of freedom=24 (X^2=27.078; df=24. X^2/df=1.12), RMSEA=0.034 ($p<0.05$), SRMR=0.050, CFI=0.91, NNFI=0.62, GFI=0.94, and AGFI=0.90. The factor loads for all items were found to 0.61 in the CFA. The diagram for the CFA is shown in Figure 2.

The mean Birth Experiences Questionnaire scores of mothers included in the study were found 34.25±2.68 (min: 31, max: 42) and mean scores of fathers were determined as 40.20±4.18 (min: 35, max: 50).

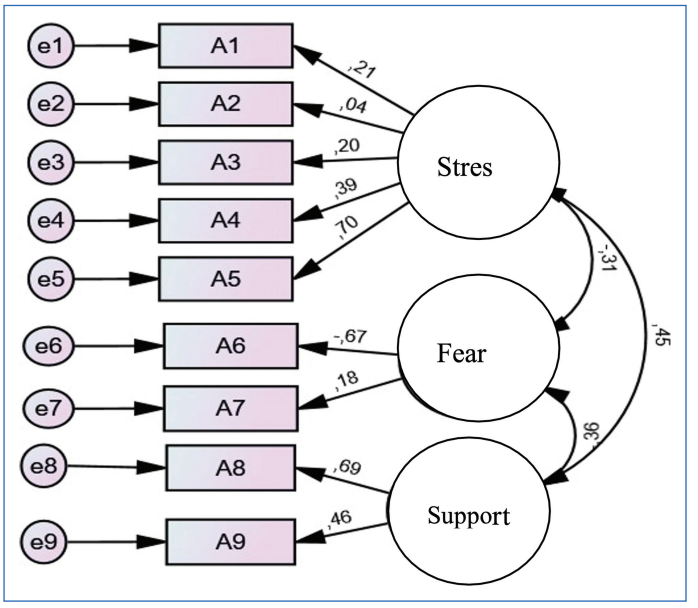

Figure 1: BEQ two-factor confirmatory factor analysis diagram.

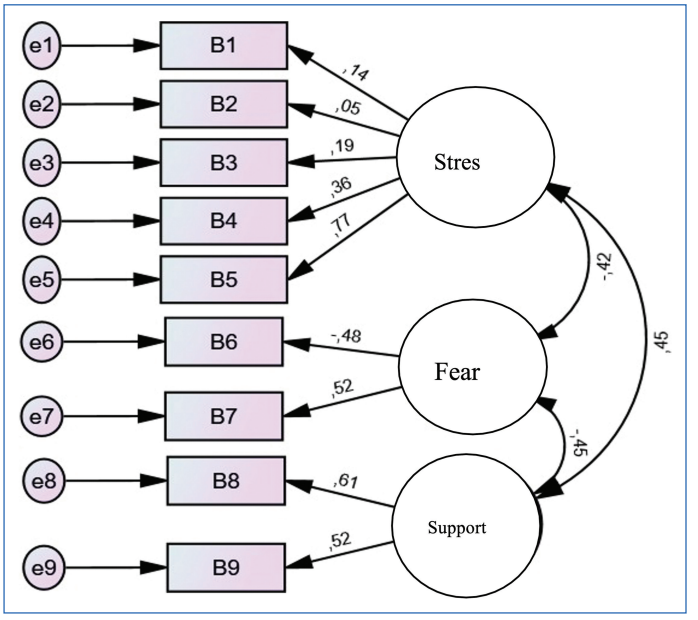

Figure 2: BEQ four-factor confirmatory factor analysis diagram.

DISCUSSION

At present study, validity and reliability study of the Birth Experiences Questionnaire was realized and the results indicated that Turkish version of the Birth Experiences Questionnaire had appropriate psychometric characteristics. As for the reliability analysis of the Birth Experiences Questionnaire test-retest, internal consistency and item analysis were utilized. Test-retest reliability is the degree to which test scores remain unchanged when measuring a stable individual characteristic on different occasions. Having statistically significant level of relation in test-retest measurement supported the reliability of scores obtained from the Birth Experiences Questionnaire with regard to stability overtime.[16–19] Another supportive finding about the reliability of the questionnaire was that it had statistically significant level of internal consistency coefficient. Cronbach alpha techniques were used to evaluate internal consistency of the questionnaire since it was suitable for Likert-type scales. A high coefficient alpha means a high degree of internal consistency that is each of items in the scale is consistent with one another and the scale consists of items that predict the elements of the same characteristics. Alpha coefficient is used to determine reliability by comparing the amount of shared variance, or covariance, among the items making up an instrument to the amount of overall variance and presented with values between 0 and 1.[16,19] In reliability study of Turkish version of the Birth Experiences Questionnaire, it was identified that Cronbach alpha reliability coefficient reached the desired level for each of the three dimensions.

If the items in a scale had equal weights and were in the form of separate units, correlation coefficient expected to be higher. Higher correlation coefficient means higher level of relation between the item and characteristic it aims to measure. Even though a standard does not exist in terms of item total score correlation's decrease the certain level, it is recommended that correlations not being negative and over 0.25 or 0.30. Higher correlation coefficient means higher reliability for the items in the scale.[16,19] When the item-total score correlations for each of the subscales regarding the reliability study of the Birth Experiences Questionnaire were examined, all the subscales were observed to meet required criteria.

The experts reviewed the items in terms of content validity and agreed on the fact that the scale demonstrated a good content validity in its original form. The high degree of experts conformity is an important finding for verifying the content validity of the Turkish version of the Birth Experiences Questionnaire.

CFA was performed for each of the subdimensions to confirm construct validity in Turkish version adaptation of the questionnaire. The most commonly employed fit tests are the Chi-square, RMSEA, SRMR, CFI, NNFI, GFI, and AGFI.[16,18] The fit statistics resulting from a CFA must be at the desired levels. For a model to be acceptable, the Chi-square value is expected to be non-significant. In this study, the Chi-square value was found to be non-significant across all dimensions. This suggested a good model fit.

RMSEA value ≤0.08 with p<0.05 (statistical significance) indicates a good model fit, while a value ≤0.10 is a poor model fit. In this study, RMSEA was found to be significant in each dimension, indicating a good fit. Factor loads should not be <0.30. The following values represent a good fit model: SRMR values of <0.10; CFI, GFI, and NNFI values equal to or greater than 0.90; and AGFI values ≥0.80.[16–19] In the statistical analysis, it was found that the Turkish version of the Birth Experiences Questionnaire satisfied all of fit criteria.

Research Limitations

The data based on self-reporting are an important limitation in this research. Since the data collected to assess birth experience based on self-reporting, a certain degree of fallibility should be taken into consideration. The function of the questionnaire that directs participants to birth psychotherapist or psychiatry clinics just by regarding the scores they obtained should be paid attention. Moreover, the couples' not admitting to the hospital being excluded from the study are another important limitation. The present study cannot be gene

ralized to all the women in postpartum period since it was conducted only with women admitting to maternity and children's hospital in the province of Istanbul.

CONCLUSION

In this study, it has been investigated the validity and reliability of the Turkish version of the Birth Experiences Questionnaire. It is recommended that the Turkish version of the Birth Experiences Questionnaire can be used as a tool to determine negative birth experiences of women together with their spouses. The questionnaire may also provide guidance to health-care professionals and be effective for identifying negative birth experiences of couples at postpartum period as well as early detection of psychological symptoms to direct them psychotherapists, psychiatrists, and other health-care professionals when needed.

Special Thanks

To experts and couples participated in the study.

Statement

Ethics Committee Approval: The Marmara University Institute of Health Sciences Ethics Committee granted approval for this study (date: 10.09.2018, number: 179).

Informed Consent: Verbal informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – FBB, MDB; Design – FBB, MD; Supervision – MDB; Resource – FBB; Materials – FBB; Data Collection and/or Processing – ST, MI; Analysis and/or Interpretation – MD; Literature Search – FBB, MD; Writing – FBB, MD; Critical Reviews – MDB.

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

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ORIGINAL ARTICLE

Five years outcomes of hysteroscopy experience in a tertiary center

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ABSTRACT

Objective: We aimed to document our hysteroscopy (HS) experience for a period of 5 years in an academic hospital.

Material and Methods: Data from patients who underwent HS for any indication were retrospectively analyzed. The clinical and histopathological outcomes of patients with diagnostic or operative HS were documented.

Results: The mean age of 202 patients included in the study was 42.83±9.58 years, their mean gravidy was 2.67±1.29, and their mean parity was 2.04±0.95. One hundred and sixty-two (80.2%) of the patients were at premenopausal period and 40 (19.8%) of them were at postmenopausal period. The most common comorbidities detected in patients were hypertension (9.4%), diabetes mellitus (4.5%), thyroid disease (4%), and breast cancer (3.5%), respectively. The mean pre-operative endometrial thickness was 12.80±6.10 mm. One hundred and thirty-five patients underwent saline infusion sonohysterography (SIS) procedure before HS, and a mass like lesion in the uterine cavity was detected in 97.8% of them. The average largest diameter of these intracavitary masses detected was 13.72±6.21 mm. Seven (3.5%) of all patients needed HS again. The most common indications for HS were menometrorrhagia (54.5%), polymenorrhea (14.4%), postmenopausal bleeding (10.9%), and infertility (9.4%). As a complication, uterine perforation was detected in 1 (0.5%) of cases and excessive bleeding in 2 (1%) of them. The most common localization of the masses in the uterine cavity was fundus (43.4%). As a result of histopathological examination, endometrial polyps were reported in 59 cases (70.3%) and myoma uteri in 21 (9.4%) cases.

Conclusion: The most common reason for HS in our clinic was endometrial polyp. The most common symptom and surgical intervention were determined as menometrorrhagia and resection of polyp, respectively. In the detection of intracavitary lesions, the use of SIS before HS was a common procedure. Our complication rate was found to be low in line with the literature.

Keywords: Diagnostic hysteroscopy, endometrial polyp, operative hysteroscopy, saline infusion sonography, submucosal myoma.

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INTRODUCTION

The uterine cavity can be evaluated by ultrasonography, hysterosalpingography, saline infusion sonohysterography (SIS), hysteroscopy (HS), and magnetic resonance imaging. With imaging methods other than HS, the clear distinction between intrauterine pathologies cannot be made with full accuracy.[1] Among these methods, HS is considered the gold standard method in the evaluation and treatment of intracavitary pathologies of the uterus.[2,3]

The first diagnostic and therapeutic HS were carried out in the mid-19th century by desormeaux, where the endometrial polyp was diagnosed and treated using silver nitrate.[4] As a result of technological developments, there have been advances in the techniques used in HS recently. HS can be used for both diagnosis and treatment. Diagnostic HS is used to examine the endocervical canal, endometrial cavity, and bilateral tubal ostia. Operative HS is also used in the treatment of intracavitary pathologies. Today, innovative technologies such as the application of mechanical, electrosurgical, or laser instruments in the operative HS offer a more widespread use for HS.[5]

Recently, HS in obstetrics and gynecology practice has become the main tool in the evaluation of infertile women, diagnosis, and management of uterine anomalies and abnormal uterine bleeding.[6] Today, the fact that minimally invasive surgery is preferred by both patients and physicians, increasing clinical experience, and production of small-scale surgical equipments have contributed to the expansion of the diagnostic and operative HS indications and its popularity.

SIS can achieve diagnostic accuracy as high as HS and can be directed to operative HS.[7] SIS is a useful diagnostic tool, especially in detecting the presence of intrauterine space-occupying pathologies.[8]

In this study, we wanted to evaluate the clinical and pathological results of all HS cases performed in our clinic in the last 5 years.

MATERIAL AND METHODS

This study was conducted on cases with HS between March 2016 and August 2020. Approval for the study was obtained from Muğla Sıtkı Koçman University Health Sciences Scientific Research Ethics Committee (Decision number: 22.09.2020-4).

Data of patients who underwent HS were analyzed retrospectively. As the inclusion criteria of the study, all diagnosic and operative HS cases performed in Muğla Sıtkı Koçman University Training and Research Hospital in the past 5 years were screened. Incomplete or inaccessible medical records were determined as exclusion criteria. All necessary information was obtained from patient files and hospital database records.

In the given period, a total of 229 patients underwent surgical or diagnostic HS procedures by our surgical team experienced in HS. Twenty-seven patients whose medical or surgical records could not be reached were excluded from the study. A total of 202 patients who underwent HS were included in the study. The characteristic and surgical parameters such as age, gravidy, parity, comorbidities, menopausal status, pre-operative symptoms, pre-operative endometrial thickness, application of SIS, mass detection in SIS, the largest mass size in pre-operative ultrasonography, mass localization in the uterine cavity, need for recurrent HS, pathology result, and HS complications (uterine perforation, fluid overload, air/gas embolism, thermal burns, excessive bleeding, and infection) were investigated.

SIS was performed in patients with suspected intracavitary lesions or abnormalities during routine transvaginal ultrasonography (TVUSG). During the SIS, an insemination cannula was inserted through the cervical os into the endometrial cavity due to its thinner size that causes less pain. To prevent echogenic artifact of air, uterine cavity was filled with sterile saline solution before the cannula was placed into the cavity. To fill the endometrial cavity, 10–30 ml of saline solution was slowly infused into the cavity accompanied by TVUSG. The thickness and regularity of the endometrium and the presence of any mass-like lesion were checked during SIS.

Diagnostic or operative HS was planned in the secretory phase of the menstrual period for patients with suspected intrauterine pathology according to TVUSG and/or SIS results. For HS procedure, 300 optical telescope, and 10 mm operative histeroscope device were used under general anesthesia (Storz, Germany). For cervical ripening, two tablets of intravaginal misoprostol were administered in selected patients with postmenopausal cervical stenosis or no history of birth 12 h before HS. Three thousand milliliters of resectisol solution were used for uterine cavity distension. Loop electrosurgical resection and correction of uterine abnormalities were performed in patients as needed. Sterile disposable blue drapes were used for sterilization during HS. Sacks with strainers and drain plugs, which are part of these drapes, were used to collect pathological materials removed after the procedure.

Statistical Analysis

The collected data were analyzed using SPSS software, version 23 (SPSS Inc, IBM, Chicago, IL, USA). The continuous or consecutive variables reported as mean±SD. The categorical variables were reported as frequency and percentage.

RESULTS

The mean age of the 202 cases included in the study was 42.83±9.58 years, their gravida was 2.67±1.29, and their parity was calculated as 2.04±0.95. 162 of the patients (80.2%) were in the premenopausal period and 40 (19.8%) were in the postmenopausal period. While 74.8% of the patients did not have any comorbidity, hypertension (9.4%), diabetes mellitus (4.5%), thyroid disease (4%), and breast cancer (3.5%) were the most common comorbidities. The mean pre-operative endometrial thickness was 12.80±6.10 mm. SIS procedure was applied to 135 of the patients before HS and a mass occupying the cavity was detected in 97.8% of them. The mean largest diameter of these intracavitary masses detected was 13.72±6.21 mm. In 7 (3.5%) of all patients, HS was needed again. All of the cases with recurrent HS were performed due to recurrence of the endometrial polyp (Table 1).

The distribution of symptoms of patients before HS was as follows; Menometrorrhagia (54.5%), polymenorrhea (14.4%), oligomenorrhea (1.5%), infertility (9.4%), incidental diagnosis (5%), postmenopausal bleeding (10.9%), lost intrauterine device (IUD)/rest piece of IUD (3%), and chronic pelvic pain (1.5%) (Table 2). All IUD dislocations were intrauterine. No IUD perforating the uterus was seen. While one (0.5%) of the cases had uterine perforation and two

Table 1: The descriptive statistics of patients who underwent hysteroscopy

Variables	Total patients (n=202) Mean±SD	%
Age (years)	42.83±9.58	
Gravidy (n)	2.67±1.29	
Parity (n)	2.04±0.95	
Menopausal status		
Premenopausal	162	80.2
Postmenopausal	40	19.8
Comorbidity		
No	151	74.8
Hypertension	19	9.4
Diabetes mellitus	9	4.5
Cardiovascular disease	6	3.0
Breast cancer	7	3.5
Thyroid disease	8	4.0
Central nervous system disease	2	1.0
Preop endometrial thickness (mm)	12.80±6.10	
SIS n (%)	135	66.8
Mass detection in SIS n (%)	132	97.8
Mass size (mm)	13.72±6.21	
Need for Re-HS	7	3.5
Complications		
Uterine perforation	1	0.5
Fluid overload	–	–
Air/gas embolism	–	–
Thermal burn	–	–
Excessive bleeding	2	1
Infection	–	–

SD: Standard deviation; HS: Hysteroscopy; SIS: Saline infusion sonohysterography.

(1%) had excessive bleeding, no complications such as excessive fluid load, air/gas embolism, thermal burn, and infection were observed. No additional procedure was needed in the case with uterine rupture. In patients with excessive bleeding, an 18 F Foley catheter was placed into the uterine cavity after HS and the balloon of Foley was inflated to 20–30 cc. These patients were followed up with vital signs, hematocrit value, and ultrasonography, and no other complications were observed.

When we analyzed the localization of the masses in the cavity detected during HS, fundus localization was the most common site (43.4%). The left lateral (16.2%), right lateral (15%), posterior (14.5%), anterior (8.1%), and cervical (2.9%) localizations were detected less frequently (Table 3).

Table 2: The distribution of pre-operative symptoms

The symptoms	Total patients (n=202)	
	n	%
Menometrorrhagia	110	54.5
Polimenore	29	14.4
Oligomenorrhea	3	1.5
Infertility	19	9.4
Incidental diagnosis	10	5.0
Postmenopausal bleeding	22	10.9
Lost IUD/Rest piece of IUD	6	3.0
Chronic pelvic pain	3	1.5

IUD: Intrauterine device.

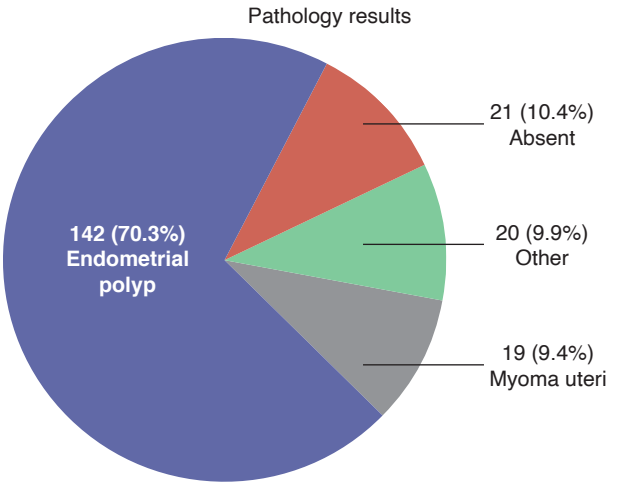
Table 3: The rates of mass localization in the uterine cavity

Location	Total patients (n=173)	
	n	%
Fundus	75	43.4
Left lateral	28	16.2
Right lateral	26	15.0
Posterior	25	14.5
Anterior	14	8.1
Cervical	5	2.9

The distribution of hysteroscopic operations according to the pathological results is presented in Figure 1. Hysteroscopic resection or endometrial sample was obtained in 181 cases for histopathological examination. Pathology results were reported as endometrial polyp in 142 cases (70.3%), and myoma uteri in 19 (9.4%) cases. The benign results other than endometrial polyp or fibroid were detected in 9.9% of the cases (necrotic decidual tissues (3.5%), proliferative endometrium (0.5%), secretory endometrium (1.5%), endometrial cancer (1.5%), atrophic endometrium (1%), simple endometrial hyperplasia without atypia (1%), polypoid adenomyoma (0.5%), and atypical polypoid adenomyoma (0.5%).

DISCUSSION

HS is used for a wide variety of diagnostic and therapeutic algorithms, such as the assessment of infertility, recurrent abortion, uterine anomalies, and the diagnosis and treatment of endometrial pathologies.[9–11] Office HS is recommended to be used as the first step, especially in the evaluation of infertile cases, as it offers very useful information and can be used practically.[12] In this study, a total of 19 cases were found to have undergone diagnostic HS due to infertility, and 183 cases operative HS. Although 8 of 19 patients who



Other: Necrotic desidual tissues, chorionic villus 3.5%, endometrium cancer 1.5%, proliferative endometrium 0.5%, secretory endometrium 1.5%, atypical polypoid adenomyoma 0.5%, polypoid adenomyoma 0.5%, atrophic endometrium 1%, simple endometrial hyperplasia without atypia 1%.

Figure 1: The pathology results of patients who underwent hysteroscopy.

underwent HS with the indication of infertility gave normal results, three uterine septum, four endometrial polyps, and two leiomyomas were detected and were found to be compatible with the literature.[13] Due to the recently opened IVF unit in our clinic, an increase in the number of HS used in infertility research is expected in the future.

SIS is another diagnostic method in investigating the causes of abnormal uterine bleeding. SIS has a distinct advantage over transvaginal ultrasound in detecting focal lesions. In the diagnosis of these lesions, SIS has a similar diagnostic accuracy value with HS. It also has the advantage to view other pelvic organs simultaneously. In the study of Bartkowiak et al.,[14] the role of vaginal ultrasound, SIS, and HS in recognizing intrauterine pathologies was investigated. They evaluated 150 premenopausal and postmenopausal patients prospectively. It has been determined that SIS is superior to vaginal ultrasound and has similar diagnostic value with HS. In the study of Nessar et al.,[15] the hysteroscopic diagnoses of the patients who were pre-diagnosed with SIS were compared and it was observed that SIS had 90.62% sensitivity and 90.48% specificity. It was also observed that SIS had 84.21% sensitivity and 100% specificity in the diagnosis of myoma. In the present study, when the pre-diagnoses of SIS and post-HS pathology results were compared, all 106 patients who were diagnosed with endometrial polyp and underwent SIS were found to have endometrial polyps after HS and the sensitivity was found to be 100%. In addition, sensitivity for fibroid was found to be 100% as a result of HS in all 18 patients who were diagnosed with fibroids and underwent SIS. The specificity could not be calculated, since there was no patient who did not have a mass finding with SIS and who had a mass after HS. SIS is currently considered as an eligible alternative method to HS due to its easy applicability, good tolerability by the patient, cheap, and outpatient application. In addition, HS has a diagnostic accuracy similar to SIS. If any pathology detected during HS procedure, it gives the advantage to treat at the same session. Thus, it has an increasing popularity in the uterine cavity pathologies.

Hysteroscopic endometrial sampling has been found to be very effective in detecting endometrial cancer and hyperplasia in patients with abnormal uterine bleeding and especially in recurrent postmenopausal bleeding cases. In our clinic, we did not have HS for the purpose of diagnosis or treatment to any patient diagnosed with endometrial cancer by pipelle or dilatation curettage method. In the samples taken in this study, endometrial cancer was detected in three (1.5%) cases after histopathological examination and all of these patients were in the postmenopausal period.

The complications of HS are rare and develop mostly due to therapeutic procedures.[16] The most common HS complications are fluid overload (5%), uterine perforation (1%), and bleeding (3%).[17] In our study, uterine perforation was observed in only one case. This perforation was a case of septum resection due to infertility. After the perforation was detected, intraoperative transabdominal ultrasonography revealed free fluid and bleeding in the abdomen. In the evaluation, the amount of bleeding did not increase, and an 18 F Foley catheter was placed from the posterior vaginal fornix to the posterior cul de sac. It was observed that there was no need for additional intervention in the patient's follow-up. This application may be an alternative method that may be useful in the follow-up of both intra-abdominal bleeding and fluid leakage during HS. In both cases, excessive bleeding occurred and the bleeding was controlled by applying balloon tamponade with the help of intrauterine Foley ballon. We attribute the fact that no fluid overload was encountered in our clinic to our experienced surgical team in HS.

The use of HS in the infertility researches is quite common. Although HS has a limited place in the detection of tubal pathologies, a few studies have been conducted on the evaluation of tubal pathologies recently. Yücel et al.[18] evaluated tubal peristalism hysteroscopically in patients with a diagnosis of unexplained infertility. In addition, Promberger et al.[19] evaluated the observation of flow effect in tubal ostia. In our clinic, we observed that at least one tube was open during hysterosalpingography in patients who underwent HS due to infertility and had fluid leakage into the abdomen. We think that the detection of fluid leakage into the abdomen after HS may bring give a positive opinion about tubal permeability. Therefore, especially in infertile patients, ultrasonography after HS can contribute not only to the control of bleeding and fluid overload but also to the evaluation of tubal permeability.

The use of misoprostol for cervical ripening before HS has not been shown to benefit cervical dilatation and surgical complications. Since increased side effects have been reported in these cases, routine application of misoprostol is not recommended. For this purpose, it is recommended that the use of misoprostol be reserved for some selected cases.[20,21] In our clinic, we do not routinely apply misoprostol for cervical ripening in the pre-operative period. In addition, we administer misoprostol only to patients not gave a birth before and who have postmenopausal cervical stenosis.

As a limitation of our study, we can say that the number of infertile patients who underwent diagnostic HS is low. However, thanks to the IVF center opened within our clinic, we think that the patient population undergoing diagnostic HS will increase in the coming days. In addition, using the same technical equipment for HS is a strong factor for standardization of the work.

HS is an indispensable intervention in gynecology clinics with its high reliability and low complication rates that can be used for diagnostic and operative purposes. The results of our study show that HS procedures performed in our clinic is a diagnostic and treatment method with high reliability and low complication rate.

Statement

Ethics Committee Approval: The Muğla Sıtkı Koçman University Health Sciences Scientific Research Ethics Committee granted approval for this study (date: 22.09.2020, number: 4).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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ORIGINAL ARTICLE

The evaluation of children with cerebral palsy admitted to the pediatric neurology outpatient department

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ABSTRACT

Objective: Cerebral palsy (CP) is a neurological condition that occurs as a result of non-progressive damage in the immature brain and is characterized by impairment of muscle tone and posture. This study aims to evaluate the risk factors and imaging findings of patients with CP.

Material and Methods: Medical records of patients with CP at the Pediatric Neurology Clinic of Cerrahpasa Medical School were evaluated retrospectively. Demographic and clinical characteristics were collected from medical records: Gestational age, birth weight, intrauterine growth retardation (IUGR), delivery mode, type of CP, risk factors, accompanying diseases, computed tomography (CT), magnetic resonance imaging (MRI), and electroencephalography findings were recorded.

Results: A total of 169 patients were enrolled in the study. The mean age at diagnosis was 27.3±26.1 months. One hundred eight (66.2%) patients were term and 55 (33.7%) were preterm. The delivery mode was vaginal in 99 (58.6%) cases and cesarean section in 70 (40.4%) cases. Ninety-six cases (56.8%) were male and 73 (43.2%) were female. Birth weights were <2500 g in 59 cases (34.9%) and 2500–4500 g in 110 cases (65%). The types of CP were spastic (n=144, 86%), dyskinetic (n=13, 7.7%), mixed (n=6, 3.6%) and ataxic-hypotonic type (n=5, 3%). In subgroup analysis, 65 (38.5%) cases were quadriparetic, 43 (25.6%) cases were diplegic, 35 (20.7%) cases were hemiparetic, and 2 (1.2%) cases were monoparetic. The reasons for CP were asphyxia (n=99, 58.9%), low birth weight (n=61, 36.1%), prematurity (n=55, 32.5%), hyperbilirubinemia (n=16, 9.5%), meningitis (n=7, 4.1%), intracranial vascular processes (n=7, 4.2%), sepsis (n=6, 3.6%), hydrocephalus (n=5, 3%), genetic anomalies (n=5, 3%), and hypoglycemia (n=1, 0.6%). No risk factors could be determined in eight (4.7%) cases. Imaging techniques (CT and/or MRI) showed encephalomalacia, which was considered as the main finding of hypoxic-ischemic encephalopathy, in 45 (26.6%) cases. Imaging results of 15 (8.9%) patients were normal.

Conclusion: This study results showed that asphyxia, low birth weight, and prematurity are the main reasons for the development of CP. Encephalomalacia is the most common imaging finding, but imaging may be also normal in some patients with CP.

Keywords: Cerebral palsy, newborn, spasticity.

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INTRODUCTION

Cerebral palsy (CP) is a postural and movement disorder that develops as a result of injury in the developing brain before, during or after birth, which may progress with permanent motor dysfunction. Prematurity, vascular, inflammatory, and traumatic causes play a role in its etiology.[1] In CP, motor retardation is often accompanied by sensory (seeing, hearing, etc.), cognitive (attention, memory, learning, interpretation, execution, etc.), communication (language, communication with body language, etc.), and behavioral (hyperactivity, impulsivity, aggression, etc.) dysfunctions, epilepsy, and secondary musculoskeletal system problems.[2] In parallel with technological advancements, new approaches are emerging in treatment and rehabilitation techniques in CP. Etiological distribution of CP, life expectancy and increased quality of life are accepted as criteria determining the development level of societies.[3] In this study, we aimed to evaluate the etiology, clinical course, and laboratory findings of patients with CP.

MATERIAL AND METHODS

The study was designed as a retrospective cross-sectional study. The study protocol was approved by the Cerrahpasa University Medical Faculty Ethics Committee. Files of the pediatric patients followed-up in the Pediatric Neurology Outpatient Clinic of the Cerrahpasa University Medical Faculty, Department of Pediatrics with the diagnosis of CP between October 01, 2003 and October 01, 2009 were retrospectively reviewed. Patients' gender, diagnosis, age at admission, delivery mode, birth weight, type of CP, risk factors, accompanying diseases, imaging, and electroencephalography (EEG) findings were recorded. Types of CP were grouped as spastic, dyskinetic, ataxic/hypotonic, and mixed type. Spastic types were further classified as quadriparesis, diplegic, hemiparesis, and monoparesis CP. Since most of the cases presented with a previous diagnosis, we considered the age at the time of admission to our outpatient clinic instead of the age at diagnosis as a criterion. We grouped ages at admission as <6 months, 6–12 months, 12–24 months, and >24 months.

Conditions known as risk factors in the etiology of CP such as gestational age, birth weight, delivery mode and intrauterine retardation, consanguineous marriage, genetic stigmata, and congenital metabolism disorders were taken into account. Gestational age, birth weight, delivery mode, and conditions that may cause intrauterine growth retardation, which are known as risk factors in the etiology of CP, were determined as follows: Delivery mode was separately evaluated as delivery at home or hospital, normal spontaneous vaginal delivery (NSVD), and cesarean section (C/S). Birth weight was classified as <2500 g, 2500–4500 g, and <4500 g. Gestational age was evaluated as term and preterm (≤37 hafta). As the risk factors; asphyxia, low-birth weight, prematurity, meningitis, sepsis hyperbilirubinemia, hydrocephalus, genetic anomalies, and vascular processes such as intracranial hemorrhage and thrombosis, acute metabolic events such as hypoglycemia and consanguineous marriage were examined separately.

Patients whose seizures were clinically supported by EEG findings were considered to have epilepsy. Patients with EEG findings, but who had no clinical seizures were accepted to have EEG anomaly. Presence of epilepsy, which is characterized by the tendency of the brain to produce continuous epileptic seizures and associated epileptiform abnormalities in EEG were recorded. Imaging findings were examined as auxiliary data in distinguishing CP subgroups and associated conditions. Accompanying diseases were determined. Types of CP, risk factors, and laboratory findings were matched and compared.

Statistical analysis was performed using SPSS 16.0. Ordinal variables were expressed as median and interquartile range. Categorical data were given as frequency and percentage Descriptive statistics were expressed as mean±standard deviation. Chi-square and ANOVA tests were used for the intergroup comparisons. P<0.05 values were considered statistically significant.

RESULTS

File records of 169 included in the study. The mean age at the time of admission was 27.3±26.1 months, 96 patients (56.8%) were boys, and 73 (43.2%) patients were girls (Table 1). Birth weight was found as <2500 g in 59 (34.9%) and 2500–4500 g in 110 (65.8%) patients. Of all patients, 108 (66.2%) were term and 55 (33.7%) were preterm. When types of CP were evaluated; spastic type was found in 144 (86%), dyskinetic type in 13 (7.7%), mixed type in 6 (3.6%). and ataxic-hypotonic type 5 (3%) patients. The other demographic features are shown in Table 1.

When the risk factors were examined separately; the most common risk factor was asphyxia in 99 patients (58.9%) followed by low birth weight in 59 patients (34.9%), prematurity in 55 patients (32.5%), and neonatal infections including meningitis in seven patients (4.1%) and sepsis in six patients (3.6%). As the other risk factors with relatively lower rates; hyperbilirubinemia was found in 16 patients (9.5%), hydrocephalus in five patients (3%), genetic anomalies in five patients (3%), vascular processes such as intracranial hemorrhage and thrombosis in seven patients (4.2%), and acute metabolic events such as hypoglycemia in one patient (0.6%). No risk factor found in eight patients (4.7%) (Table 2).

When imaging (computed tomography [CT] and magnetic resonance imaging [MRI]) findings of the patients were evaluated; encephalomalacia, which is accepted as the main finding of hypoxic ischemic encephalopathy (HIE), was found in 45 patients (26.6%). Imaging evaluation was normal in 15 patients (8.9%). It was found that imaging had not been performed in 21 patients (12.4%) (Table 3).

When the cases are evaluated considering the possibility of epilepsy accompanying CP; epilepsy was observed in 60 patients (35.5%). Regardless of the presence of epilepsy, EEG abnormality was found in 56 of 83 patients who had EEG (33.1% of all patients) (Table 1). When the types of CP, gender, gestational age, birth weight, delivery mode and the presence of birth trauma were matched and compared; no statistically significant difference was found between type of CP and gender, low birth weight (<2500 g) and the presence of birth trauma (p>0.05) (Table 4).

DISCUSSION

CP is the most common physical disability in childhood, but it is very heterogeneous etiologically and clinically. Movement disorders associated with CP are categorized as spasticity, dyskinesia, ataxia or

Table 1: Patients' gender, mean age at admission, type of cerebral palsy, birth weight, gestational ages, delivery mode, place of birth, risk factors, and electroencephalography abnormality findings

Findings	n	(%)
Gender		
Boy	96	56.8
Girl	73	43.2
Age of admission (month)		
<6	25	14.8
6–12	21	12.4
12–24	50	29.6
>24	73	43.2
Type of CP		
Spastic quadriparesis	65	38.5
Spastic diplegia	43	25.6
Spastic hemiparesis	35	20.7
Dyskinesia	13	7.7
Mixed	6	3.6
Ataxia-hypotonia	5	3
Spastic monoparesis	2	1.2
Birth weight (g)		
<2500	59	34.9
2500–4500	110	65
>4500	0	0
Gestational age (week)		
Term (≥38)	108	66.2
Preterm (≤37)	55	33.7
Delivery mode		
Vaginal	99	56.8
Cesarean	70	40.4
Place of birth		
Home	17	10
Hospital	152	90
Risk factor		
1	92	54.4
2	50	29.5
≥3	19	11.2
Epilepsy		
No	8	8.7
Yes	60	35.5
Electroencephalography abnormality		
No	86	50.9
Yes	56	33.1

CP: Cerebral palsy.

Table 2: Risk factors of the patients in the study

Risk factors	n	%
Asphyxia	99	58.9
Prematurity (≤37)	55	32.5
Low-birth weight (<2500 g)	59	34.9
Hyperbilirubinemia	16	9.5
Neonatal meningitis	7	4.1
Neonatal sepsis	6	3.6
Thrombosis-intracranial hemorrhage	7	4.2
Genetic anomaly	5	3.0
Hydrocephalus	5	3.0
Hypoglycemia	1	0.6
Unknown	8	4.7

Table 3: Imaging findings of the patients

Imaging findings	n	%
Encephalomalacia (HIE)	45	26.7
Dysgeneses		
Holoprosencephaly	2	1.2
Porencephalic cyst	2	1.2
Polymicrogyria	5	3
Schizencephaly	1	0.6
Corpus callosum anomaly	9	5.3
Choroid plexus cyst	1	0.6
Arnold chiari malformation	1	0.6
Basal ganglia hyperintensity	18	10.6
Cortical atrophy	33	19.5
Cerebral infarction	7	4.1
Hydrocephalus	4	2.4
Normal	15	8.9
Imaging not performed	21	12.4

mixed/other. Spasticity is the most common movement disorder seen in 80% of children with CP.[2]

The incidence of CP differs between genders. CP is reported to me more common among boys.[4] It is claimed that this tendency in male gender is based on a number of factors ranging from biological vulnerability and possible differences in brain organization to genetic disorders or the effect of female hormones to reduce the possible effects of brain damage. Therefore, gender is reported to have an effect in increasing the risk of developing CP. In studies investigating possible gender differences in specific forms of CP, it is not exactly clear whether gender will also affect the severity of the motor impairment.[5] In our study, the boy/girl ratio was 1.3/1 and similar to the previous studies, the rate of males was higher.

Table 4: Comparison of the types of cerebral palsy with gestational week, gender, birth weight, delivery mode, low-birth weight, and asphyxia in patients included in the study

	Spastic quadriparesis	Spastic diplegia	Spastic hemiparesis	Other	n
GW Mean±SD	37.01±4.6	34.9±5.1	38.4±3.8	36.9±4.6	ns
Distribution	28–40	26–40	27–40	28–40	p<0.05
Boy/Girl (n)	33/30	24/19	24/11	14/10	ns
Preterm (≤37) (n)	18	23	6	8	
Term (≥38) (n)	44	18	28	16	p<0.05
Birth weight Mean±SD	2674.5±841.7	2284.9±858.7	2875.6±742.2	2579.2±688.6	
Distribution	1000–4000	980–4000	900–4500	1200–4200	p<0.05
Low-birth weight (<2500 g) (n)	21	21	7	9	ns
Asphyxia (n)	35	24	22	14	ns

GW: Gestational week; C/S: Cesarean section; NSVD: Normal spontaneous vaginal delivery; ns: Not significant; SD: Standard deviation; Distribution: Median value (25^{th}–7^{th} percentiles).

Since early diagnosis will bring healing, timely diagnosis of CP cases is very important. Early physiotherapy has been reported to provide significant positive improvements in CP. In a study of 202 cases by Eriman et al.,[6] it has been reported that CP symptoms were noticed by the family in 102 cases, pediatrician in 97 cases, and environment in three cases. In our study, when the age of recognition of CP symptoms was questioned; it was found that CP symptoms were noticed in the neonatal period in 74 patients, between 0 and 6 months in 55 patients and after 1 year of age.

Although age at diagnosis of CP varies according to socioeconomic levels of countries, it has been generally reported between 12 and 24 months.[7] It has been reported that establishing a diagnosis before 6 months of life is inadequate especially in mild or hypotonic cases.[7,8] The mean age at diagnosis was found as 8.98 months by Vurucu et al.[9] and 8.2 months by Bruck et al.[10] Kabakuş et al.[11] reported the mean age at admission as 23.4±3.8 months and found that 42% of the cases were diagnosed before 1 year of age, 38% between 1 and 2 years and 20% after 2 year of age. The age of admission to our neurology outpatient clinic with the diagnosis of CP was under 6 months old in 25, between 6 and 12 months in 21, 12, and 24 months in 50 and >24 months of life in 73 and the mean age at admission was 27.3±26.1. We think that early CP awareness is sufficient in our country, because in our study age at the time of admission was in infancy (<24 months) and patients who presented in the following months of age had been diagnosed in other centers.

CP has been reported to be more commonly developed in asphyxia cases than other risk factors.[12] In our study, asphyxia was one of the most common causes of CP. When the frequency of asphyxia was evaluated according to the age of birth; it was found that asphyxia was 3 times more common in term cases. In our series, there was no patient with a birth weight >4000 g. Therefore, it was thought that it would be appropriate to investigate the reasons other than high birth weight when evaluating asphyxia in term infants.

In CP screening studies from abroad and countries known to be at different socio-economic levels, the incidence of asphyxia has been reported in a wide range between 3% and 50%.[12] Whereas, in studies conducted in our country, this rate has been reported between 30% and 45%.[13] In our study, the rate of asphyxia was 58.9%, remarkably higher than all reported. Among this; life and birth conditions and thus socio-economic level should be primarily discussed. In a series of 102 cases by Adın et al.[14] from the Inonu University, the rate of asphyxia was reported as 51.9% in CP. This rate is the closest to our rate of asphyxia in the literature.

It has been reported that the majority of CP cases are delivered by normal vaginal method. In a study by Bringas-Grande et al.[15] 68% of CP cases were reported to be delivered by normal vaginal method and 32 by C/S. In a study by Vurucu et al.[9] 77.8% of the cases were delivered by normal vaginal method and 22.2% by C/S, while in another study by Kabakuş et al. 60% of the cases were delivered by normal vaginal method and 40% by C/S.[11] In our study, 56.8% of the patients were delivered by normal vaginal method and 39.6% C/S.

It has been reported in the literature that preterm births are the most important risk factor for the development of CP.[2] It has been stated that as neonatal care units become more widespread, the number of infants kept alive has increased and gestational week has decreased, leading to an increase in the prevalence of CP in preterm births.[12] It is known that prematurity and low-birth weight are the most common reasons in the countries where intensive care conditions are better and living chances are higher. Periventricular leukomalacia and intraventricular hemorrhage (IVH) are two main causes of CP development in premature infants.[16] Furthermore, in our study, prematurity was among the important etiological factors.

Low-birth weight in CP seems to be an important reason for an effect that begins in the intrauterine period. However, when low birth weight is evaluated in the literature, some confusion of concepts as in the evaluation of the age of prematurity is remarkable. Some authors accepted <2500 g as the low-birth weight criterion,[17] while others determined the low-birth weight considering gestational age,[9] and some authors mentioned the concept only as a low-birth weight and did not explain their criteria sufficiently. In our study, 59 patients were

low birth weight infants and 55 were preterm. The difference between them reflected the small for gestational age.

Dyskinetic type CP is seen in late infancy and childhood due to bilirubin encephalopathy.[18] Among the risk factors, hyperbilirubinemia was found in our 16 (9.5%) patients. In studies reported from our country, hyperbilirubinemia has been reported as a cause of CP by 1–20%.[6,7,9,11] Different rates were attributed to the level features of the centers where the studies were conducted.

In our study, we gathered vascular pathologies among CP risk factors in two subgroups as hemorrhagic and thrombotic, but under the same title. However, the result can be associated with vascular pathology in HIE. In this case, the potential of evaluating asphyxia together with thromboembolic and hemorrhagic factors increases. We concluded that a clear classification of vascular pathologies is difficult especially in units that are reference centers such as our outpatient clinic. Namely, it was unclear whether HIE might have occurred in the presence of hypoxia, thromboembolism, or hemorrhagic diathesis in the patients with leukomalacia findings verified with imaging, and especially in those with late admission. Therefore, in our study, patients with a definitive diagnosis of thromboembolic or hemorrhagic diathesis were gathered under vascular pathologies and the remaining encephalomalacia patients under the diagnosis of HIE. Looking at other studies, we found that clear classification of the cases was not possible and there was no explanation on this issue. In ethnic communities, where consanguineous marriages are common, the frequency of genetic etiology increases in CP. In a study conducted in Asia, CP was reported to be more common in ethnic societies where consanguineous marriages are common.[13] According to the studies conducted in Turkey, the frequency of consanguineous marriage is between 21% and 33%.[8,19] In a study from Turkey, among the prenatal causes consanguineous marriage was found as 24% and the most common etiologic factor in CP.[20] In our study, consanguineous marriage was found in 38 (22.5%) cases.

The most common type of CP is spastic type with the majority being spastic diplegic type.[21] In our study, the most common type of CP was spastic CP with the most common subgroup being spastic quadriplegic CP. Comparing birth weights and types of CP, Gulati et al. reported that the incidence of spastic quadriplegia and spastic diplegia was statistically significant.[22] In our study, when gestational weeks and birth weights were compared with the types of CP, these factors were found to be statistically significantly correlated with the development of spastic hemiparesis and spastic diplegia ($p<0.05$). The most common types of CP are diplegia and tetraplegia in preterm infants. In fact, spastic diplegia and quadriplegia have been more commonly reported in the developed countries in parallel with the increasing rate of keeping premature infants at the lower gestational week alive.[8] Since asphyxia is a severe picture involving all motor pathways in terms of the location of involvement, while an even distribution is observed in spastic SP subtypes as in our study, spastic diplegia and quadriplegia CP types were more common, because periventricular area was more markedly involved in the preterm infants.

Magnetic resonance imaging (MRI) showed abnormalities in more than 80% of patients with CP. A MRI classification system (MRICS) was developed by the Surveillance of CP in Europe (SCPE). Here, the aim is interpretation and classification of brain MRI results in a simple way by both clinicians and other specialists caring CP patients. Due to the myelination development in the 1st years of life, SCPE recommends classifying MRI images performed after the child reaches 2 years of age according to the MRICS system unless previous images show a specific pathology.[7,23,24] Diffusion MRI should be preferred, because classical MRI is limited in identifying white matter pathways precisely. Similar to the literature, in our study, CT and MRI showed various abnormalities that can be grouped as cerebral atrophy, encephalomalacia, cerebral infarction, intracranial hemorrhage, hydrocephalus, cortical-subcortical dysgenesis, and intensity changes (Table 3).

Epilepsy may also occur in the follow-up of children with CP. In our study, EEG abnormality was found in 56 of our CP patients whose EEG examination was performed due to presumed epilepsy. In a screening study by İpek et al.[7] on CP, epilepsy was found by 35.8%; with EEG abnormality was found in 31.2% of these patients. In line with the other studies, in our study, EEG abnormality was found in 56 of 169 patients (33.1%).

CONCLUSION

Retrospective cross-sectional design of the study was the main limitation. In conclusion, results of our study indicate that asphyxia is one of the main causes of CP development in our country. CP screening studies, which are accepted as an indicator of the socio-economic and cultural structure, require standardization. Considering central nervous system maturation, brain plasticity and changing clinical picture, the definitive diagnosis of CP cannot be made before 1 year of age. However, occasionally symptoms showing possibility of CP may be seen in early infancy. Although there are studies investigating diagnostic tools that enable early diagnosis in premature infants with abnormalities in neuroimaging, determining the exact age at which CP should be diagnosed is still a subject open to research.

Statement

Ethics Committee Approval: The Cerrahpaşa University Faculty of Medicine Clinical Research Ethics Committee granted approval for this study (date: 24.11.2009, number: D-008).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – SPK; Design – HHT; Supervision – HHT; Resource – HHT; Materials – SPK; Data Collection and/or Processing – HHT; Analysis and/or Interpretation – HHT; Literature Search – HHT; Writing – HHT; Critical Reviews – HHT.

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ORIGINAL ARTICLE

Turkish adaptation of the postpartum hemorrhage-specific self-efficacy scale; validity; and reliability

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ABSTRACT

Objective: The aim of the study is to define the validity and reliability of the Turkish version of postpartum hemorrhage-specific self-efficacy scale.

Material and Methods: The study was conducted in methodological type. The sample of the study consisted of 238 physicians, nurses, and midwives, working in the delivery room, postnatal, and birth emergency areas for at least 2 years. The data were collected by introductory information form, generalized self-efficacy scale, and postpartum hemorrhage-specific self-efficacy scale in February-December 2018. The structural validity of the scale was evaluated by exploratory factor analysis. In the context of reliability analyses, Cronbach's alpha, the item-total score correlation and the parallel test methods were used.

Results: According to the factor analysis results, it was found that the two-factor structure explained 69.38% of total variance and that item loads ranged between 0.31 and 0.88. Item total score correlations were found to be between 0.42 and 0.77. Cronbach's alpha value was 0.92 for the whole scale. Positive and middle level correlation was found between both scales as a result of parallel testing (r=0.301; p=0.000). It was determined that the self-efficacy sub-dimension of the scale consisted of eight items and the collective efficacy sub-dimension of 13 items, and a total of 21 items. Fit indices were found to be at an acceptable level as a result of the confirmatory factor analysis (χ^2/df=3.08, RMSEA=0.09, GFI=0.91, AGFI=0.77, IFI=0.92, CFI=0.92, NFI=0.89, RFI=0.87).

Conclusion: The Turkish version of the Postpartum Hemorrhage-Specific Self-Efficacy Scale was found valid and reliable. The scale can be used to evaluate physicians, nurses, and midwives' self-efficacy perception specific to postpartum hemorrhage.

Keywords: Bleeding, postpartum hemorrhage, reliability, self-efficacy, validity.

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INTRODUCTION

Maternal deaths, which are important criteria in determining countries' development level, are a universal health problem affecting developing countries the most.[1] The World Health Organization (WHO) and the United Nations (UN) tried to reduce maternal mortality by making various decisions in their health policies and set various goals.[2] The WHO and UN many international non-governmental organizations strive to achieve these goals by organizing joint studies and programs.[1,3] While maternal mortality was ranked fifth in the UN's Sustainable Development Goals (SDG) between 1990 and 2015, it rose to the third place in the SDGs determined for 2016–2030, and globally it is aimed to reduce the maternal mortality rate to below 70 per hundred thousand live births.[2–4] In 2017 reports of the WHO, it was stated that maternal deaths occurred during pregnancy, birth, or post-birth in 295,000 cases. The number of deaths out of 100,000 live births was 415 in underdeveloped countries, 543 in sub-Saharan African countries, 10 in European countries, 18 in North American countries, 211 globally, and 17 in Turkey.[3] In light of this data, it can be said that maternal mortality is globally decreasing. However, it is still quite far from the objective to decrease it below 70 out of 100,000 live births specified by the UN within the scope of SDG for 2016–2030, and the problem remains severe to this day.

Hemorrhage comes first in maternal mortality reasons globally and Turkey. One out of four maternal deaths (27.1%) in the world and one out of five maternal deaths (19.2%) in Turkey result from postpartum hemorrhage (PPH).[5,6] PPH is the most important obstetrical state of emergency that can develop following vaginal or cesarean birth.[7] Occupying an important place in maternal mortality, PPH is one of the preventable reasons for maternal mortality.[7] While PPH does not have a universally accepted definition, which refers to PPH as a type of hemorrhage that is more than 500 ml and occurs within 24 h of birth, and obstetrical bleedings causing a hemodynamic disturbance and threatening the mother's life.[8] Prevention of PPH and the awareness of health personnel (doctors, nurses, and midwives) about current implementations of its treatment and their active usage play a crucial role in preventing maternal deaths caused by hemorrhage.[9] Therefore, courses with various qualities have been being organized for 15–20 years to update health personnel's (doctors, nurses, and midwives) knowledge, remind them of the importance and sensitivity of the issue, and prepare them for obstetrical emergencies such as PPH.[10] In Turkey, Emergency Obstetric Care courses have been organized by the Turkish Ministry of Health General Directorate of Public Health, Department of Women's Health and Reproduction since 2009. The ministry has also published Emergency Obstetric Care Guide for health personnel to give a qualified, standard, and trustworthy service and provide unity in implementation in emergency obstetric situations.[11] Midwives/nurses are the health personnel that can specify abnormalities as fast as possible by monitoring the bleeding and involution of the mother during the postpartum period.[8] Today, postpartum bleedings are generally evaluated subjectively, as in visual guesses such as "very little," "little," "moderate," and "severe" bleeding in many clinics.[9–11] However, conducted studies put forward that visual guesses are not absolute. They tend to underestimate bleedings.[12,13] Only one out of nine women with PPH is diagnosed correctly, and even sometimes experienced gynecologists can be wrong.[14] Therefore, even the bleeding evaluation requires a certain professional experience, and wrong evaluations can lead to undesired results such as hemorrhagic shocks and mortality by delaying the PPH diagnosis.[13]

In this respect, health professionals (doctors, nurses, and midwives) monitoring the new mother during the postpartum period must have a high level of self-efficacy and self-sufficiency perception that can enable them to correctly implement the decisions they make in the face of an important obstetrical emergency, which could result in maternal death, such as PPH, besides having professional skills and experience that will help them be aware of abnormalities. The perception of self-efficacy and self-sufficiency demonstrates an individual's belief in his/her ability to determine and implement the required path to succeed in certain situations.[15]

Individuals with high self-efficacy and self-sufficiency perception choose to do harder work and direct themselves to achieve their goals. The higher the perceived self-efficacy and self-sufficiency is, the more efficient their efforts are.[16] Therefore, self-efficacy and self-sufficiency are important for health professionals (doctors and midwives/nurses) who can intervene in such a challenging obstetrical emergency as PPH.

Midwives/nurses must be aware that they cannot fight with a state of emergency such as PPH by themselves and take emergency action only after they call for help[8] because such a challenging obstetrical state of emergency as PPH requires fine teamwork.[17] In short, in PPH management, besides the self-efficacy of midwives/nurses and doctors, team efficacy is important. Team efficacy is defined as the shared belief in a team's ability to organize and manage the action phases required to produce certain skills.[18]

It is important to determine the health personnel's self-efficacy and team efficacy levels (doctors and midwives/nurses) who specialize in a vital field such as PPH. Therefore, Egenberg et al.[7] realized that there was no scale tool to determine the self-efficacy and team efficacy levels of health personnel. They developed a scale evaluating self-efficacy perception specific to PPH. In Turkey, it has been observed that there is no scale evaluating self-efficacy perception specific to PPH. This study is thought to contribute to the literature related to the field in question and provides researchers studying in this field with a scale tool that they can use. In this respect, this study has been designed to evaluate the validity and reliability of the scale for perceived PPH-specific self-efficacy for Turkish. In this study, answers will be sought for the questions of;

1. Is the Scale for Perceived PPH-Specific Self-Efficacy valid for Turkish doctors, nurses, and midwives?
2. Is the Scale for Perceived PPH-Specific Self-Efficacy reliable for Turkish doctors, nurses, and midwives?

MATERIAL AND METHODS

Type of Study

This study has been conducted as methodological.

The Sample and Population of the Study

Midwives, nurses, and gynecologists working in birthing, birthing emergency, and postpartum clinics at a private hospital specializing in gynecology located in the Anatolian side of Istanbul province be-

tween February and December 2018 have composed the population of this study. Midwives, nurses, and doctors who accepted to participate in the study and had at least 2 years of experience in birthing, birthing emergency, and postpartum clinics constituted its sample. In scale development studies, it is stated that data points must be 5–10 times more than the number of questions.[19] Within the scope of this study, considering that the Scale for Perceived PPH-Specific Self-Efficacy, projected to be adapted into Turkish, is composed of 21 items, the sample number was planned to be composed of at least 210 individuals, and the study was completed with 238 participants.

Data Collection Tools

Introductory Information Form, General Self-Efficacy/Sufficiency Scale, and the Scale for Perceived PPH-Specific Self-Efficacy Scale were used in data collection. These tools were handed to the individuals meeting the criteria to be included in the sample, and they were collected back 1 week later.

Introductory Information Form

This form, prepared by researchers following the literature, is composed of six questions evaluating the socio-demographical features of the participants (age, gender, education, profession, experience, and experience in the birthing field).

General Self-Efficacy Scale

This scale, whose validity and reliability check for Turkish was carried out by Gözüm and Aksayan (1999), was developed by Sherer and Maddux in 1982. Not belonging to any subjective field, it measures general self-efficacy perception. It is created as a 5-Likert type scale composed of 23 items. It generates at least 23 and at most 115 points. Participants are asked to choose one of the choices "1 – Does not define me; 2 – Somewhat defines me; 3 – Indecisive; 4 – Defines me well; 5 – Defines me extremely well" from every item, and points assigned to each item are taken as a basis. The scale has four subscales. The items 2, 4, 5, 6, 7, 10, 11, 12, 14, 16, 17, 18, 20, and 22 are reverse-scored. High points reflect a high general self-efficacy perception. Gözüm and Aksayan stated the Cronbach alpha internal consistency coefficient of the scale as 0.81.[20] The Cronbach alpha coefficient of the General Self-Efficacy Scale, used as a parallel scale in the study, was found to be 0.82.

The Scale for Perceived PPH-Specific Self-Efficacy

The scale for perceived PPH-specific self-efficacy was developed by Eggenberg et al.,[7] who was inspired by Bandura's self-efficacy concept, in 2017. It is a scale developed to evaluate health personnel's individual and collective efficacy levels when facing PPH. Self-efficacy and collective efficacy items were focused on the individual discipline and team sufficiency perceptions, respectively, in the face of PPH. While the first eight items in the scale measure PPH-specific individual self-efficacy, the items 9–21 measure collective efficacy. All the items except for the second one are reverse-scored. The total item points evaluate the scale. The points to be possibly earned from the scale range from one to eight, and while points close to eight reflect an increased self-efficacy, points close to one reflect a decreased self-efficacy in the two sub-scales and the whole scale.

Egenberg et al.[7] found the Cronbach alpha coefficient of the PPH-Specific self-efficacy sub-scale and collective efficacy subscale to be 0.95 and 0.96, respectively.

Evaluation of the Data

In evaluating the data, besides descriptive statistics such as percentage, frequency, mean, and standard deviation, the scale's language and construct validity were tested for its validity analysis. Construct validity test was carried out with exploratory and confirmatory factor analysis. Varimax rotation method was used in exploratory factor analysis. The data were deemed interpretable after the analysis of KMO and Bartlett's test results. Internal consistency analysis, item-rest and item-total correlations, and the parallel test method were used for reliability analysis.

Ethical Aspect of the Study

For the study to be carried out, ethical approval was obtained from the Clinical Research Ethics Committee of the hospital where the study was conducted (Approval Date: 22.12.2017; Decree No: 168), and institutional permission was attained from the institutions where the study was carried out. Before starting to collect data, the objective of the study was explained to participants, who then obtained general information about the study. The individuals who accepted to participate voluntarily in the study gave their written and verbal consent. Permission was obtained from Egenberg et al.,[7] the developer of the scale, for the Turkish adaptation of the scale.

RESULTS

The mean age of the participants was 38.35±8.38, and 83.12% of them were female, while 16.9% were male, and 36.9% were nurses, and their mean experience in years in the field of obstetrics and gynecology was 8.60±7.06. The socio-demographic data of the sample group are given in Table 1.

Validity Analysis

Language Validity

For the language validity of the scale, five translators having full knowledge of both English and Turkish languages first translated the original scale into Turkish. Then, the researchers selected the best statements among all the translations. After that, three translators re-translated into English with full command of both languages and different from the first group. The original scale and the English translations were compared. After necessary corrections, the Turkish form was created, and to evaluate its suitability in terms of meaning and clarity, the items in the scale were presented to Women's Health Nursing faculty members (n: 10) to obtain an expert opinion.

Content Validity

To assess the content validity, the opinions obtained from ten experts were analyzed with the Davis technique. In this technique, experts assess the scale items with a four-point rating system. The content validity rate (CVR) is calculated for each item and is obtained by dividing the number of the items with 3 or 4 points on the expert forms

Table 1: Socio-demographic data of the participants

Characteristics	n	%
Age (year), Mean±SD	38.35±8.38	
Experience (year), Mean±SD	9.53±8.58	
Experience in obstetrics (year), Mean±SD	8.60±7.06	
Gender		
Female	198	83.1
Male	40	16.9
Educational level		
High school	7.1	17
Associate degree graduate	4.6	11
Undergraduate	51.3	122
Faculty of medicine	15.9	38
Postgraduate	7.6	18
Doctorate/expertise in medicine	13.4	32
Profession		
Doctor	29.4	70
Midwife	34.5	82
Nurse	36.1	86

SD: Standard deviation.

by the total number of experts. The content validity index (CVI) is obtained by calculating the mean CVRs. It is recommended that the CVI be above 0.80 and the items with a CVR below 0.80 be eliminated (Şencan, 2005). In the analysis results, the items' CVRs were found to range from 0.90 to 1, and the CVI was observed to be 0.97.

Pilot Study

The final form of the scale in which its items were arranged was assessed in a ten-person group outside of the sample with the aim of the pilot study. During this pilot study, the researchers met face-to-face with the participants and assessed whether any items could not be understood on first reading. As a result of the researchers' pilot study, it was concluded that the items were understandable and clear.

Construct Validity

The factor analysis of the scale was carried out with exploratory and confirmatory factor analyses. Varimax rotation technique was used in exploratory factor analysis. The factor analysis was deemed interpretable after the analysis of KMO and Bartlett's test results. The KMO and Bartlett's test values were found to be 0.93 and 0.000, respectively.

On looking at the distributions of items to factors using the Varimax rotation technique, the scale was seen to accumulate in two factors. The two-factor construct was observed to explain 69% of the variance (Table 2). The scree plot graphic also confirmed the two-factor construct of the scale (Fig. 1). As it fits the original construct of the scale, the first factor comprises eight items, while the second is composed of 13 (Table 2). As shown in Table 2, the item factor loading

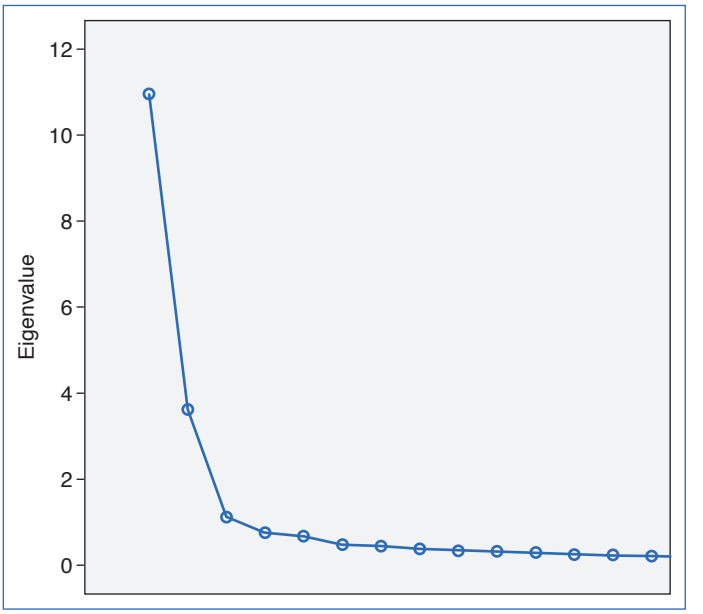

Figure 1: Scree plot graphic.

values were observed to range between 0.31 and 0.88. Item number 2 was found to have reverse loading just as in the original scale and receive loading from both factors.

Based on the confirmatory factor analysis, the scale's structural equation modeling result was significant with a value of P = 0.000, and the 21 items and the two sub-scales of the scale were determined to be related to the construct of the scale. Improvements were implemented on the modeling. During these improvements, the variables decreasing the fit level were specified, and among the remaining values, new covariances were created for the ones with a high covariance. The accepted values for the fit index were then met in fit index calculations, as shown in Table 3. The ratio of the Chi-square value to the degree of freedom (536.487/174) was determined to be 3.083. On reviewing the other fit indexes, the determined values were as follows; RMSEA=0.09, NFI=0.89, GFI=0.91, CFI=0.92, and AGFI=0.77. The model where the standardized parameter estimations related to the factors and the scale items are given is presented in Figure 2.

Reliability Analysis

In the item-total item-test analysis conducted for the reliability analysis of the scale, all the items' correlations were found to range between 0.42 and 0.77 (Table 2).

For internal consistency, the Cronbach alpha coefficient was calculated for the scale and its sub-scales. Item number 2 was re-coded for pre-analysis. The Cronbach alpha value was calculated to be 0.92 for the whole scale. The Cronbach alpha values for the Self-Efficacy and Collective efficacy sub-scales were 0.91 and 0.97, respectively (Table 4).

The parallel test method was implemented to determine the consistency coefficients within the scope of the reliability analysis of the scale. As shown in Table 4, a positive significant correlation between both scales was detected as a result of Spearman's correlation analysis (r=0.301; p=0.000).

Table 2: Factor analysis results of the scale for perceived postpartum hemorrhage-specific self-efficacy

Items	Factor load		Item total correlations
	1	2	
Item 14 As a team we help each other to prevent excessive PPH	0.88		0.76
Item 16 As team we can cope with PPH	0.87		0.77
Item 21 When PPH arises, our team is able to take action	0.87		0.68
Item 20 The team can handle PPH	0.86		0.69
Item 18 The team has usually a clear leadership in emergency situations like PPH	0.85		0.73
Item 17 As a team we are able to carry out the necessary actions to treat PPH	0.85		0.73
Item 15 I think that every member of the team will express clear messages during PPH	0.84		0.73
Item 19 As a team we communicate clearly and efficiently whenever PPH arises	0.83		0.68
Item 13 Everyone knows what to do during an ongoing PPH	0.83		0.75
Item 9 We are supportive towards each other when we are in demanding situations	0.79		0.72
Item 12 We are able to identify PPH in an early stage	0.77		0.72
Item 11 I think the team will share tasks in an appropriate way during PPH	0.74		0.73
Item 10 We as a team remain calm during situations with PPH	0.72		0.70
Item 2 PPH will make me paralyzed/unable to act. (reverse item)	-0.53	-0.31	0.57
Item 3 I can handle PPH whenever it happens		0.88	0.61
Item 7 I am confident in how to treat PPH		0.87	0.67
Item 6 I am able to identify PPH in an early stage		0.85	0.62
Item 4 I remain calm when handling PPH		0.85	0.62
Item 5 I have experienced that I am able to act in situations with PPH		0.85	0.56
Item 8 I can carry out the necessary actions to handle PPH		0.82	0.61
Item 1 I am able to stay calm in emergency situations		0.56	0.42
Variance It explains			
Factor 1	52.15%		
Factor 2	17.22%		
Total	69.38%		

PPH: Postpartum hemorrhage.

DISCUSSION

To test whether the sample magnitude was sufficient for exploratory factor analysis, the KMO and Bartlett's test values were taken as a basis. The KMO produces a value ranging from 0 and 1, and the closer to 1 a value is, the more sufficient the sample magnitude is reflected to be.[21,22] In this study, the KMO value was found to be 0.93. This value reflects that the sample magnitude is sufficient for factor analysis. Furthermore, a significant Bartlett's test value ($p<0.05$) demonstrates that the data set has multivariate normality.[21,22] The Bartlett's value was found to be 0.000 for this study, which shows that the factor analysis is interpretable.

After factor analysis, the scale was seen to display a two-factor construct. In the analysis of the scree plot graphic, it can be seen that the line between two points is a factor, and the distance between the points after the second factor is small and similar. This graphic confirms the two-factor construct of the scale.[21] The two-factor construct was seen to explain 69% of the variance (Table 2). The amount of total explained variance is expected to be above 30% in multifactor scales,[23] and each sub-scale is supposed to have at least 10% variance.[22] Egenberg et al.[7] stated the variance value of the two-factor construct of the original scale to be 43.8%. In this respect, the explained variance value obtained for this scale in the study is regarded as fit.

It was observed that the item factor loading values ranged from 0.31 to 0.88, and the item total correlations calculated for the reliability analysis of the scale were aligned between 0.42 and 0.77. The item factor loading value is supposed to be at least 0.32 or above during the scale development and adaptation process.[21,22] Furthermore, the item-total correlation value being 0.30 or above is stated to reflect that the items are sufficient in distinguishing the feature to be measured and fitted with the scale total.[21] The items with an item

Table 3: Fit index results from confirmatory factor analysis

	Fit indices	Recommended values
χ^2/df	3.08	≤5
RMSEA	0.09	≤0.08
GFI	0.91	≥0.85
AGFI	0.77	≥0.85
IFI	0.92	≥0.90
CFI	0.92	≥0.90
NFI	0.89	≥0.90
RFI	0.87	≥0.90
	χ^2: 536,487, df: 174, P: 0.000	

RMSEA: Root Mean Square Error of Approximation; GFI: Goodness of Fit Index; AGFI: Adjusted Goodness of Fit Index; IFI: Incremental Fit Index; CFI: Comperative Fit Index; NFI: Normed Fit Index; RFI: Relative Fit Index.

Table 4: Reliability analysis results of the scale for perceived postpartum hemorrhage-specific self-efficacy

	C. Alpha	Mean±SD	Parallel test	
		Min–Max	r*	p
General self-efficacy scale		141.09 (19.66)	301	0.000
		79.00–168.00		
Postpartum hemorrhage self-efficacy scale	0.92	6.71 (0.93)		
		3.76–8.00		
Self-efficacy	0.91			
Collective efficacy	0.97			

*: Spearman's correlation test used. P<0.001.

factor loading value below 0.32 are recommended to be excluded from the scale. However, some views defend that no item should be discarded to remain faithful to the original scale in scale adaptation studies. In this study, item number 2 is a reverse item and receives -0.31 load from the first factor and -0.53 load from the second factor. Even though the load amount that item number 2 receives from the second factor, it was deemed fit that this item would be included under the first factor to remain faithful to the original construct of the scale. The item factor loading values of the original scale was seen to range from 0.62 to 0.91. In scale adaptation studies, item clarity is affected by cultural and linguistic differences. Such differences were thought to cause lower item loading values to be obtained in the Turkish version of this scale.

After evaluating the fit statistics obtained from CFA, it was concluded that the GFI and AGFI indexes being above 0.85 and the IFI, RFI, NFI, and CFI indexes being above 0.90 reflect an acceptable

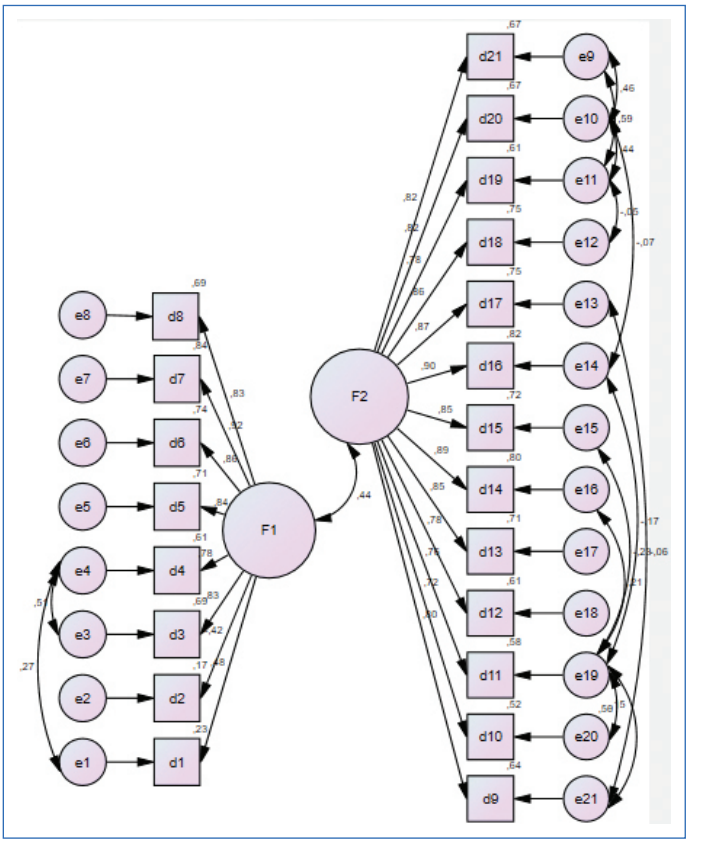

Figure 2: CFA results of the perceived postpartum hemorrhage-specific self-efficacy scale.

fitness.[23–25] The NFI and RFI indexes for this scale were seen to be extremely close to acceptable values. The CFI and IFI indexes being above 0.90 show that they have good fit values. It is also stated that an RMSEA value below 0.08 reflects the goodness of fit, while below 0.10 demonstrates an acceptable fit level, while the ratio of the chi-square value to the degree of freedom being below 5 indicates a good fit level.[23–25] For this scale, the RMSEA index was seen to be 0.09, extremely close to the acceptable fit criterion. After analyzing the CFA results, the ratio of the Chi-square value to the degree of freedom was seen to be 3.083 (p=0.000). This value being below 5 reflects a good fit level.[23–25] After reviewing the goodness of fit indexes obtained from the confirmatory factor analysis, the model is regarded as fit.

The Cronbach alpha value, calculated to determine the scale's internal consistency reliability, was found to be 0.92 for the whole scale, 0.91 for the self-efficacy sub-scale, and 0.97 for the collective efficacy sub-scale. In the original scale, Egenberg et al.[7] calculated the internal consistency coefficients to be 0.95 for the self-efficacy sub-scale and 0.96 for the collective efficacy sub-scale. These coefficients are seen to be close to the Turkish version. Scales with a reliability coefficient of 0.70 or above during scale development and adaptation processes are stated to be reliable.[22,23] In this respect, the Cronbach alpha values were high for the whole scale and its sub-scales.

In determining the parallel form reliability, the correlation between the points obtained from two-scale tools is looked at by implementing a

different scale tool that has the same qualities to the same individuals at the same time. The general self-efficacy/sufficiency scale, whose validity and reliability have been proven in the Turkish language, was referred for the parallel form reliability. A positive significant correlation was found between the general self-efficacy/sufficiency scale and the scale for perceived PPH-specific self-efficacy (r=0.301; p=0.000). A correlation value between 0.70 and 1.00 reflects a high-level correlation, while a value between 0.30 and 0.70 demonstrates a mid-level correlation.[23] A mid-level positive significant correlation was found between the general self-efficacy/sufficiency scale and the scale for perceived PPH-specific self-efficacy used in this study. This result is important in terms of the reliability of the scale.

CONCLUSION

The results obtained from the study have shown that the exploratory factor analysis and confirmatory factor analysis results of the Turkish version of the scale for perceived PPH-specific self-efficacy are acceptable, and its reliability indexes are high. In this respect, the two-factor and 21-item form of the scale has been regarded as a valid and reliable tool that could be used to measure the perceived PPH-specific self-efficacy/sufficiency levels Turkish doctors, nurses, and midwives working in the field of gynecology.

Study Limitations

The results of this study are limited to the health professionals of the hospital where it was carried out. Therefore, the inability to generalize the results of this study to every health personnel working in gynecology is one of the limitations of the study. The small number of doctors and male health professionals participating in the study constitutes another limitation.

Statement

Ethics Committee Approval: The Zeynep Kamil Women and Children Diseases Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 22.12.2017, number: 168).

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CASE REPORT

Report of a pregnant woman with mosaic Turner syndrome

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ABSTRACT

Spontaneous pregnancy in women with Turner syndrome is rare (5%) and relatively high risk. A number of methods to preserve fertility in such women have been discussed. Careful follow-up is required during these pregnancies due to the high incidence rates of neonatal, obstetric, maternal, and cardiovascular complications. A 39-year-old multigravid woman (G5, P3, A2) with mosaic Turner syndrome with a history of three spontaneous pregnancies and two miscarriages was evaluated at our clinic. The analysis showed mos 45,X [9]/46,XX [38] mosaic Turner syndrome. Her first and fourth pregnancies resulted in miscarriages during the first trimester. Here, we discuss a pregnant woman with mosaic Turner syndrome with unaffected fertility but with a history of spontaneous pregnancies/miscarriages, with reference to the current literature.

Keywords: Mosaic turner syndrome, spontaneous pregnancy, turner syndrome.

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INTRODUCTION

Turner syndrome is characterized by the absence of all or part of a normal second sex chromosome in females,[1] which often leads to a constellation of physical findings, including congenital lymphoedema, short stature, and gonadal dysgenesis.[2] Turner syndrome has an incidence of 1 in 2500 live births and is one of the most common chromosomal abnormalities worldwide.[3,4] The majority of patients have a short stature, infertility, and absence of secondary sex characteristics. The classic form of Turner syndrome is associated with a 45,X karyotype, accounting for approximately half of all cases. The mosaic form (45,X/46,XX) accounts for 15–25% of Turner syndrome cases, while the remaining cases have structural abnormalities in the X chromosome.[5] The syndrome is caused by partial or complete loss of one of the X chromosomes, which leads to haploinsufficiency of genes involved in the development or maintenance of ovarian reserve. Approximately 1–2% of women with Turner syndrome can become pregnant naturally. Several studies have reported that the rates of spontaneous pubertal development and menarche, as well as unassisted pregnancy, are greater in Turner syndrome with mosaicism than in monosomy X patients.[6] Here, we report a 39-year-old woman with 45,X [9]/46,XX [38] Turner syndrome mosaicism who had spontaneous puberty and a history of three spontaneous pregnancies and two miscarriages. The incidence of, and prognostic counseling topics for, spontaneous adolescence, menarche, and fertility is discussed in relation to this case and the current literature.

CASE REPORT

A 39-year-old multigravid woman (G5, P3, A2) with mosaic Turner syndrome who had a history of three spontaneous pregnancies and two miscarriages was evaluated at our clinic. The patient's parents appeared healthy and were of normal height and weight. There was no history of hereditary or congenital disease in the family. There was no special follow-up. She had achieved normal developmental milestones and spontaneous puberty with regular menses. She was not using contraception. Here height and weight were 150 cm and 65 kg, respectively, indicating a body mass index of 28.9. The first clinical finding that led to karyotype analysis was a growth rate limitation at the age of 18 years. Cytogenetic analysis of blood lymphocytes revealed a karyotype of Turner syndrome mosaicism with 45,X (9 cells)/46,XX (38 cells). The analysis showed mos 45,X [9]/46,XX [38] mosaic Turner syndrome (Fig. 1). Echocardiography showed a normal aorta and aortic valve. Ophthalmologic examination and audiography were normal. The patient's initial echocardiography did not show any cardiovascular malformations associated with Turner syndrome, including normal thoracic aortic dimensions (aortic size index 2.0 cm/m^2) without coarctation symptoms. The patient was followed up from gestational week 25 of her pregnancy to delivery.

Arterial blood pressure was monitored regularly throughout the course of pregnancy and found to be normal, ranging between 110/70 mmHg and 120/80 mmHg. Typical blood screening tests (cytomegalovirus, rubella, Toxoplasma gondii antibodies, total blood cell count, blood biochemistry, thyroid function, and hemoglobin electrophoresis), a glucose tolerance test, urinalysis, general urine culture, and antenatal ultrasonography were all normal. She had a history of three spontaneous pregnancies and two miscarriages. Her first and fourth pregnancies resulted in miscarriages during the first trimester, while the second and third pregnancies resulted in live births by cesarean section. The patient gave birth to a normal healthy 3550 g live baby girl at gestational week 38.

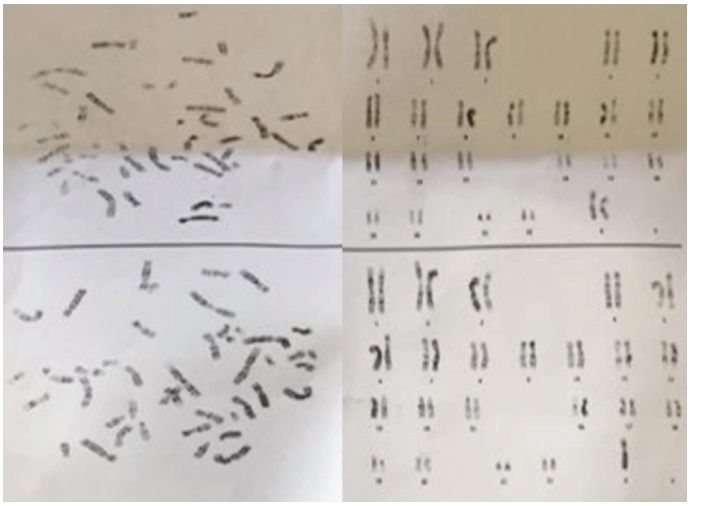

Figure 1: The cytogenetic analysis report of mos 45,X [9]/46,XX [38] mosaic Turner syndrome.

DISCUSSION

Turner syndrome is a chromosomal abnormality caused by complete or partial loss of one X chromosome and is usually characterized clinically by a short stature and primary ovarian failure. Classical Turner syndrome is the result of complete loss of an X chromosome in all cells, resulting in a 45,X karyotype, and accounts for half of all cases. The most common karyotype in mosaic Turner syndrome is 45,X/46,XX, which accounts for approximately 15–25% of cases.[7] Jacobs et al.[8] reported that among 84 cases of Turner syndrome with a standard karyotype (45,X), 16% had mosaicism with a second cell type containing a ring X chromosome (45,X/46,X,r(X)). Later, adolescence, even during menstrual cycle and women with menstrual cycle, even deterioration and only 2–8% of spontaneous pregnancy. Most of these pregnancies (87–92%) occur in women with mosaicism.[6,9]

In a previous study of 1648 women with Turner syndrome, 86 women achieved spontaneous conception (5.2%), 128 live infants were delivered, and most patients (76.7%) presented with the 45,X/46,XX karyotype.[6] The frequency of spontaneous pregnancy ranged from 1.26% to 5.6%. With regard to gestational outcome, an expressive number of children born, and abortions were observed, the latter with values of 54.9% and 34.6%. In another study, 62 Turner syndrome patients achieved spontaneous pregnancy, with a total of 153 pregnancies. Most patients in this cohort had the 45,X/46,XX karyotype (42 patients). The minimum and maximum ages at pregnancy were 21 and 32 years, respectively.[10] The present study evaluated patients with Turner syndrome and spontaneous pregnancy with mosaic (more frequent) and pure karyotype.[6,9–12]

In a few studies, it is believed that the rate of spontaneous pregnancy in Turner syndrome was underestimated because many individuals with Turner syndrome are not diagnosed due to the wide phenotypic variability associated with this chromosomal abnormality.

Therefore, diagnosis is difficult in those without significant dysmorphism. Thus, many affected individuals may have spontaneous pregnancies, and a cytogenetic diagnosis cannot be made or is delayed. On the other hand, a previous study described a Turner syndrome patient with the 45,X/47,XXX karyotype who had five miscarriages by the age of 26 years old; the first, third, fourth, fifth, and sixth pregnancies resulted in miscarriages during the first trimester. Her second pregnancy resulted in the birth of a healthy girl with karyotype 46,XX. The 45,X/47,XXX karyotype is rare, accounting for only 1.5% of Turner syndrome patients.[13]

Spontaneous pregnancies are rare, and recurrent pregnancy even rarer, in women with Turner syndrome.[14] Considering the chance of spontaneous pregnancy, even in mosaic cases, protection of fertility by oocyte vitrification and/or ovarian tissue freezing should be discussed at a relatively young age, preferably immediately after pubertal development (age 13–15 years), when the ovaries are still functional. Therefore, a number of methods for preserving fertility in such cases have been discussed. Careful follow-up is required during these pregnancies due to the high incidence of neonatal, obstetric, maternal, and cardiovascular complications. Regardless of the type of pregnancy, all pregnancies in women with Turner syndrome should be considered high risk and should be monitored closely for obstetric complications. It is recommended that a multidisciplinary team composed of specialists in the fields of maternal–fetal medicine, cardiology, and endocrinology closely monitor Turner syndrome patients during pregnancy due to risks of worsening cardiovascular diseases during pregnancy and specific complications. However, there are very few reports on spontaneous pregnancy in Turner syndrome, and therefore, more research is needed to clarify the true frequency of spontaneous conception in such women. In addition to rigorous neonatal follow-up, the team should provide assistance to patients who wish to continue to conceive, before they become pregnant, to provide comprehensive risk assessment and genetic consultation.[15]

CONCLUSION

We present a woman with Turner syndrome with a history of spontaneous pregnancies and live births and discussed our observations in relation to the current literature.

Statement

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – YET, SKT; Design – YET, AİG; Supervision – SKT, EPTY; Resource – YET, AİG; Materials – YET, EPTY; Data Collection and/or Processing – SKT, EPTY; Analysis and/or Interpretation – YET, AİG; Literature Search – YET, EPTY; Writing – YET, SKT; Critical Reviews – YET, AİG.

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CASE REPORT

Recurrent pericarditis caused by familial Mediterranean fever: A case report

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ABSTRACT

Familial Mediterranean fever (FMF) is characterized by clinically recurrent fever attacks and inflammation associated with serositis. The Mediterranean fever gene is found in 16p13.3 and its mutations are known to lead to FMF. Here, we present a patient with FMF and recurrent pericarditis who responded to colchicine treatment. Therefore, regular follow-up of FMF patients who are mutation carriers is important in terms of cardiovascular risk.

Keywords: Familial Mediterranean fever, Mediterranean fever gene, recurrent pericarditis.

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INTRODUCTION

Familial Mediterranean fever (FMF) is an autosomal recessive disorder and frequently observed among the nations of the Mediterranean populations, such as Jews, Armenians, Turks, and Arabs.[1]

Mediterranean fever gene (*MEFV*) resides on 16p13.3 and its mutations are known to lead to FMF. *MEFV* encodes a protein called pyrin. The pyrin protein has a role in regulation of apoptosis, inflammation. *MEFV* consists of 10 exons and most patients have mutations associated with exon 10. M694V, V726A, M680I, and M694I (in exon 10) are common mutations that lead to FMF and are responsible for more than 80% of FMF cases in the Middle Eastern region.[2]

FMF is clinically characterized by recurrent episodes of fever and inflammation associated with serositis. Usually, peritonitis is typically the first manifestation of FMF. Other findings of FMF are synovitis, pleuritis, and rarely pericarditis and meningitis. The incidence of pericarditis in FMF is low, ranging between 0.7% and 1.4%.[3,4] Recurrent pericarditis as the initial finding has been reported in a few case with FMF.[5–7]

Here, we report a patient with suspected FMF and recurrent pericarditis who responded to colchicine therapy.

CASE REPORT

A 27-year-old Turkish man applied to the emergency department with acute chest pain, which was aggravated with deep inspiration and rotation. There is no history of cigarette, alcohol, and drug use. Serum C-reactive protein (CRP) was 12 mg/dl. Electrocardiogram showed normal sinus rhythm, however, echocardiogram revealed mild pericardial effusion. The patient was diagnosed with acute pericarditis and indomethacin 800 mg/day was administered. CRP level decreased to 1.1 mg/dl. Chest pain was relieved and the patient was discharged.

Three weeks later, the patient applied to the emergency department with similar chest pain. At the time of admission, the patient's temperature, pulse rate, and blood pressure were normal. His heart sounds were clear without audible murmurs or pericardial friction rub. His breath sounds were normal, and no crackles were detected. Serum CRP was increased (27.16 mg/dl) and showed slightly increased white blood cell count of 11.63/µl (normal 3.8–10.0/µl) (73% neutrophils, 16.3% lymphocytes, 8.4% monocytes, 2.1% eosinophils, and 0.2% basophils). Serum alanine aminotransferase was mildly elevated at 98 IU/l (12–55 IU/l), however, aspartate aminotransferase, lactate dehydrogenase, and gamma-glutamyl transferase levels were normal. In addition, serum protein electrophoresis showed an acute-phase pattern. Serum-free triiodothyronine and free thyroxine were within the normal ranges.

Echocardiogram showed only mild pericardial effusion. Computed tomography of the chest showed mild pericardial effusion with mild left pleural effusion.

During this second episode of pericarditis, indomethacin 800 mg/day and colchicine 1 mg/day were started. As the patient's symptoms did not improve, colchicine dose was increased to 2 mg/day. With this treatment continued for 12 months, his complaints disappeared, and all laboratory values were within normal limits and no episodes of pericarditis recurred. The sequencing *MEFV* gene revealed compound heterozygous mutation for M694V/R202Q. We performed *MEFV* mutation analysis on the patient's parents. The mother had a heterozygous M694V mutation. The father had a heterozygous R202Q mutation.

DISCUSSION

Idiopathic recurrent pericarditis (IRP) is defined as repeated episodes of acute pericarditis with unknown origin.[8] Autoimmune and autoinflammatory mechanisms have been accounted for the etiology of IRP. The safety and efficacy of colchicine have been shown in patients with recurrent pericarditis and colchicine decreases the recurrence rate after the first attack of acute pericarditis.[9,10]

Recurrent pericarditis can present as the only initial findings of FMF. Okutur et al.[5] described a 25-year-old Turkish woman who presented with IRP. After a few episodes, she was treated with colchicine and episodes of pericarditis were terminated. *MEFV* mutation analysis showed that this patient was compound heterozygous for M694V and M680I.

Tutar et al.[6] described an 8-year-old Turkish girl who had three attacks of pericarditis within a 3-month period. After the third attack, colchicine was started, which ended the episodes of pericarditis. During the subsequent 20 months under the colchicine treatment, no FMF attacks or acute pericarditis episodes were observed. She was compound heterozygous for E148Q and L695A.

Yoshioka et al.[7] described a 56-year-old man who had a high fever, CRP level, and periodic episodes of acute pericarditis. The patient was treated with colchicine, became afebrile and CRP level decreased. No recurrence was shown. *MEFV* mutation analysis showed compound heterozygosity for E84K and G304R.

Our patient's *MEFV* mutation analysis showed compound heterozygosity for M694V and R202Q. M694V is the most commonly mutation in the Turkish population. Tunca et al.[4] reported that 51.4% of 1090 FMF patients had M694V mutation in Turkish population, which is followed by M680I (14.4%) and V726A (8.6%). Another study by Yilmaz et al.[11] reported that the allele frequency in FMF patients was 51.1% for M694V. M694V homozygosity is associated with a severe form of the disease and the most serious complication of the disease, amyloidosis, is reported at a higher incidence in cases homozygous for M694V.[12]

R202Q has previously been reported as a common polymorphism.[13] However, its clinical significance is still controversial. No significant association was found between demographic and clinical characteristics of patients and R202Q genotype in some studies.[14–16]

Yigit et al.[15] reported that there was a high association between the R202Q and FMF, however, they state that R202Q may not have an effect on disease in heterozygous state but can be a cause of illness in homozygous state and should be included in routine mutation screening of FMF.

In one study from Greece, Giaglis et al.[16] showed that R202Q homozygosity was found in 48% of cases with FMF in whom no other *MEFV* mutation could be detected. Researcher supports that R202Q polymorphism may have a diagnostic correlation in the homozygous state.

Table 1: Causes of pericarditis

Idiopathic pericarditis	Pericardial fat necrosis, Loffler syndrome, Thalassemia, drug reactions (procainamide, hydralazine)
Infectious pericarditis	Viral: Coxsackie A and B, influenza, HIV, hepatitis A, B, C
	Bacterial: *Tuberculosis, Streptococcus, Pneumococcus*
	Mushrooms
	Parasitic: Ekinokok, Entamocba histolytica, cysticercus
	Other: Rickettsial, spiroketal, mycoplasma, infectious mononucleosis
Autoimmune/vasculitis	Rheumatoid arthritis, rheumatic fever, SLE, scleroderma, Sjögren syndrome, Reiter's syndrome, ankylosing spondylitis, Wegener granulomatosis, Behçet's syndrome, FMF, polyarteritis nodosa
Metabolic	Renal failure, myxedema, gout, skorbit
Neighboring tissue diseases	Myocardial infarction, aortic dissection, pleural and pulmonary disease
Neoplasms	Mesothelioma, sarcoma, fibroma, metastatic, carcinomas, sarcomas
Trauma	Penetrating, iatrogenic, radiation, dissecting aneurysm

FMF: Familial Mediterranean fever.

R202Q mutation located at exon 2 of the *MEFV* gene, which was reported as a frequent polymorphism with linkage disequilibrium with M694V mutation (http://fmf.igh.cnrs.fr/infevers/). In the study of Oztürk et al.,[13] R202Q was observed in a different haplotype which is not in linkage with M694V mutation. This denoted that it might be a disease-causing mutation. This may also confirm their hypothesis in two cases with amyloidosis. The R202Q frequency is high in their control group. It seems that it has no effect when it is in heterozygous state, however, when combined with another disease-causing mutation, the clinical spectrum appears. This shows that R202Q alteration is important for diagnosis.

Chronic pericarditis is a disease that maintains its importance today due to various etiological reasons. It may progress with non-specific symptoms and present with a serious clinical picture such as cardiac tamponade. Histological, cytological, and biochemical examinations are performed for diagnosis. Diagnosis and treatment processes are mostly carried out together. The classification of pericarditis for etiology is shown in Table 1.[17]

Pro-inflammatory cytokines and acute-phase reactants increase during FMF attacks. Therefore, it is thought that chronic inflammation that occurs may also be associated with increased cardiovascular risk in patients with FMF.[18] In the study conducted by Salah et al.[19] with pediatric patients diagnosed with FMF, it showed that approximately half of the patients affected by valvular disease. In another study, different degrees of tricuspid regurgitation were reported.[20]

In a recent study, two patients diagnosed with FMF and their family members evaluated in terms of cardiovascular involvement. In echocardiographic examination, different degrees of valvular insufficiency were reported. In addition, considering that all family members with the compound M694V, R202Q mutation has at least one cardiac valve disease, it can be said that it is important to follow these mutation carrier FMF patients in terms of cardiovascular involvement.[21]

According to these studies, M694V/R202Q mutation may suggest etiology of recurrent pericarditis in our patient. Mutation analysis of *MEFV* gene should keep in mind in patient with IRP to provide a proper diagnosis and treatment.

Statement

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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DERLEME / REVIEW

Dudak ve/veya damak yarığı olan bebeklerde beslenme problemlerine yaklaşım

Approach to feeding problems in babies with cleft lip and/or palate

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ÖZET

Dudak ve/veya damak yarığı en yaygın kraniyofasiyal doğumsal anomalilerden biri olup, en sık orofasiyal bölgede görülür. Yenidoğan bebeklerde bu doğumsal anomalinin görülme sıklığı %15 civarındadır. Bu konjenital malformasyonların patogenenezi tam olarak bilinmemekle beraber, hem beslenme hem de genetik faktörlerin rol oynadığına dair kanıtlar bulunmakta ve bu kanıtlar gün geçtikçe artmaktadır. Dudak ve/veya damak yarığı olan çocuklar, doğumdan sonra beslenme güçlükleri nedeniyle yetersiz beslenebilirler. Bu deformitelere sahip çocukların büyümesi genellikle sağlıklı çocuklara kıyasla bozulmuştur. Bu bebeklerin değerlendirilmesi için multidisipliner bir yaklaşım zorunludur. Başlangıçta dudak ve/veya damak yarığı olan yenidoğanların beslenmesi ebeveynler için büyük bir endişe kaynağıdır. Emzirme, modifiye edilmiş biberonlar ve/veya meme ucu, tıkayıcı plakalar ve anne danışmanlığı ve destek gibi beslenme müdahalelerine ihtiyaç duyulur. Bu yazıda, bu konudaki bazı beslenme sorunlarının ve uyarlamalarının gözden geçirilmesi amaçlanmıştır.

Anahtar sözcükler: Yarık dudak, yarık damak, beslenme.

ABSTRACT

Cleft lip and/or palate is one of the most common craniofacial congenital anomalies and is most common in the orofacial region. The incidence of this congenital anomaly in newborn babies is around 15%. Although the pathogenesis of these congenital malformations is not fully known, there is evidence that both dietary and genetic factors play a role, and this evidence is increasing day by day. Children with cleft lip and/or palate may be malnourished after birth due to nutritional difficulties. Children with these deformities are often impaired in growth compared to healthy children. A multidisciplinary approach is mandatory for the evaluation of these babies. Feeding newborns with cleft lip and/or palate in the beginning is a major concern for parents. Nutritional interventions such as breastfeeding, modified bottles and/or nipple, occlusive pads and maternal counseling and support are needed, so this article aims to review some nutritional issues and adaptations in this regard.

Keywords: Cleft lip, cleft palate, nutrition.

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GİRİŞ

Oral yarık, yenidoğanda en sık görülen kraniyofasiyal malformasyondur. Bu hastalığın birçok sınıflandırması vardır. Bu sınıflandırmalardan en basit olanı üç ana oral yarık türü olan, tek başına yarık dudak, yarık damaklı yarık dudak ve tek başına yarık damaktır. Dudak ve/veya damak yarığı (DDY), günümüzde öne çıkan, coğrafik bölgelere ve etnik kökenlere göre değişiklik gösteren, beslenme problemlerini de içine alan bir anomalidir.[1] Üst çene kemiği ve ağız tavanını meydana getiren kemik ve yumuşak dokuları oluşturan embriyonik uzantıların yetersiz birleşmesinden kaynaklanmaktadır.[2] Genel olarak yarık tipi, hem lateralitesi (tek taraflı, iki taraflı veya orta hat) hem de yerine göre tanımlanır. Tek başına yarık dudak, yarık olgularının %25'inde, dudak ve damak yarığı kombine olarak olguların %51'inde, izole yarık damak ise olguların %24'ünde görülür.[3] Damak yarıkları konuşma, işitme ve orta yüz bölgesinde kemik gelişimi ile ilgili fizyolojik dengeleri etkileyerek fonksiyonel ve estetik bozukluklara yol açmaktadır. Dudak ve/veya damak yarıkları için bugüne kadar birçok sınıflandırma yapılmıştır, ancak uluslararası ideal bir sınıflandırma halen yoktur.[4] Bugüne kadar yapılan sınıflandırmalar arasında en çok kabul gören sınıflandırma embriyo patolojik temele dayanan sınıflandırmadır.[4]

İlerleyen yıllarda yarık dudak ve yarık damaklı çocukların beslenme ihtiyaçlarının karşılanmasında zorluklar devam edebilmektedir (Şekil 1a–c). Bu nedenle beslenme yetersizlikleri ve beslenme komplikasyonları açısından tıbbi izlemede olmaları gerekmektedir.[5] Normal koşullar altında bile emzirme hem anne hem de yenidoğan için karmaşık ve öğrenilmesi gereken bir süreçken DDY'li bebeklerde beslenme süreci daha da komplike hale gelebilmektedir (Şekil 1d).

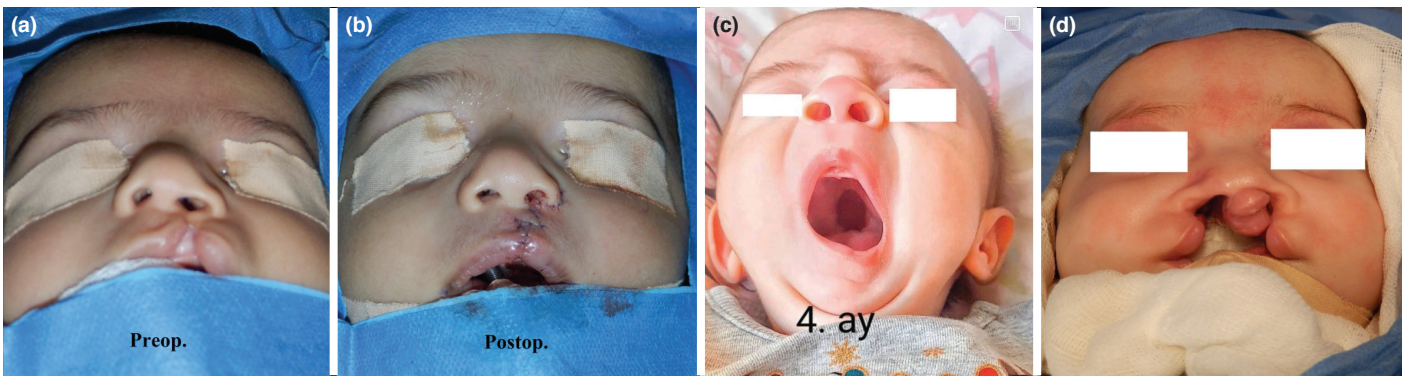
Dudak ve/veya damak yarıklarının tanısı, tedavisi ve takibi multidisipliner bir yaklaşım gerektirmektedir. Bu derlemede, DDY'li bebeklerde beslenme problemlerine yaklaşımdan bahsedilmiştir.

Dudak ve/veya Damak Yarığı Olanlarda Epidemiyoloji

Yarık dudak ve yarık damak, çevresel faktörler ve sosyoekonomik koşulların yanı sıra coğrafi köken, ırk ve etnik gruplar arasındaki değişkenlik nedeniyle ortaya çıkabilecek en yaygın doğum anomalilerinden biridir. Dudak ve/veya damak yarığı prevalansı, Asya ve Amerikan popülasyonlarında en yüksek, Afrika popülasyonlarında en düşük oranlardadır. Dudak ve/veya damak yarığının cinsiyet dağılımı genel olarak eşit değildir. Dudak ve/veya damak yarığının insidansı erkeklerde kadınlara göre iki kat daha fazla iken, sadece damak yarığının oranı kadınlarda daha yüksektir.[6] Dudak ve/veya damak yarığı insidansları, 2003 yılında Dünya Sağlık Örgütü'nün İnsan Genetiği Programı aracılığı ile kurulan Uluslararası Perinatal Tipik Orofasiyal Yarıklar Veritabanı tarafından yapılan bir çalışmada bildirilmiştir. Coğrafi bölgelere göre değerlendirilen kayıtlara göre DDY olguları; Japonya, Meksika, Batı Avrupa, Kanada, Amerika Birleşik Devletleri, Avustralya, Britanya Adaları, Doğu Avrupa, Birleşik Arap Emirlikleri, Güney Avrupa ve Güney Afrika'da belirlenmiştir. Dudak ve/veya damak yarığı insidansı, Japonya'da en yüksek, Güney Afrika'da en düşük olarak bildirilmiştir.[7] Dünya genelinde genel kabul gören DDY insidansı 1/1000'dir.[6] Dudak ve/veya damak yarığı insidansı Afrika popülasyonlarında 0.3/1000, Avrupa popülasyonlarında 0.7–1.3/1000, Asya popülasyonlarında 1.4–2.1/1000 ve Amerikan popülasyonlarında 3.6/1000'dir.[6,8] Türkiye, Orta Doğu, Avrupa ve Asya'yı birbirine bağlayan eşsiz coğrafi konumu nedeniyle yüksek derecede göçe maruz kalmıştır. Nüfustaki artışla birlikte değişkenlik, Türkiye'de karmaşık bir heterojen etnik tablonun oluşmasına ve mevcut popülasyonda çok çeşitli önemli genetik varyasyonlara yol açmıştır.[6] Bölgesel olarak incelendiğinde, Türkiye'nin doğu bölgelerinde izole dudak ve/veya damak yarığı olgularının diğer bölgelere göre daha yüksek sayıda olduğu tespit edilmiştir.[9] Ülkemizde yarık dudak anomalilerinin 1/1000, yarık damak anomalilerinin ise 1/2500 oranında görüldüğü bildirilmiştir.[5]

Dudak ve Damak Yarıklarının Embriyolojisi

Kraniyofasiyal gelişim, hücre örüntüsü, göç, çoğalma ve farklılaşmanın karmaşık bir etkileşimini temsil eder. Yüz dokusunun çoğu, düzenleyici, yapısal ve konumsal genler tarafından yönetilen embriyonik nöral krest hücre göçünden kaynaklanır. Dudak yarığı; normalde, dudağın tamamen kapanması, lateral nazal, medyan nazal ve maksiller mezodermal süreçler birleştikçe, gebe kaldıktan 35 gün sonra tamamlanır. Üç normal füzyon bölgesinden herhangi birinin kapanmaması, tek taraflı (en yaygın), iki taraflı (daha az yaygın) veya medyan (nadir) dudak yarıklarını oluşturabilir. Yarık damak, damak raflarının orta hat füzyonu gerçekleşmediğinde ortaya çıkar. Programlanmış hücre ölümündeki anormallikler, bu mekanizma tartışmalı olsa da damakta füzyon eksikliğine katkıda bulunabilir.[10] Yüz gelişiminin büyük bir bölümü 4–8. gebelik haftaları arasında gerçekleşmektedir. Onuncu hafta sonunda anlaşılır bir yüz görünümü ortaya çıkmaktadır. Damak, gebeliğin beşinci haftasında oluşmaya başlar. En kritik aşama altıncı ve dokuzuncu hafta arasında olmasına rağmen gelişim 12. haftaya kadar devam eder. Yarık dudak ve yarık damak sıklıkla birlikte görülmelerine rağmen, farklı embriyolojik kökenlere sahiptir. Yarık dudak, bir veya her iki tarafta maksiller ve medial burun yük-



Şekil 1: Preoperatif **(a)** ve postoperatif **(b)** yarık dudak. **(c)** izole yarık damak, **(d)** bilateral yarık damak ve dudak.

selmelerinin başarısız bir şekilde birleşmesinden kaynaklanır. Yarık damak, lateral palatinin birbirleriyle buluşup kaynaşması sürecindeki başarısızlıktan kaynaklanır. Yarık damak daha sık bir sendrom ile ilişkilendirilirken, yarık dudak çoğunlukla izole bir kusurdur.[11]

Dudak ve Damak Yarıklarının Etiyolojisi

Dudak ve/veya damak yarığı nedenleri karmaşıktır, hem genetik hem de çevresel faktörlere bağlı gelişebilir.[12] Muhtemel sebepler arasında; ileri yaş gebeliği, akraba evliliği, oligohidramniyoz, gebelikte kötü beslenme, radyasyon ve teratojenik ajanlara maruz kalma, stres, geçirilen infeksiyonlar (toksoplazma ve rubella), sigara ve alkol kullanımı, maternal fenilketonüri, hipertermi, hidantoin, gestasyonel obezite, pregestasyonel diyabet, folat ve çinko eksikliği, gebelik döneminde kullanılan ilaçlar (steroidler, trimetadion, metotreksat, aminopterin, antikonvülzan ve hidantoin grubu antiepileptikler), uyuşturucu kullanımı ve kalıtım sayılabilir.[13,14] Yoksul ve daha düşük eğitim seviyesine sahip kadınların çocukları arasında DDY görülme sıklığı daha fazladır.[15,16] Maternal beslenme ile DDY arasındaki ilişkiyi araştıran çalışmaların çoğu multivitamin ve folik asit takviyeleri ile ilgilidir.[17,18] Yapılan bir çalışmada, gebelik döneminde yalnız folik asit takviyeleri değil aynı zamanda gıda kaynaklı folatın da DDY ile yakından ilişkili olduğu bildirilmektedir.[19] Yapılan başka bir çalışmada, DDY'li bebeklerin annelerinin gebelikteki beslenme durumları araştırılmış ve diyetsel makro besin ögesi ve vitamin alımlarının sağlıklı kontrol gebelere göre daha düşük bulunduğu, gebelerin lif, askorbik asit, demir ve magnezyum, çinko alımları ile sebze ve meyve tüketiminin DDY'yi önlemede önemli faktörler olduğu rapor edilmiştir.[20]

Oral yarıkların çoğu sendromik değildir (gen-gen ve gen-çevre etkileşimleri vb.). Gebeliği planlayan kadınlar, bu malformasyon ile ilişkili ilaçları bırakmak için doktorlarının görüş ve önerileri doğrultusunda ilaç kullanarak, sendromik olmayan oral yarığı olan bir çocuk sahibi olma riskini azaltabilirler. Örneğin, antikonvülzan ilaçların daha güvenli olanlarla değiştirilmesi, sigaranın bırakılması, alkollü içeceklerden kaçınılması, diyet veya takviyeler yolu ile folat eksikliğinin giderilmesi gibi rutin gebelik tavsiyelerine uyabilirler.

Sendromik olgular, tek bir gendeki varyantlardan veya bir genomik bölgenin silinmesinden veya kopyalanmasından (kopya) kaynaklanabilir. Yüzden fazla sendromda oral yarık defekti görülmüştür. Van der Woude sendromu, otozomal dominant bir bozukluktur ve olguların %1 ila %2'sini oluşturan en yaygın sendromik yarık şeklidir.

Yüksek kromozom anormallikleri riski nedeniyle, fetal oral yarıkların ultrason bulguları ve ilişkili anomalileri olan kadınlara amniyosentez önerilmelidir. Spesifik paneller veya tam ekzom sekanslama yolu ile daha fazla genetik analiz, aile geçmişi ve spesifik ilişkili anomaliler dikkate alınarak olgu bazında değerlendirilebilir.

Görünüşe göre gen-çevresel etkileşimlerin daha fazla incelenmesi ve anlaşılması gerekmektedir. Daha fazla genetik ve epidemiyolojik araştırmalar nihayetinde oral yarıkların oluşumuna ilişkin anlayışımızın gelişmesi mümkün kılınacaktır.

Dudak ve Damak Yarıklarında Büyüme ve Gelişmenin İzlenmesi ve Antropometrik Ölçümler

Dudak ve/veya damak yarığının fiziksel büyümeye etkisini gösteren antropometrik veriler, eski yıllara aittir. Bunların tümü ortalama vücut ağırlığı ve ortalama boy uzunluğunu içeren eski göstergelerdir.[21,22] Bazı çalışmalarda yarık defekti olan çocukların daha düşük doğum ağırlıklarına sahip oldukları, aylar ve yıllar içinde genel büyümelerinin daha yavaş olduğu öne sürülmektedir.[23–25] Literatürde DDY'li infantlarda malnütrisyon görülme sıklığının yüksek olduğu bildirilmektedir.[26]

İzole damak yarığı olan bebeklerin sıklıkla intrauterin büyüme kısıtlılığı gösterdikleri, doğum ağırlıklarının 2500 g, boy uzunluklarının 49 cm'nin altında, baş çevresinin de 33 cm'nin altında olduğu bildirilmiştir.[25] Farklı çalışmalarda vücut ağırlık kazanımının sadece damak yarığı olanlarda en az olduğu bildirilmiştir.[27,28] Dudak ve/veya damak yarığı olan bebek ve çocuklarda, özellikle başka sağlık riskleri de eşlik ediyorsa, vücut ağırlıklarının normal çocuklardan daha yavaş arttığı bildirilmiştir.[29]

Yenidoğan Yönetimi

Doğum sonrası yenidoğan bakımının ilk odak noktası, bebeğin hava yolu ve emme yeteneğinin değerlendirilmesidir. Şiddetli Pierre Robin sekansı (mikrognati ile ilişkili) olan bebekler, güvenli bir hava yolunu korumak için doğumdan sonra uzman desteğine ihtiyaç duyabilir. Damak yarığı olan bebekler genellikle sütü biberondan veya göğüsten etkili bir şekilde emmek için yeterli negatif ağız içi basınç oluşturamazlar, ancak sıklıkla mama veya sağılmış anne sütü ile uyarlanabilir beslenme ekipmanıyla (örn. sıkılabilir biberon, değiştirilmiş meme başı, kaşık) beslenirler.[30] Aksine, yarık dudağı olan ve palatal anormalliği olmayan bebekler, genellikle özel cihazlar olmaksızın biberon veya göğüsten beslenebilirler.[31] Bu alanda bir bebek besleme/emzirme uzmanına danışılması önerilir.

Birincil dudak onarımları genellikle üç aylıkken yapılır. Bu onarımlar altı aylıkken palatal onarımlarla birlikte de yapılabilir. Bu bebek ve çocuklarda ek ameliyatların yanı sıra konuşma ve ortodontik tedavilere sıklıkla ihtiyaç duyulmaktadır.[32] Amerikan Yarık Damak-Kraniyofasiyal Derneği, hastanın genel gelişimsel, tıbbi ve psikolojik ihtiyaçları çerçevesinde değerlendirme ve tedavilerinin uygun şekilde sıralanmasıyla koordineli bakımı vurgular ve ebeveynler için önemli destek ve bilgiler sağlar (acpa-cpf.org).

Dudak ve/veya Damak Yarığı Olan Bebeklerde Beslenme

Bebeklerin ve çocukların fiziksel büyümesi, önemli bir sağlık göstergesidir. Yetersiz fiziksel büyüme çoğu zaman yetersiz beslenme, kronik sağlık durumu, genetik bozukluk durumu veya bir sendromu içeren bir dizi problemin varlığına işaret edebilir.[25] Dünya Sağlık Örgütü bebeklerin doğumdan itibaren ilk altı ay boyunca, su ve başka sıvı ve katı besinler almadan, sadece anne sütü ile beslenmelerini, altıncı aydan sonra tamamlayıcı besinlerle birlikte emzirmenin iki yaş ve üzerine kadar sürdürülmesini önermektedir.[33]

Solunum ve yutma, bazı ortak anatomik yapıları ve fizyolojik olayları paylaşan koordine sistemlerdir. Disfaji, yutma biyomekaniklerini etkileyen koordinasyon bozukluğu, obstrüksiyon veya zayıflık nedeniyle anormal yutma olarak tanımlanır.

Optimal yutma için, uygun olgunlaşma, duyusal gelişim ve ince motor koordinasyon gibi gelişim faktörleri zorunludur. Prematürite, nörolojik olumsuz koşullar, reflü ve konjenital malformasyonların tümü ve prematürite ile eşlik eden bazı yaygın tıbbi bozukluklar disfajiye neden olabilir. Prematüre bebekler, ağızdan beslenme için gerekli olan çeşitli aktiviteleri koordine etmekte ve tolere etmekte zorlanırlar. Yetersiz gelişmiş oral motor sistemin bir sonucu olarak kötü

Tablo 1: Emzirme güçlüğü olan durumlar ve öneriler[41]

Durum	Negatif basınç oluşumu	Oral motor becerisi	Besleme tekniği
Dudak ve damak yarığı	-	+/-	Emzirme zordur
			Ağız içine süt boşaltımı
Sadece sert damak yarığı	±	+	Emzirme bazen başarılıdır
			Geniş delikli biberon başlığı
			Ağız içine süt boşaltımı
Sadece yumuşak damak yarığı	±	+	Emzirme, uzun boyunlu emzikli biberon ile besleme
Tek taraflı yarık dudak	±	+	Emzirme, geniş tabanlı emzikli biberon ile besleme
Pierre Robin sekansı	±	-	Emzirme olası değildir
			Biberonla pozisyon önemli
			Uzun boyunlu geniş tabanlı emzikli biberon
			Orogastrik/nazogastrik besleme

emme meydana gelir. Kötü emme, oral motor güç ve koordinasyonun az gelişmiş olması ile az gelişmiş oral motor gücü ve olgunlaşmamışlık veya yanaklardaki destek dokulara bağlı emme gücünün tamamen gelişmemiş olmasının bir sonucu olarak ortaya çıkar. Ayrıca gelişmemiş akciğerler solunum ve yutma koordinasyonu için zorluklar yaratır.[34] Esas olarak yutma hareketi üç ana evrede gerçekleşir: oral, faringeal ve özofageal besin oral yoldan alınıp hazırlandıktan sonra tükürükle işlemlenerek besin içeriği istemli olarak farinkse gönderilir, böylece istemsiz faringeal evre tetiklenir. Yumuşak damak nazofarinksi kapatır, larinks yükselir ve öne eğilir, gerçek ve yalancı vokal kordlar kapanır ve faringeal konstriktörler sıralı şekilde kasılarak besin bolusunu özofagusa iter. Üst özofagus sfinkteri eş zamanlı olarak gevşer ve yemek içeriğini almak için açık kalır. Daha sonra bu besin içeriği, peristaltik hareketlerle mideye iletilir. Bu evrelerden birindeki veya hepsindeki sorunlar yutma bozukluklarına (orofaringeal disfaji) neden olur. Yarık damak emme için gerekli basıncın sağlanamaması ve/veya nazal regürjitasyonla, yarık dudak ise memenin etrafında labial kapalılığın sağlanamaması nedeni ile fonksiyon kaybına yol açarak yutmayı olumsuz yönde etkiler.[35]

Dudak ve/veya damak yarığı olan bebeklerde ağız bölgesinde nöromusküler fonksiyon bozukluğu olması nedeniyle beslenme sorunu ilk olarak karşımıza çıkan önemli bir problemdir. İntraoral nöromusküler disfonksiyon veya kraniyofasiyal malformasyonu olan infantlarda sıklıkla beslenme ile ilgili sorunlarla karşılaşılmaktadır.[34] Dudak ve/veya damak yarığı olan bebeklerin çoğunda beslenme için gerekli olan oral motor beceri, dağınık veya etkisiz olarak saptanmıştır. Bu bebeklerde yutma fonksiyonu normaldir fakat emme fonksiyonunda problem vardır.[36,37] Literatürde DDY'li bebeklerin beslenme problemlerini çözecek tek ve uygun bir yöntem bulunmamaktadır.[38] Yarıkla doğan bebeğin, başka hiçbir sistemik sorunu söz konusu olmadığı sürece sağlıklı bebeklerle benzer beslenme gereksinimleri vardır.[39] Birinci öncelik yeterli sürede yeterli beslenmenin mümkün olduğunca normale yakın şekilde gerçekleştirilmesi, ikinci öncelik ise uygun beslenme yönteminin saptanmasıdır.[40] Dudak ve/veya damak yarığı olan bebekler beslenirken diğer bebeklere kıyasla çok çabuk yorulurlar, beslenme süreleri daha uzun olabilmekte ve oral içerik sıklıkla nazal bölüme kaçabilmektedir. Yapılan bir çalışmada, bu bebekler arasında 0–18 aylar arasında solunum yollarına bağlı hastalıklar ve intestinal rahatsızlıklar tanımlanmış, bu nedenle de bu tür bebeklerin kilo artışı ve boy uzamalarının daha yavaş olduğu bildirilmiştir. Dudak ve/veya damak yarığı olan bebeklerin çoğunda gerekli olan oral beceri dağınık ve etkisiz olup yutma fonksiyonunun normal, emme fonksiyonunun ise problemli olduğu bildirilmiştir.[27,38]

Bu olgularda üç anatomik problem tanımlanmıştır. Birincisi iki taraflı dudak yarıklarında premaksillanın aşırı projeksiyonu nedeniyle meme ucuna adaptasyonun bozulması, ikincisi geniş damak yarıklarında nazal tarafa kaçan meme başının dil tarafından sıkıştırılıp emilememesidir. Üçüncüsü ise, dilin retrograd yerleşimi ile öne uzanamaması ve bu nedenle meme başının sıvazlanmasının yetersizliğidir. Yutkunma, ağız içinde süt birikince dil yardımıyla önce orofarinkse ardından mideye yönlendirilmesi olarak tanımlanır. İzole dudak ve/veya damak yarığı olgularında yutkunma problemine pek rastlanmaz. Yutkunma problemleri daha çok Pierre Robin sekansında (glossopitozis nedeniyle), nöromusküler yetersizliklerde, daha seyrek olarak da özofagus anomalilerinde görülebilir. Bu tür bebeklerde nazogastrik beslenme gibi farklı beslenme tedavileri uygulanır.[38]

Farklı yarık defektlerinde emme ve beslenmenin değerlendirilmesi Tablo 1'de özetlenmiştir.[41]

Farklı derecelerde beslenme sorunlarına yol açan ve farklı tip defektleri olan bu bebekler için özel beslenme ekipmanları kullanılarak sorun çözülebilir. Bu ekipmanlar özel tasarlanmış emzikler, özel tasarlanmış biberonlar, yumuşak başlıklı kaşık veya ucu kaşık olan biberonlar, çanaklar ve beslenme şırıngalarıdır (Şekil 2).[37,38,42] Çok sayıda besleme cihazı olmasına rağmen, cihaz seçimi kadar besleme tekniği de önemlidir. Bebeği beslemede birinci yöntem sütü arka tarafa ileten özel biberonların veya meme uçlarının kullanılmasıdır. Bebek bu özel biberon veya meme uçları ile sütü yutar. Bebeği besleyen ile bebek arasında bir ritim öğrenilir. Bu yöntem, bebeğin gerçekten emmesine ve yardımcı emme yöntemlerine ihtiyacını azaltmaya dayanır ve böylece bebeğin beslenme sürecindeki sorumluluğunun öncelikle yutmak haline getirilmesi amaçlanır.

Damak yarığı olan bebeklerde beslemeye yönelik diğer bir yöntem ise obturator (damak protezi) kullanımıdır. Kullanılan yapay da-

Şekil 2: Dudak ve/veya damak yarığı olan bebekler için özel tasarlanmış biberonun bir örneği.

mak plakaları (maksiller protezler ve oral obturatorlar) yarığı tıkar, bebeğin meme ucuna bastırıp sütü çekebileceği sert bir yüzey oluşturur, boğulma ve sütün nazal boşluğa akma riskini azaltır.[42] Bu tür bir aletin yerleştirilmesi, bebeğin sütü göğüsten veya biberon meme ucundan çekmesi için yeterli emmeye izin verecek ve burun boşluğundan dışarı akan sıvı miktarını azaltacak yeterli negatif basınç oluşturma yeteneğini kolaylaştıracaktır. Oral obturatorlar, regürjitasyonu azaltır, dilin damak yarığına kaçarak o bölgeyi genişletmesini önler, maksillar kollapsı kısıtlar ve de beslenme süresini azaltabilir. Ülserasyon oluşması, hijyen problemleri ve büyüme ile beraber ölçülerin değişmesi oral obturatorların dezavantajlarıdır.[38]

Pierre Robin sekansı olan bebeklerde tedavi planı yapılırken solunum sıkıntısı ve beslenme sorunu birlikte ele alınmalı, tedavi buna göre düzenlenmelidir. Hafif olgular dışında anneyi emerek beslenme sıklıkla olanaksızdır. Hafif olgularda bebek yan yatırılarak emzirme denenmelidir. Biberonla beslenme denenirken yüzüstü ya da yan yatış durumunda, damak yarıklarında kullanılan uzun emzikli ve geniş delikli biberonlar kullanılarak sağılmış anne sütü verilmelidir. Damak yarığı olan bebeklerde obturator (damak protezi) denenebilir. Beslenme ve kilo alımı sorunu olan bebeklerde orogastrik tüp ile beslenme ya da gereğinde geçici olarak gastrostomi ile beslenme seçilmelidir. Yeterli beslenmenin sağlanması kilo alımının yanı sıra erken çene gelişiminin hızlanması, dil kaslarının olgunlaşması açısından da önemlidir.[43]

Yeterli kilo alımının sağlandığından ve sürdürüldüğünden emin olmak için bebeği özellikle ilk haftalarda ve aylarda dikkatle izlemek önemlidir. Tüm bu beslenme sorunlarına rağmen, bir yarıkla doğan bebeklerde, infeksiyona karşı direncini arttırmak ve cerrahi müdahalelere izin verebilmek için yeterli kilo alımı sağlanmalı, stresin üstesinden gelmek için güç oluşturmaya yardımcı olmak amacıyla yeterli besin alımı sürdürülmelidir.

Emzirme

Yumuşak damakta küçük yarıkları olan bebekler emmeyi başarabilirler fakat yumuşak ve/veya sert damakta büyük yarıkları olan bebekler genellikle emmeyi başaramazlar. Yenidoğanlar ve prematüre bebekler daha büyük bebeklere kıyasla daha düşük emme basınçları oluştururlar. Yarık dudaklı bebeklerin emmesi daha kolaydır ancak sadece yarık dudak olan bebeklerde, emzirme sırasında dudak koruyucusu kullanılmalıdır. Yarık damak veya yarık dudak ve damak kombine olan bebekler emme oluşturmada güçlük çekerler, çünkü beslenme sırasında ağız boşluğu burun boşluğundan yeterince ayrılamaz. Bu bebekler için olumsuz sonuçlar, emzirme sırasında yorgunluk, uzayan beslenme süreleri ve bozulmuş büyüme ve beslenmedir. Emzirme sonuçlarını açıklayan literatür sınırlıdır.[40] Küçük yarık damaklı geç preterm bebekler tipik olarak küçük yarık damaklı term bebeklere göre daha az emerler. Yarık damaklı bebekler için damak protezi kullanmak, memeden sütü iyi bir şekilde emme yeteneğini kolaylaştırabilir.

Besleme veya emzirme yarı oturur pozisyonda bebeğin başı hafif fleksiyondayken yapılmalıdır. Bebeğin sık sık gazı çıkarılarak, 60–90 mL için 30 dakikayı aşmayacak sürede beslenmelidir.[38,39] Bebeğin yeterli beslenip beslenmediği, beslenme süresi ve ağırlık kazanımından takip edilebilir (Tablo 2).[38,44] İki taraflı ve bazen tek taraflı yarıkları olan bebekler, belirgin emme verimsizliği nedeniyle genellikle emmede zorluk çekerler ve bu bebeklerde yumuşak bir şekilde "yardımlı beslenme" gerekli olabilmektedir.[45]

Yine yarık dudak veya yarık damaklı bebeklerin vücut ağırlığı kazanımı daha uzun sürebilir. Bir bebekten günde 5–6 ıslak bez alınıyorsa ve düzenli hareketleri varsa, sağlıklı ve uyanıksa, yeterince beslendiğinin belirtileridir.[39] Eğer bebek emziriliyorsa, emzirmenin günde 8–10 kez iki veya üç saatte bir 10 dakika süreyle yapılması önerilmektedir.[45] Bebek ememiyorsa anne sütü sağılıp biberonla verilmeye çalışılmalıdır. Anne sütünü saklama koşullarına yönelik farklı çalışmalarda farklı uygulamalar olduğu görülmektedir.[46] Anne sütünü uzun süreli saklamak için sert plastik veya camdan yapılmış sert kenarlı kaplar tercih edilmelidir. Bu kaplar hava geçirmez özellikte olmalıdır. Anne sütünü kısa süreli (72 saatten daha az) saklamak

Tablo 2: Beslenme kapasitesi protokolü (0–3 ay)[38,44]*

	İyi	Orta	Kötü
Uygun beslenme şeklinin bulunma süresi	Doğumdan sonra ilk 48 saat	Birkaç gün	Haftalar
Beslenme süresi	<20 dakika	20–40 dakika	40–60 dakika
Haftalık kilo alımı	>200 gram	<200 gram	Düzensiz kilo alımı ve kaybı

*: Tablonun başlık kısmı kaynaklar incelenerek ve modifiye edilerek hazırlanmıştır.

için steril plastik poşetler kullanılabilir. Kalan sütün atılmaması için az miktarlarda depolanmalıdır. Anne sütü buzdolabında saklanacaksa 2–4ºC sıcaklıktaki buzdolabının orta rafında ve arka tarafında saklanmalıdır. Çözdürülmüş süt buzdolabında dört saate kadar saklanabilir, ancak tekrar dondurulmamalıdır. Sağılmış anne sütü mikrodalga fırında ısıtılmamalıdır, çünkü mikrodalga, sütün bazı immünolojik özelliklerine zarar vermektedir. Dondurulmuş sütün buzu buzdolabında ya da ılık suyun içinde çözdürülmelidir. Bebeğe vermeden önce kabı sallayarak sıcaklığın karışması sağlanmalı ve sütün sıcaklığı kontrol edilmelidir. Sütün sıcaklığı bileğin iç kısmına birkaç damla süt damlatılarak kontrol edilebilir.[46] Sağılan süt oda sıcaklığında (22ºC) 6–10 saat, buzdolabında (+4ºC) 12 saat saklanabilir.[38]

Yarığı olan bebeklerde, özellikle süt akışı çok yavaş veya çok hızlı ise, beslenme sırasında normalden daha fazla hava yutulabilir, bu sebeple besleme süresinde iki veya üç kez beslemeye ara verip bebeği daha dik bir pozisyonda tutmak ve gazını çıkartmak faydalı olabilmektedir.[42] Emzirme mümkün olmuyorsa sıkılabilir biberon kullanmak faydalı olabilir, emzik ucu artı şeklinde kesilerek sütün daha fazla gelmesi sağlanabilir ve bebeğin yorulması önlenebilir.[38] Bu çocuklarda anne sütü veya mama dışında tamamlayıcı beslenmeye başlanması altıncı aydan sonra önerilmektedir, ek gıda yumuşak olmalı ve asitli olmamalıdır. Turunçgiller ve domates gibi bazı yiyecekler asidik yapıya sahip oldukları için burun geçişini tahriş edebilir, bu tür yiyeceklerin çocuk daha fazla kontrole sahip olduktan sonra verilmesi uygun olur.[47]

Yapılan bir çalışmada şırınga, bardak ve kaşıkla beslenen DDY'li bebekler sırasıyla 10 ile 14 haftada ağırlık kazanımları açısından karşılaştırılmıştır. En fazla vücut ağırlık artışı anne sütünü şırınga ile alan bebeklerde görülmüştür. Dudak ve/veya damak yarığı olan bebeklerde 10. haftada 0.7 kg, 14. haftada 0.8 kg vücut ağırlık artışı olmuş, bardak ve kaşıkla beslenen DDY'li bebeklerde ise 0.4 kg vücut ağırlık artışı tespit edilmiştir. Normal emzirilen bebeklerin ise 10. haftada 0.6 kg, 14. haftada 0.7 kg vücut ağırlık kazanımları olmuştur. Mama ve anne sütünü karışık olarak kaşıkla alan DDY'li bebekler 10. haftada 0.5 kg, 14. haftada 0.6 kg vücut ağırlığı kazanmışlardır. Normal bebekler ise 10. haftada 1.0 kg, 14. haftada 1.7 kg vücut ağırlığı kazanmışlardır. Ortalama beslenme süreleri altıncı hafta için şırınga ile beslenenlerde 10 mL/1.25 dakika, fincan ve kaşıkla beslenen DDY'li bebeklerde 10 mL/2.08 dakika olarak bildirilmiştir. Yapılan bir çalışmada, düşük doğum ağırlıklı damak yarığı olan bebeklerin, ikinci ve dördüncü haftalar arasında sağılmış anne sütü ile nazogastrik bir tüpten beslendiklerinde, bebeklerde haftada 0.119 kg vücut ağırlık artışı sağlandığı saptanmıştır.[48]

Ameliyat Sonrası Besleme

Dudak ve/veya damak yarığının güncel cerrahi yaklaşımı erken onarım olup, onarımın üç aylık bebeklerde (10'lar kuralının gereklerini tamamladığı zaman), 12 aylıkken, 5–10 kg vücut ağırlığına ulaşıldığında ve 400–700 mL arasında total kan hacmine sahip bebeklerde yapılması önerilmektedir.[49]

Yarığı olan bebeğin ameliyattan sonra emzik kullanması önerilmez. Beslenme ile ilgili de farklı görüşler vardır. Erken dönemde biberon kullanımına izin veren görüşler olduğu gibi, ilk 72 saat oral beslenmeye izin vermeyen, sonrasında da kaşıkla veya şırıngayla ön vestibül bölgesinden beslenmeye izin veren görüşler de vardır.[38,50] Anne sütü ile beslenebilen bebeklerde anne sütü ile beslenmeye başlanır. Ek gıda alanlarda ise partikülllü besinler tercih edilmez ve mamanın su oranı arttırılır, beslenme sonrasında da su içirilmesi önerilir. Ameliyat sonrasında 2.5–3 hafta süresince bebeğin sıvı gıda ile beslenmesi önerilir.[1] Yoğurt, çorba gibi sıvı gıdalar tercih edilmemelidir. Yarık dudaklı bebeklerin beslenmesi ameliyat gününden itibaren olmak üzere kaşıkla gergin onarım hattına zarar vermeyecek şekilde oturur pozisyonda uzun saplı yumuşak başlıklı bir kaşık ile yapılmalıdır. Yarık damaklı bebeklerin en azından ilk 48–72 saatte mamaları partikülllü olmamalı ve berrak gıda almaları sağlanmalıdır. Başlangıçta bakımı zor olmasına rağmen ağız içindeki kesiler 3–4 gün içinde hızla iyileşir.[51] Ameliyat sonrasında kullanılan kaşık, biberon, emzirme arasında kilo alımı, yara komplikasyonları ve beslenme miktarı açısından bir fark bulunmadığı bildirilmektedir.[38] Yarık dudak ameliyatı sonrası dönemde emzirme ve biberonla beslenme önerilmez.[50]

Tablo 3: Operasyon geçirmiş 2–6 yaş arası dudak ve/veya damak yarığı olan çocukların makro besin ögesi alımlarının sağlıklı çocuklarla karşılaştırılması[52]

	Ortalama değerler		
Besin ögesi	**Normal**	**DDY**	**p**
Enerji (kcal)	1165.58	1337.57	**0.215**
Protein (g)	42.05	45.08	**0.163**
Yağ (g)	34.26	45.08	**0.021**
Karbonhidrat (g)	168.03	182.08	**0.513**

DDY: Dudak ve/veya damak yarığı.

Yapılan bir çalışmada, ameliyat olmuş 2–6 yaş arası çocukların besin alım düzeyleri araştırıldığında, DDY'li çocukların, makro besin ögeleri açısından normal çocuklara benzer diyetsel alım gösterdikleri bildirilmiştir (Tablo 3).[52]

Sonuç ve Öneriler

Dudak ve/veya damak yarıkları çok çeşitli tiplerde olduğundan ve bazılarında birlikte görülen ek anomaliler ve sendromlar da olabileceğinden doğum sonrası bir süre bunların tetkik edilmesi için çocuk doktorları bebeğin yoğun bakım ünitesinde bakılmasını uygun bulmuş veya bulacak olabilirler. Bu durum ebeveynleri korkutmamalıdır. Unutulmaması gereken başlıca noktalar; hiçbir aperey yarığı tamamen kapatmaz, damak yarığının ön tarafını kapatır, arkası açık kalır, zaten kapatırsa çocuk nefes alamaz, bu nedenle arkadan burnuna besin kaçışı olabilir. Apereyler bebek ve anne tarafından her zaman çok kolay kullanılamazlar. Bunların da ayrı bir bakımı ve bebek büyüdükçe belli aralıklarla değiştirilmesi gereklidir. Bu nedenle ortodonti doktoru ile yakın iş birliği ve bunların bakımına hazırlarsa kullanılmaları uygundur. Asıl önemli olan bebeğin 45–60 derece açı ile dik beslenmesi, mutlaka gazının çıkarılması ve yan yatırılmasıdır. Beslenme sırasında bebeğin dinlenme aralarının olacağı ve sonra tekrar emeceği unutulmamalıdır. Beslenme miktarının aynı aydaki diğer bebekleri yakalaması gereklidir. Bunun için uğraşmak gere-

kebilir ama beslenme süreçleri çok uzun da olmamalıdır. Beslenme araları belki aynı aydaki bebeklerden biraz daha sık olabilir, ancak yarım saat gibi çok sık aralara inerse bebek yine bütün enerjisini emmeye harcadığı için kilo alamaz. Beslenmede en önemli konu annenin bebeğini kucağına alması, kendisine ve bebeğe en uygun ve rahat pozisyonu bulması ve onunla rahat ve konforlu bir şekilde beslenmeyi sürdürmesidir. Bebek anneyi ememiyorsa bile ten teması sağlanmalıdır. Mümkünse anne bebeğini beslerken konuşmamalı ve sadece onunla ilgilenmelidir. Anne beslenme sırasında çok yorulacağı için bebeğin gazının çıkarılması baba veya bu konuda tecrübeli ve yardımcı olabilecek diğer aile bireyleri tarafından yapılmalıdır. Bu bebekler ne kadar dik durumda olurlarsa o kadar rahat ederler. Ayrıca psikolojik açıdan da bu kıymetlidir. Beslenme miktarları ve mama çeşitliliği her bebek gibi ayına göre artacaktır. Her bebekte olduğu gibi ek besinlere geçiş de bu bebeklerde aynı zamanda ve acele etmeden olmalıdır. Zaten 6–7 aylık olduğunda bebek destekle veya desteksiz oturur durumda olacağı için beslenme nispeten daha kolay olacaktır. Bütün bunlara dikkat edilmesi ile en çok korkulan beslenme sırasında akciğerlere besin kaçma ihtimali azalacaktır ama yine de olabileceği akılda tutulmalıdır. Bebek bu durumda öksürerek bunu atmaya çalışır. Böyle bir durum olduğunda veya beslenme sırasında morarma görüldüğünde beslenme hemen kesilip bebeğin sırtına vurularak ona yardımcı olmaya çalışılmalıdır. Bu durum, aslında her bebekte olabilir ama bu bebekler biraz daha fazla hava yuttukları için, daha fazla kusarlar ve kusma sırasında da ciğerlere kaçma durumu olabilir. O nedenle dik besleme, gazının çıkarılması ve biraz kucakta tutulup yan yatırılma çok önemlidir.

Sonuç olarak, DDY'li bebekler, nüfusun önemli bir bölümünü oluşturmaktadır. Dudak ve/veya damak yarıkları sık görülen doğum anomalilerindendir. Bu anomaliler, genetik ve çevresel faktörlerin etkisi ile meydana gelmektedir. Bu faktörlerin belirlenip ortadan kaldırılması önemlidir. Dudak ve/veya damak yarıklarının önlenmesinde ve tedavisinde multidisipliner çalışma gerekir. Birey, aile ve topluma danışmanlık hizmeti verilerek, risk altındaki gruplar tespit edilerek ve gebe olan veya gebelik planlayan kadınların takibi sağlanarak, dudak ve/veya damak yarığı olan çocuğa sahip olma riski azaltılabilir. Birinci basamakta dudak ve/veya damak yarıklarının oluşumunda rol oynayan risk faktörleri azaltılmaya çalışılıp bu konuda toplum bilinçlendirilebilir. Bu tür hastalar yetersiz beslenme ve çeşitli sağlık sorunları açısından riskli bebeklerdir. Kanıta dayalı müdahaleler ve beslenme teknikleri oral beslenmede başarılı olabilir ve bebek sağkalımı artabilir. Beslenme müdahaleleri ve ailenin eğitimi ile ailenin yaşadığı stres azaltılmalıdır. Bu konuda sağlık kuruluşlarında uzmanlaşmış bir ekip kurulmalıdır. Kadın hastalıkları ve doğum uzmanı tarafından, üç ve dört boyutlu ultrasonografinin kullanılması ile prenatal yarık dudak ve damak tanı oranları artmıştır. Çocuk hekimi tıbbi ve genetik öyküleri aldıktan sonra ayrıntılı fizik muayeneleri yapmalı ve sağlık sorunlarını gidermek için gerekli tıbbi tedavi protokolleri hazırlamalıdır. Doktor, diyetisyen ve hemşire tarafından hastanın tıbbi beslenme ve tedavisi sağlanmalı ve aileye beslenme eğitimi verilmelidir. Plastik ve rekonstrüktif cerrah ile maksillofasiyal cerrahi bilim dalları, anatomik defektin onarımından sorumludur. Kulak burun boğaz uzmanı ve odyolog olası işitme bozukluğu açısından, konuşma terapisti ise çocuğu konuşma ve dil problemleri açısından düzenli olarak takip eder. Dişlerinin normal düzeninde çıkması ve düzensizliklerin önlenebilmesi için ortodontist tarafından takip edilmelidir. Aile hekimi, çocuğun büyüme ve gelişmesinin takibi ve gerekli uzmanlık dallarına zamanında yönlendirilebilmesi için ekibin önemli bir parçasıdır. Böylelikle sağlık masrafları azaltılabilir, beslenme yükü ve hem ebeveynler hem de bebekler için zorluklar hafifletilebilir. Emzirmenin nütrisyonel olduğu kadar bebek için sosyal ve psikolojik ihtiyaç olduğu asla unutulmamalıdır.

Açıklama

Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastalardan alınmıştır.

Hakem Değerlendirmesi: Dış-bağımsız.

Yazar Katkıları: Fikir – FS, AAE; Tasarım – FS, AAE, AGP; Denetleme – FS, AAE, OEA, ABA, EC, AGP; Kaynak – FS, OEA; Malzemeler – FS, OEA; Veri Toplanması ve/veya İşlemesi – FS, AAE, OEA, ABA, EC, AGP; Analiz ve/veya Yorum – FS; Literatür Taraması – FS, AAE, OEA, ABA, EC, AGP; Yazıyı Yazan – FS, AAE; Eleştirel İnceleme – FS, AAE, OEA, ABA, EC, AGP.

Çıkar Çatışması: Yazarların beyan edecek bir çıkar çatışması yoktur.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

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