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Clinical Investigations

Factors associated with breastfeeding
Emzirme ve ilişkili faktörler
Elif Yılmaz, Fatma Doğa Öcal, Zehra Vural Yılmaz, Meryem Ceyhan, Osman Fadıl Kara, Tuncay Küçüközkan; Ankara, Amasya, Turkey

Quality of intrapartum care in vaginal births
Vajinal doğumlarda intrapartum bakımın kalitesi
Zekiye Karaçam, Döndü Arslan Kurnaz, Gizem Güneş; Aydın, Turkey

Prevalence of gestational diabetes mellitus
Gestasyonel diyabet prevalansı
Evren Akgöl, Sedat Abuşoğlu, Faik Deniz Gün, Ali Ünlü; Şanlıurfa, Konya, Turkey

Evaluation of ductus venosus in the second trimester
İkinci trimesterde duktus venozusunun değerlendirilmesi
Gökhan Karakoç, And Yavuz, Serenat Eriş Yalçın, Mehmet Özgür Akkurt, Nuri Danışman; Ankara, Isparta, Turkey

Preterm neonates' incidence, factors, and mortality
Preterm yenidoğan insidansı, risk faktörleri ve mortalitesi
Nadin M. Abdel Razeq, Yousef S. Khader, Anwar M. Batieha; Amman, Irbid, Jordan

Fecal incontinence and vaginal delivery
Fekal inkontinans ve vajinal doğum
Süleyman Kargın, Sami Çifçi, Adnan Kaynak, Hüseyin Ataseven, Cengiz Kadıyoran, Murat Çakır; Konya, Karaman, Turkey

Vesicovaginal fistulas after gynecologic surgery
Jinekolojik cerrahi sonrası vezikovajinal fistüller
Burak Tatar, Taylan Oksay, Fatma Selcen Cebe, Sedat Soyupek, Evrim Erdemoğlu; Isparta, Turkey

Predicting lymph-node metastasis in endometrial cancer
Endometrium kanserinde lenf nodu metastazının öngörülmesi
Tayfun Toptaş, Tayup Şimşek, Şeyda Karaveli; Antalya, Turkey

Cycle characteristics in poor ovarian responders
Düşük yanıtlı hastalarda siklus özellikleri
Tayfun Kutlu, Enis Özkaya, Pınar Kumru, Habibe Ayvacı, Belgin Devranoğlu, İlhan Sanverdi, Yavuz Şahin, Beyhan Sağlam, Ateş Karateke; İstanbul, Turkey

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STROBE statement-checklist of items that should be included in reports of observational studies (http://www.strobe-statement.org/),

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Systematic review	300 words	6,250 words (~25 pages)	4	60
Current commentary	250 words	3,000 words (~12 pages)	4	12
Procedure and Instruments	200 words	2,000 words (~8 pages)	4	10
Letters	NA	350 words	4	5

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TURKISH JOURNAL OF OBSTETRICS AND GYNECOLOGY

CONTENTS

Clinical Investigations

1 Early initiation and exclusive breastfeeding: Factors influencing the attitudes of mothers who gave birth in a baby-friendly hospital
Emzirmeye başlama ve sadece anne sütüyle besleme: Bebek dostu bir hastanede doğum yapmış annelerin yaklaşımlarını etkileyen faktörler
Elif Yılmaz, Fatma Doğa Öcal, Zehra Vural Yılmaz, Meryem Ceyhan, Osman Fadıl Kara, Tuncay Küçüközkan; Ankara, Amasya, Turkey

10 Evaluating the content and quality of intrapartum care in vaginal births: An example of a state hospital
Vajinal doğumlarda intrapartum bakım hizmetlerinin kapsam ve kalitesinin değerlendirilmesi: Bir devlet hastanesi örneği
Zekiye Karaçam, Döndü Arslan Kurnaz, Gizem Güneş; Aydın, Turkey

18 Prevalence of gestational diabetes mellitus according to the different criterias
Farklı kriterlere göre gestasyonel diyabet prevalansı
Evren Akgöl, Sedat Abuşoğlu, Faik Deniz Gün, Ali Ünlü; Şanlıurfa, Konya, Turkey

23 The significance of reverse flow in ductus venosus between sixteen and twenty weeks' gestation
On altıncı ve yirminci gebelik haftaları arasında değerlendirilen duktus venozus ters akımının önemi
Gökhan Karakoç, And Yavuz, Serenat Eriş Yalçın, Mehmet Özgür Akkurt, Nuri Danışman; Ankara, Isparta, Turkey

28 The incidence, risk factors, and mortality of preterm neonates: A prospective study from Jordan (2012-2013)
Preterm yenidoğan insidansı, risk faktörleri ve mortalitesi: Ürdün'den prospektif bir çalışma (2012-2013)
Nadin M. Abdel Razeq, Yousef S. Khader, Anwar M. Batieha; Amman, Irbid, Jordan

37 The relationship between fecal incontinence and vaginal delivery in the postmenopausal stage
Postmenopozal dönemde görülen fekal inkontinansların vajinal doğumla ilişkisi
Süleyman Kargın, Sami Çifçi, Adnan Kaynak, Hüseyin Ataseven, Cengiz Kadıyoran, Murat Çakır; Konya, Karaman, Turkey

45 Management of vesicovaginal fistulas after gynecologic surgery
Jinekolojik cerrahi sonrası oluşan vezikovajinal fistüllerin yönetimi
Burak Tatar, Taylan Oksay, Fatma Selcen Cebe, Sedat Soyupek, Evrim Erdemoğlu; Isparta, Turkey

52 Prognostic risk factors for lymph node involvement in patients with endometrial cancer
Endometrium kanseri hastalarında lenf nodu tutulumu için prognostik risk faktörleri
Tayfun Toptaş, Tayup Şimşek, Şeyda Karaveli; Antalya, Turkey

58 Clinical analyses of successful and previously failed intracytoplasmic sperm injection cycle parameters in patients with poor ovarian reserve
Düşük over rezervli olgularda başarılı ve başarısız siklusların klinik analizi
Tayfun Kutlu, Enis Özkaya, Pınar Kumru, Habibe Ayvacı, Belgin Devranoğlu, İlhan Sanverdi, Yavuz Şahin, Beyhan Sağlam, Ateş Karateke; İstanbul, Turkey

Review

64 Intra-cesarean insertion and fixation of frameless intrauterine devices
Çerçevesiz rahim içi araçların sezaryen esnasında uygulanımı ve fiksasyonu
Ateş Karateke, Abdulkadir Turgut, Özkan Özdamar, Dirk Wildemeersch; İstanbul, Turkey, Ghent, Belgium

Case Reports

67 Chondrosarcoma mimicking an adnexal mass: A very rare case report
Adneksiyal kitleyi taklit eden kondrosarkom: Çok nadir bir olgu sunumu
Hüseyin Çağlayan Özcan, Aynur Mustafa, Zehra Bozdağ, Seyhun Sucu, Özcan Balat; Gaziantep, Turkey

TURKISH JOURNAL OF OBSTETRICS AND GYNECOLOGY

CONTENTS

70 Mayer-Rokitansky-Kuster-Hauser syndrome associated with rectovestibular fistula
Rektovestibüler fistülle ilişkili Mayer-Rokitansky-Kuster-Hauser sendromu
Charu Tiwari, Hemanshi Shah, Mukta Waghmare, Kiran Khedkar; Mumbai, India

Letter to the Editor

74 A rare case of complete penoscrotal transposition with hypospadias in a newborn
Yenidoğanda nadir görülen bir anomali olarak komplet penoskrotal transpozisyon ve hipospadias
Fatma Beyazıt, Eren Pek, Hakan Aylanç; Çanakkale, Turkey

TURKISH JOURNAL OF OBSTETRICS AND GYNECOLOGY

LETTER FROM THE PRESIDENT

Dear Colleagues,

It is our pleasure and privilege to invite you to join the 25th European Congress of Obstetrics and Gynaecology which will be held in the beautiful city of Antalya, between the 17th and 21st May 2017, in conjunction with the 15th Congress of Turkish Society of Obstetrics and Gynecology.

These organizations will serve as invaluable opportunities to enhance our knowledge on the broad domains of obstetrics and gynecology. They also promise to offer you unique opportunities to participate in top quality scientific programmes.

The European Board and College of Obstetrics and Gynecology (EBCOG) will also be running a second programme for specialists; European Fellow in Obstetrics and Gynaecology EFOG-EBCOG in Antalya.

Doctors from anywhere in the world will be able to sit a "Knowledge Based Assessment" examination during congress. The exciting social and scientific activities will be organized for participants in Antalya.

We thank all of our colleagues and Prof. Dr. Eray Çalışkan for their contribution to this issue of journal.

We hope you will enjoy the meeting and we are looking forward to welcoming you to Antalya.

Sincerely
Ateş Karateke, Prof. MD
President of TSOG

TURKISH JOURNAL OF OBSTETRICS AND GYNECOLOGY

EDITORIAL

Dear Colleagues,

This is the first issue of Turkish Journal of Obstetrics and Gynecology to be evaluated by PubMed Central. Our editorial team is eager to evaluate and respond to all pioneering research in the area of obstetrics and gynecology. Unfortunately due to the limited number of articles published in the area our acceptance rate is decreasing and only those studies that contributes significantly to the field of obstetrics and gynecology will be accepted.

There are two studies in this issue which may contribute to baby friendly hospital and mother friendly hospital strategy initiated by the Ministry of Health of Turkey. One of them aims to evaluate the content and quality of the intrapartum care offered in vaginal births in Turkey by Karaçam et al. and the other one was conducted by Yılmaz et al. on the initation time of breastfeeding, exclusive breastfeeding rates and complementary feeding practices during the first six months of life among mothers. Both issues are utmost important topics for perinatal practices and will guide the clinicians working in the area.

I am proud to anounce that this year a new course on how to prepare a guideline will be held. This course will be organised by Prof. Dr. Berna Dilbaz as part of an education programme by Turkish Society of Obstetrics and Gynecology. Prof. Dr. Berna Dilbaz is a member of our Editorial Board and those who want to join this course can mail to the Editor.

Increasing cesarean section rate and all preventive measures to increase vaginal delivery rate are hot topics. As an Editor in Chief of the journal I would like to call for studies that address the problem in all aspects including malpractice claims, pregnant womens opinions and obstetrician's point of view.

Best wishes

Eray Çalışkan, Editor

Clinical Investigation / Araştırma

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Early initiation and exclusive breastfeeding: Factors influencing the attitudes of mothers who gave birth in a baby-friendly hospital

Emzirmeye başlama ve sadece anne sütüyle besleme: Bebek dostu bir hastanede doğum yapmış annelerin yaklaşımlarını etkileyen faktörler

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Abstract

Objective: To investigate the initation time of breastfeeding, exclusive breastfeeding rates, and complementary feeding practices during the first six months of life among mothers who gave birth in a baby-friendly hospital.

Materials and Methods: A cross-sectional study was conducted with 350 mothers. Demographic characteristics, obstetric history and information about breastfeeding initiation were collected at the hospital. Information about factors affecting breastfeeding duration and feeding practices of the infants were obtained at the end of six months.

Results: Some 97.4% of the mothers initiated breastfeeding, 60.1% within the first hour. Exclusive breastfeeding was maintained for six months in 38.9%. Low education levels of mother/father, random breastfeeding, rare breastfeeding at night, nipple problems, bottle/pacifier use, and lack of social support were found associated with early cessation. Planned pregnancy [odds ratio (OR=2.02)] and vaginal delivery (OR=0.3) were found as the most important factors in early initiation, whereas antepartum breastfeeding education (OR=7.17) was the most important factor for exclusive breastfeeding duration in the logistic analysis. More than half (61.1%) of the infants were partially/bottle fed for six months; the most common reason was the belief that breast milk was insufficient.

Conclusion: Efforts to encourage mothers and society to breastfeed exclusively should be made as part of a primary public health strategy to prevent early cessation of breastfeeding.

Keywords: Breastfeeding initiation, exclusive breastfeeding, complementary feeding

Öz

Amaç: Çalışmanın amacı bebek dostu bir hastanede doğum yapmış annelerin ilk emzirmeye başlama zamanlarını, yaşamın ilk altı ayında sadece anne sütü verme oranlarını ve bebeklerini besleme uygulamalarını etkileyen faktörlerin araştırılmasıdır.

Gereç ve Yöntemler: Kesitsel tipteki bu çalışmaya toplam 350 anne dahil edildi. Annelerin, demografik bilgileri, obstetrik öyküleri ve emzirmeye başlama zamanları ile bilgiler hastanede yattıkları dönem içerisinde kaydedildi. Postpartum altıncı ayda anneler tekrar aranarak, emzirme süresini etkileyen faktörler ve diğer besleme yöntemleri ile ilgili bilgiler elde edildi.

Bulgular: Annelerin %97,4'ü emzirmeye başlamış olup, ilk bir saat içerisinde bebeğini emzirenlerin oranı %60,1 olarak bulundu. İlk altı ay sadece anne sütü verme oranı %38,9 idi. Anne/babanın düşük eğitim düzeyi, düzensiz emzirme, gece seyrek emzirme, meme ucu problemleri, emzik/biberon kullanımı ve çevre desteğinin olmayışı emzirmenin erken sonlanmasında etkili faktörler olarak saptandı. Lojistik analizde, planlı gebelik [göreceli olasılıklar oranı (OR=2,02)] ve normal vajinal doğum (OR=0,3) erken emzirmeye başlamada, gebelikte emzirme eğitimi alma (OR=7,17) ise ilk altı ay sadece anne sütü ile beslemede en etkili faktörler olarak saptandı. Kısmen/tamamen formüla alan bebeklerin oranı %61,1 olup, en önemli nedeninin annelerin sütlerinin yetersiz olduğunu düşünmeleri olduğu saptandı.

Sonuç: Bir halk sağlığı stratejisi olarak emzirmenin erken sonlanmasının engellenmesi ve emzirme devamlılığının sağlanması için gerekli çaba harcanmalı, anneler ve toplum bilinçlendirilmelidir.

Anahtar Kelimeler: Emzirmeye başlama, sadece anne sütü ile besleme, tamamlayıcı besleme

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Introduction

The recommendation of the World Health Organization (WHO) is exclusive breastfeeding (EBF) of infants during the first six months of life, and breastfeeding (BF) for two years or beyond with complementary foods for achieving optimal growth and health[1]. In addition to providing essential nutrients to infants, breastmilk has been shown to be related to decreased sudden infant death syndrome, respiratory-gastrointestinal tract infections, and allergic diseases, as well as a lower risk of developing obesity, cardiovascular disease, diabetes, and hematologic malignancies in future life[2-4]. Reduction in postpartum blood loss due to increased uterine activity and greater weight loss compared with mothers who bottle feed are the reported benefits of BF for mothers[2,3].

Despite all recommendations of the WHO, the rates of initiation and duration of BF are still far from expectations worldwide. According to the United Nations Children's Fund (UNICEF), EBF rates for the first 6 months have not changed significantly since 1990 and are around 36%[5].

Various factors have been shown associated with both the initiation and duration of BF. It has been shown that advanced age, higher maternal educational level, higher socioeconomic status, BF education, social support, and an infant with birthweight over 3 kg and >38 weeks gestation have a positive affect on BF[6-11]. The belief of mothers that their milk is inadequate, the failure to provide adequate information and support from healthcare workers, breast problems due to incorrect BF, and the increased use of bottle-feeding/pacifiers are important causes for early discontinuation of BF[7,12-14].

According to the Turkish Population and Health Survey (TPHS) 2013 report, BF is very common in Turkey, with 96% of children breastfed for some period. However, despite many encouraging studies condected in our country, both early initiation and exclusive BF rates are still far below the desired levels. Only 50% of childen are breastfed within the first hour and the median duration of EBF is only 1.2 months. The rate of EBF during the first six months fell to 30.1% in 2013, which was 41.6% in 2008[15,16].

The main objective of the present study was to determine the initation time of BF and complementary feeding practices during the first six months of life among Turkish mothers who gave birth in a baby-friendly hospital, risk factors associated with lack of early initiation, and EBF.

Materials and Methods

A cross-sectional study was performed in the maternity ward of a tertiary hospital, one of the major maternity centers in Ankara, the capital of Turkey, between March and October 2015. A total of 350 mothers aged ≥20 years who gave birth in the hospital participated in the study on a voluntary basis. The exclusion criteria were multiple pregnancies, preterm births (<37 weeks), foreign patients, women with health problems, babies with health problems, and those who required the neonatal intensive care unit or intubation. The study was approved by the Keçiören Training and Research Hospital Local Ethics Committee (approval no: 2012-KAEK-15/1073) and was performed in accordance with the ethical standards described in an appropriate version of the 1975 Declaration of Helsinki, as revised in 2000.

Our hospital is a certificated baby-friendly institution and all mothers are explained the benefits of breastmilk and given BF education after delivery by lactation consultants.

After being informed about the study, informed written consent was obtained from the mothers. A questionnaire consisting of questions about demographic characteristics, obstetric history, and BF history was completed by two research assistants 12-24 hours after birth. The survey also investigated whether the infant received prelacteal feeds and their nature. Information about gestational age, birth weight, sex of the infant, and type of birth were obtained from hospital records. When discharging from the hospital, all patients were informed that they would be called by the research assistant at the end of the sixth month postpartum in order to get the infant's nutritional information and feeding practices. During this call, information about BF, factors affecting BF and its duration, and feeding practices of the infant were obtained.

Initiation time and related factors were assessed for over 350 patients. Assessments related to BF duration and EBF were peformed with 329 patients, excluding the 21 patients that could not be reached at the end of six months.

Definitions

Definitions included in the study:

-Early breasfeeding was defined as BF within one hour postpartum.

-Initiation time of first breastfeed was the time at which the baby was first breastfed after delivery.

-Exclusive breastfeeding was defined as BF only since birth and no other supplemental fluids.

-Partial breastfeeding was defined as mainly BF combined with supplemental foods.

-Bottle-feeding was defined as only feeding with formula or non-human milk without BF.

-Complementary feeding was defined as transition from EBF to family foods.

Statistical Analysis

The analyses were performed using Statistical Package for the Social Sciences software version 15.0 (SPSS Inc., Chicago, IL, USA). Results are presented as mean ± standard deviation and n (%). The suitability of continuous variables to normal distribution was analyzed using the Kolmogorov-Smirnov test. Nominal data were expressed using cross tables depending on initiation times before or after one hour, and EBF more or less than six months. Differences between groups were assessed using χ^2, Fisher or Yates tests for categorical variables. Multivariate logistic regression analysis was used to determine

which factor best predicted BF within one hour postpartum, and which factor predicted EBF for six months. The Hosmer-Lemeshow test was used to determine the goodness of fit of the logistic regression model. A p value of <0.05 was considered statistically significant.

Results

Socio-demographic and obstetric characteristics

The mean age of the study group at birth was 27.58±5.4 years (range, 20-42 years), and the mean gestational age was 38.7±1.2 weeks (range, 37-41 weeks). The majority of the mothers were housewives, 11.7% were working mothers, and 68.4% were with their babies at home during the first six months. Regarding education, 64% of the mothers were educated at primary school or illiterate. Just under half (47.7%) of the women experienced a vaginal delivery and 4% of the babies weighed <2500 gr. The mean birthweight of babies was 3234.34±436.1 g (range, 2080-4800 g), and 55.1% of the babies were girls.

Breastfeeding initiation and influencing factors

In total, 97.4% of the mothers in this study initiated BF. Of the 341 patients, 60.1% initiated BF within the first hour, and 22.6% within the second hour after birth. Of the mothers who gave vaginal birth, 76.8% initiated BF within the first hour, whereas this ratio was 44.6% in the cesarean group. The mean first BF time was 1.67±1.0 hours postpartum (range, 1-6 hours), 1.33±0.7 hours for vaginal delivery, and 1.97±1.1 hours in the cesarean group.

Table 1 shows the characteristics of the study group according to the BF initiation time. Planned pregnancy and vaginal delivery were found as factors that had an affect on the initiation time of BF.

Planned pregnancy and vaginal delivery were found as significant factors for early BF in the logistic regression analysis (Table 2). Early BF was significantly higher in the vaginal delivery group.

Breastfeeding patterns, rates and infant feeding practices of the study group

Bottle feeding from birth was reported in 2.7% of the mothers, 88.3% of the mothers stated that breast milk was the first food taken by the newborns, the rest of the newborns were fed with other fluids before breast milk and then breastfed. The number of mothers who stated that they stopped BF from the first to fifth months were 12, 15, 29, 30, and 54 mothers, respectively. Partial bottle feeding was disclosed by 61.1% of the mothers, and 38.9% exclusively breastfed until six months from birth (Table 3).

When the partial feeding group was asked why they were giving formula/other drinks, the most common responses were concerning the insufficiency of breastmilk (39.6%), a family belief that the baby's weight gain was inadequate (25.5%), supplementing BF (21.9%), and convenience of the mother (13%). EBF rates fell whereas partial/bottle feeding rates increased as babies grew older (Table 4).

Table 1. General characteristics of the study group according to the initiation time

Characteristics	Initiation time		p
	≤1 hour n (%)	>1 hour n (%)	
Maternal age, years			
≤25	95 (61.7)	59 (38.3)	
26-34	95 (58.6)	67 (41.4)	0.858
≥35	15 (60)	10 (40)	
Maternal education level			
Elementary school/ lower	136 (63)	80 (37)	
High school	56 (55.4)	45 (44.6)	0.367
University	13 (54.2)	11 (45.8)	
Maternal employment status			
Employed	22 (55)	18 (45)	0.595
Unemployed	183 (60.8)	118 (39.2)	
Health security			
Yes	17 (70.8)	7 (29.2)	0.370
No	188 (59.3)	129 (40.7)	
Family structure			
Nuclear	186 (60.4)	122 (39.6)	0.899
Extended	19 (57.6)	14 (42.4)	
Planned pregnancy			
Yes	143 (55.6)	114 (44.4)	0.005
No	62 (73.8)	22 (26.2)	
Antepartum breastfeeding education			
Yes	51 (54.8)	42 (45.2)	0.223
No	154 (62.1)	94 (37.9)	
Regular antepartum care (≥4 times)			
Yes	158 (59)	110 (41)	0.401
No	47 (64.4)	26 (35.6)	
Parity			
1	54 (60.7)	35 (39.3)	0.901
2+	151 (59.9)	101 (40)	
Delivery type			
Vaginal	126 (76.8)	38 (23.2)	0.001
Abdominal	79 (44.6)	98 (55.4)	
Sex			
Female	112 (60.2)	74 (39.8)	0.968
Male	93 (60)	62 (40)	
Infant birth weight, grams			
<2500	5 (41.7)	7 (58.3)	0.304
≥2500	200 (60.8)	129 (39.2)	

Table 2. Logistic regression analyses for factors associated with initiation time of breastfeeding (a) and with exclusive/predominantly breastfeeding (b)

a			
Variables	OR	95% CI	p
Planned pregnancy	2.019	1.044-3.905	0.037
Antepartum breastfeeding education	1.622	0.820-3.208	0.165
Vaginal birth	0.304	0.175-0.527	<0.001
Parity	1.140	0.641-2.028	0.656
b			
Variables	OR	95% CI	p
Maternal employment status	0.394	0.118-1.315	0.130
Family structure	1.554	0.439-5.506	0.494
Antepartum breastfeeding education	7.172	3.309-15.546	<0.001
Parity	1.181	0.658-2.122	0.577

OR: Odds ratio, CI: Confidence interval

Table 3. Breastfeeding, feeding patterns, and breastfeeding rates of the study group

Feeding pattern	No	%
Breastfeeding		
No breastfeeding	9	2.6
Any breastfeeding	341	97.6
Initiation time*		
≤ one hour	205	60.1
> one hour	136	39.9
First food of the infant		
Breastmilk	309	88.3
Formula, water or else	41	11.7
Frequency of breastfeeding**		
As suggested (at least 3 hours)	138	43.1
Randomly	182	56.9
No. of breastfeeds at night**		
0-1	105	32.8
2-3	127	39.7
≥4	88	27.5
Exclusive breastfeeding (6 months)***		
Yes	128	38.9
No	201	61.1
Feeding pattern***		
Exclusive	128	38.9
Partial/Bottle	201	61.1

*No breastfeeding group (n=9) excluded, **At the end of six months, except for the missed group (n=21) and no breastfeeding group (n=9), ***At the end of six months, except for the missed group (n=21)

Some 39.8% of the infants in the study group were introduced to solid foods before 6 months, which is the recommended age by the WHO. Solid foods were more commonly initiated around 4-6 months (6.9% at 4 months, 12.8% at 5 months, 20.1% at 6 months, and 60.2% at the end of six months). The mean infant age at which solid foods were introduced was 5.33±0.9 months and for formula milk it was 2.23±1.8 months.

Exclusive breastfeeding duration and influencing factors

EBF for 6 months was maintained by 38.9% of the mothers. The mean duration of BF was 4.86±1.6 months, and the mean duration of EBF was 3.66±2.3. Table 5 summarizes the maternal and infant characteristics of the EBF group compared with the early cessation groups. Low education levels of mother and father, not receiving antepartum BF education, random BF, rare BF at night, nipple problems, bottle/pacifier use, and lack of social support were found as variables associated with early cessation of BF. In the multivarite analysis, antepartum BF education was found as the most significant factor in EBF duration (Table 2).

Discussion

This study presents the BF and complementary feeding practices of Turkish mothers, with a focus on risk factors associated with lack of early initiation and EBF. Planned pregnancy and vaginal delivery were found as the most important factors in early initiation, whereas antepartum BF education was the most important factor for EBF duration in logistic analysis. Education level of mother and father, frequency of BF, number of BFs at night, nipple problems, bottle/pacifier use, and social support were found as other factors that had statistically significant effects on the duration times of EBF.

In our study, the percentage of early initiation was 60.1%. This ratio can be considered in the good group according to the classification of WHO [poor (0-29%), fair (30-49%), good (50-89%), and very good (90-100%)][17]. Although this result is not at the desired level, it is better than the initiation times found in other studies conducted in our country, which determined rates between 9.9%-50%[16,18,19]. Being a baby-friendly hospital and providing all mothers with lactation consultancy after birth may have had an effect on these results. Despite the efforts on BF education all over the country, the premature introduction of other fluids before BF (11.2%) is still common because of a superstition among people.

One of the most important factors found to affect early initiation in our study was delivery type, consistent with the literature. Mothers who gave birth vaginally were significantly more likely to initiate early BF compared with cesarean deliveries. As was shown by several studies, cesarean birth is one of the most important obstacles that causes a delay in the initiation times of BF[18,20,21]. Pain after surgery, significant discomfort in holding and positioning the baby, delayed skin-to-skin contact, delay in the production of breastmilk, limited mobility, and needing extra help for BF could account for this delay. Women

Table 4. Infant feeding patterns during the first six months

Feeding methods	1st day	1-4 weeks	5-8 weeks	9-12 weeks	13-16 weeks	17-20 weeks	21-24 weeks
Exclusively breastfeed (only breast)	309 88.3%	278 84.5%	243 73.9%	206 62.6%	180 54.7%	153 46.5%	128 38.9%
Partial/Bottle (formula/other milk/water &breast)	41 11.7%	51 15.5%	86 26.1%	123 37.4%	149 45.3%	176 53.5%	201 61.1%
Total	350	329	329	329	329	329	329

Table 5. General characteristics of the study group according to breastfeeding type

	Breastfeeding type		
Characteristics	Exclusive	Partially/Bottle	p
Maternal age, years			
≤25	54 (37)	92 (63)	
26-34	63 (39.9)	95 (60.1)	0.755
≥35	11 (44)	14 (56)	
Maternal education level			
Elementary school/lower	69 (29.1)	146 (70.9)	
High school	49 (49)	51 (51)	0.001
University	19 (82.6)	4 (17.4)	
Education level of father			
Elementary school/lower	51 (33.1)	103 (66.9)	
High school	55 (37.2)	93 (62.8)	0.001
University	22 (81.5)	5 (18.5)	
Maternal employment status			
Employed	21 (55.3)	17 (44.7)	0.043
Unemployed	107 (36.8)	184 (63.2)	
Employment status of father			
Employed	123 (39.5)	188 (60.5)	0.455
Unemployed	5 (27.8)	13 (72.2)	
Health security			
Yes	120 (39.3)	185 (60.7)	0.716
No	8 (33.3)	16 (66.7)	
Family structure			
Nuclear	119 (40.2)	177 (59.8)	0.209
Extended	9 (27.3)	24 (72.7)	
Planned pregnancy			
Yes	95 (39.7)	144 (60.3)	0.609
No	33 (36.7)	57 (63.3)	
Antepartum BF education			
Yes	60 (68.2)	28 (31.8)	0.001
No	68 (28.2)	173 (71.8)	

who undergo cesarean delivery may need additional help to attain comfortable and correct positioning of their infant for BF. In recent years, cesarean section rates are above the expected levels around the world. According to Turkey Health Statistics, 50% of all births were performed by cesarean section in 2013, similar to our results (52.3%)[22]. Developing policies to

Table 5. Continued

Characteristics	Breastfeeding type		p
	Exclusive	Partially/Bottle	
Regular antepartum care (≥4 times)			
Yes	104 (40.2)	155 (59.8)	0.450
No	24 (34.3)	46 (65.7)	
Frequency of breastfeeding			
As suggested (at least 3 hours)	100 (72.5)	38 (27.5)	0.001
Randomly	28 (14.7)	163 (85.3)	
No. of breastfeeds at night			
0-1	7 (6.1)	107 (93.9)	
2-3	54 (42.5)	73 (57.5)	0.001
≥4	67 (76.1)	21 (23.9)	
Nipple problems			
Yes	10 (7.4)	125 (92.6)	0.001
No	118 (60.8)	76 (39.2)	
Bottle/Pacifier use			
Yes	7 (4.1)	163 (95.9)	0.001
No	121 (76.1)	38 (23.9)	
Parity			
1	29 (33.7)	57 (66.3)	0.251
2+	99 (40.7)	144 (59.3)	
Starting to work before 6 months			
Yes	2 (16.7)	10 (83.3)	0.004
No	19 (73.1)	7 (26.9)	
Social support			
Yes	107 (57.5)	79 (42.5)	0.001
No	21 (14.7)	122 (85.3)	
Delivery type			
Vaginal	60 (39)	94 (61)	0.985
Abdominal	68 (38.9)	107 (61.1)	
Sex			
Female	66 (36.3)	116 (63.7)	0.274
Male	62 (42.2)	85 (57.8)	
Infant birth weight, grams			
≤2500	8 (57.1)	6 (42.9)	0.250
>2500	120 (38.1)	195 (38.1)	

BF: Breastfeeding

reduce cesarean rates is essential, but it should also be noted that providing special lactation consultancy and emphasizing skin-to-skin contact in patients where cesarean is mandatory is necessary.

In the study group, the initiation times of BF in women who gave birth after a planned pregnancy were significantly less than for women with unplanned pregnancies. Consistent with our results, Taylor and Cabral[23] found a stronge inverse association between unwanted pregnancies and BF in their study of 6733 first singleton live births. Kost et al.[24] reported that women with unwanted pregnancies were less likely to breastfeed their babies than those who intended to conceive. Therefore, as a woman's attitude toward her baby can affect her likelihood of baby-care and consequently her decision to breastfeed, the importance of lactation consultancy should be kept in mind for women with unplanned pregnancies.

The majority of mothers in the study group initiated BF, but only 38.9% of them exclusively breastfed their infants for six months. Although this result is better than the 30.1% detected in the TPHS 2013 report, it is still far behind the desired levels. According to UNICEF, global rates of BF have remained stagnant since 1990, with only 36% of children aged less than six months were exclusively breastfed in 2012, worldwide[5]. The higher results of our study compared with the TPHS and UNICEF may be explained by the fact that our hospital is in a semi-urban region that serves a relatively better income group who have higher antepartum follow-up and BF education rates compared with other regions of our country. Also, our hospital is a baby-friendly hospital that aims to promote and support BF, and this might have had an influence on the results. It should be kept in mind that there still exists a need for encouraging mothers to exclusively feed their babies with breast milk for up to six months. Mothers should be informed about the benefits of breast milk, BF techniques, and how to avoid circumstances that would negatively affect this.

Both maternal and paternal education were found as effective factors for BF duration in our study. Similar to our results, low maternal and paternal education were found as risk factors for early weaning of BF in the literature[6,10]. Maternal working status has been previously negatively linked to BF, EBF in housewives was reported more than in working mothers[12,20]. Interestingly, this finding is in contrast with our results. The higher EBF rates in the working mothers in our study group may be associated with their late return to work and being at home, especially during the first six months.

In our study group, mothers who breastfed more frequently during the day and the night, as suggested by our health staff, breastfed their infants significantly longer than did mothers who breastfed their infants upon demand. It is known that maternal milk production is positively correlated with the demand of the infant and frequent feeding maintains breast milk supply[1,25]. The findings of our study also support this information.

Bottle/pacifier use and nipple problems were reported as negative influencing variables of BF duration[26]. It is known that the use of bottle/pacifier possibly changes the baby's oral dynamics and sucking pattern and may lead to both a reduction in BF frequency and breast demand. For improving EBF, effective strategies to reduce bottle/pacifier should be developed for use among infants, especially those younger than 6 months. Nipple problems are common among BF mothers. Lack of information about BF positions and poor latch of the baby are the most frequent cause of damage to nipples[27]. As these problems are the common causes of early weaning of BF, health staff should pay special attention to mother's breasts in the early postpartum period. Proper BF education by a lactation consultant is essential in the prevention of these problems and ensuring the continuity of BF.

Regression analysis indicated that antepartum BF education was the most significant predictor for the duration of BF. One of the top reasons for the early cessation of BF is mothers' inadequate knowledge about the importance of breast milk and BF techniques. Successful BF starts when the mother thinks she is going to breastfeed her baby and believes that she can accomplish it. The affect of antepartum BF education on increasing EBF rates has been shown in several studies[28,29]. In a study performed in Israel to explore the effect of BF education given in the perinatal period, it was found that both the initiation and the duration rates of BF were increased[30]. Therefore, antepartum education should be considered by health staff to increase the self-confidence of mothers.

In the present study, the most commonly reported reason for starting supplementary drinks was the belief of breastmilk insufficiency. The concern about milk insufficiency among mothers is still very common and stems from having insufficient information on the proper techniques to increase breast milk. Mothers should be relaxed so that they are able to produce enough breastmilk for the proper growth of their infants, and informed about the importance of frequent feeding with the correct technique for stimulating optimal milk production[1,25]. Similar to our study, results of early introduction of complementary foods, contrary to WHO recommendations are of great concern, especially in developing countries. Mothers should be warned about the impact of premature introduction of complementary foods on early termination of EBF, without conferring any growth advantage over EBF[20].

Study Limitations

There are several limitations to our study. The nature of data collection was retrospective and the responses were self-limited, which may have led to over or under estimation of BF practices and duration. To minimize these errors, all the questionnaires were completed by the same author to ensure consistent technique. Enough time was allocated to all patients to avoid rushing and insufficient thinking time of the patients for the questions. Also, the cross-sectional nature of the study prevented determining causal relationships of knowledge,

attitudes, or interest with the rates of BF. However, the hospital where the study was conducted is a large women's health center located in a semi-urban region, which exhibits a close profile to the entire country. At the same time, the study is important in indicating the effectiveness of baby-friendly hospital practices, especially postpartum BF education. Larger prospective studies are needed to clarify BF duration rates, factors that affect these practices, and practical things that should be done to increase these rates in our country.

Conclusion

In conclusion, this study reported important factors that affect the initiation and the duration of BF. Despite all the efforts spent on this subject, both the initiation and duration of BF rates are still below the desired levels in our country. The results of our study indicate the importance of awareness of both mothers and their family members regarding the significance and benefits of BF. Efforts should therefore be made to ensure both professional and social support to mothers to prevent early cessation of BF.

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Ethics

Ethics Committee Approval: The study was approved by the Keçiören Training and Research Hospital Local Ethics Committee (Approval number: 2012-KAEK-15/1073), Informed Consent: Consent form was filled out by all participants.
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Authorship Contributions

Surgical and Medical Practices: M.C., F.D.Ö., Concept: E.Y., O.F.K., Design: E.Y., T.K., Data Collection or Processing: E.Y., Z.V.Y., Analysis or Interpretation: E.Y., F.D.Ö., Literature Search: Z.V.Y., Writing: E.Y.
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Evaluating the content and quality of intrapartum care in vaginal births: An example of a state hospital

Vajinal doğumlarda intrapartum bakım hizmetlerinin kapsam ve kalitesinin değerlendirilmesi: Bir devlet hastanesi örneği

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Abstract

Objective: The purpose of the research was to assess the content and quality of the intrapartum care offered in vaginal births in Turkey, based on the example of a state hospital.

Materials and Methods: This cross-sectional study was conducted between January 1st, 2013 and December 31st, 2014 at Aydın Maternity and Children's Hospital. The study sample consisted of 303 women giving vaginal birth, who were recruited into the study using the method of convenience sampling. Research data were collected with a questionnaire created by the researchers and assessed using the Bologna score. Numbers and percentages were assessed in the data analysis.

Results: The mean age of the women was 25.14±5.37 years and 40.5% had given one live birth. Of the women, 45.2% were admitted to hospital in the latent phase, 76.6% were administered an enema, 3.3% had epidural anesthesia, 2.6% delivered using vacuum extraction, and 54.1% underwent an episiotomy. Some 23.8% of the women experienced spontaneous laceration that needed sutures. The babies of two women exhibited an Apgar score below 7 in the fifth minute. When the quality of the intrapartum care given to the women was assessed with the Bologna score, it was found that 92.7% went into labor spontaneously, 100% of the births were supervised by midwives and doctors, 97.7% of the women had no supporting companion, and the nonsupine position was only used in 0.3% of the women. A partogram was used to follow up on the birth process in 72.6% of the women, and 82.5% achieved contact with their babies within the first hour after birth. Induction was applied in 76.6% of the women and fundal pressure in 27.4%.

Conclusion: The study revealed that the quality of intrapartum care in vaginal births was inadequate. Reformulating the guidelines regarding intrapartum care in accordance with World Health Organization recommendations and evidence-based practices may contribute to improving mother and infant health.

Keywords: Intrapartum, care, quality of health care, Bologna score

Öz

Amaç: Araştırmanın amacı, bir devlet hastanesi örneğinde, Türkiye'de vajinal doğumlarda verilen intrapartum bakım hizmetlerinin kapsam ve kalitesini Bologna skoru kullanarak incelemektir.

Gereç ve Yöntemler: Bu kesitsel araştırma, 1 Ocak 2013 ve 31 Aralık 2014 tarihleri arasında Aydın Kadın Doğum ve Çocuk Hastalıkları Hastanesi'nde yapılmıştır. Araştırmanın örneklemine normal doğum yapan ve gelişigüzel örnekleme yöntemi ile belirlenen 303 kadın dahil edilmiştir. Araştırma verileri araştırmacılar tarafından hazırlanan anket formu ve Bologna skoru ile toplanmıştır. Verileri sayı ve yüzde ile analiz edildi.

Bulgular: Kadınların yaş ortalaması 25,14±5,37 idi ve %40,5'i bir kez canlı doğum yapmıştı. Kadınların %7,3'ünün doğum eyleminin spontan başlamadığı, %45,2'sinin latent fazda hastaneye kabul edildikleri, %76,6'sına lavman, %3,3'üne epidural anestezi, %2,6'sına vakum ve %54,1'ine epizyotomi uygulandığı saptanmıştır. Kadınların %23,8'inde dikiş gerektiren spontan laserasyon oluşmuştu. İki kadının bebeğinin beşinci dakikadaki Apgar skoru 7'nin altında idi. Kadınlara verilen intrapartum bakımın kalitesi Bologna skoru ile değerlendirildiğinde, %92,7'sinin doğum eyleminin spontan olarak başladığı, tüm doğumların ebe ve doktorlar tarafından yaptırıldığı, %97,7'sinde destekleyici bir kişi bulunmadığı ve kadınların sadece %0,3'ünde nonsupin pozisyon kullanıldığı saptanmıştır. Kadınların %72,6'sının doğumlarının izleminde partogram kullanılmış ve %82,5'inin anne ve bebek teması doğumdan sonraki bir saat içinde gerçekleştirilmişti. Kadınların %76,6'sının doğumunda indüksiyon ve %27,4'üne fundal basınç uygulanmıştı.

Sonuç: Bu çalışma, vajinal doğumlarda intrapartum bakım kalitesinin yeterli olmadığı sonucunu ortaya koymuştur. İntrapartum bakım hizmetlerinin Dünya Sağlık Örgütü'nün önerileri ve kanıta dayalı uygulamalara uygun biçimde yeniden düzenlenmesi ile anne-bebek sağlığının gelişimine katkı sağlanabilir.

Anahtar Kelimeler: İntrapartum, bakım, sağlık bakım kalitesi, Bologna skoru

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PRECIS: Using the Bologna score, we evaluated the content and quality of the intrapartum care offered in vaginal births in Turkey, based on the example of a state hospital.

Introduction

The high birth rate and percentages of maternal and infant deaths in Turkey continue to occupy a priority as major health issues. The World Health Organization (WHO)[1] calls attention to the fact that the number of midwives, midwifery care outcomes, and quality are essential in reducing maternal and infant mortality rates and in reaching related global goals. Monk et al.[2] reported that spontaneous vaginal birth rates are higher among women who give birth in maternity units that are under the direction of midwives and that newborn health indicators exhibit similar or even better outcomes when this is practiced. On the other hand, because statistics on maternal and infant mortality do not reflect the quality of maternal healthcare services, the process of caregiving must be evaluated separately[3]. In this context, the content and quality of intrapartum care is of vital importance in putting an end to mother and infant mortality and morbidity rates that are a consequence of preventable causes[4].

Researches in recent years and evidence-based practices have led to important changes in intrapartum care. With the rise in the use of technological methods such as electronic fetal monitorization and induced labor, length of stay in the hospital has been reduced and the scope of midwifery, nursing, and medical care has changed[5].

The strategies of the WHO[6] designed to end preventable maternity mortality have pointed to the need to prioritize the basic care and follow-ups of women and newborns throughout the process of labor and birth. In addition, in the effort to end preventable maternal and infant mortality and morbidity, it is stressed that every pregnant woman and newborn needs to receive evidence-based basic care from well-trained healthcare professionals and to have this in a supportive environment[4]. From another perspective, research points to the probable association between intrapartum care practices and the rise in cesarean rates, so it is important to avoid elective induction practices and to maintain professional teamwork if cesarean rates are to be reduced[7].

Intrapartum care constitutes an important part of healthcare directed toward women in Turkey. The technological developments of recent years have significantly affected the scope of intrapartum care. Elective cesarean and general cesarean section birth rates have steadily increased, rising to 48.1%[8]. Despite reports that epidural anesthesia raises the risk with cesareans[9], there has been a rising trend toward the use of epidural anesthesia. At the same time, there has also been an increasing trend toward interventions with which restricted use is recommended, such as episiotomy (20%) and induction (10%)[10,11]. It is known that practices such as the lithotomy position (used in almost all births), unnecessary palpation, shaving of the perineum, enema, use of catheters, establishing vascular access, restriction of eating and drinking water, amniotomy (60%), and fetal monitorization are widespread[11,12]. Moreover, there are serious issues with providing emotional and physical support during labor and with practicing nonpharmaceutic pain management methods. These are matters about which adequate assistance is not provided. From a different perspective, however, there are some positive developments in Turkey in the context of intrapartum care. Almost all births (97.2%) take place in the hospital and with the assistance of healthcare professionals (97.4%)[8]. Rates of early bonding between mother and child and starting breastfeeding are considerably high (70.2%)[13].

There are no studies in the national literature that address the content and quality of intrapartum care. There are certain criteria used in evaluating the quality of intrapartum care[14]. This study employed the standard measurement instrument, the Bologna score, which is based on the WHO recommendations for evaluating the quality of care in vaginal deliveries, which was drawn up by Chalmers and Porter[15] and used by Sandin-Bojö and Kvist[16-18]. The purpose of this research was to assess the content and quality of intrapartum care offered in vaginal births in Turkey, based on the example of a state hospital and using the Bologna score.

Materials and Methods

The research was of cross-sectional design. The study was conducted between January 1st, 2013 and December 31st, 2014 at Aydın Maternity and Children's Hospital with 303 women giving birth by vaginal delivery who were recruited on the basis of a convenience sampling. The number of vaginal births at this hospital in 2013 was 3051. The number of women recruited into the study was determined as 341 at a confidence level of 95% (s=0.05), with p=0.50 and n=3051. A total of 360 women who expected a vaginal delivery were invited into the study. Of these women, 48 were taken in for emergency cesarean section and data could not be collected for 9, resulting in the final analysis being performed with a total of 303 women. The study protocol was approved by the Adnan Menderes University Faculty of Medicine Ethics Committee (approval number: 2012/111).

In the 150-bed Aydın Maternity and Children's Hospital where the research was conducted, midwives provide care for women going into vaginal delivery. At this hospital, women are generally placed in the lithotomy position, with their back slightly raised, their legs in stirrups and mediolateral episiotomy is performed, particularly on primigravidae. Moreover, the practice in this hospital proscribes vaginal delivery after cesarean section has been performed once. In the two-year period in which this research took in the hospital (2013-2014), the rate of primary cesarean births was 15.63% (n=1397/8937), the total cesarean rate was 31.08% (n=2778/8937), and the rate of operative delivery (vacuum) was 1.18% (n=73/6191).

The researchers collected data for the research using a questionnaire that was developed based on the pertinent literature[19,20], and assessed using the Bologna score. The questionnaire's 36 items probed the women's sociodemographic and obstetric characteristics; whether their pregnancies had been planned and wanted; whether they had received antenatal care; their height and weight; smoking status; cervical dilation upon admittance to hospital; whether an enema, epidural anesthesia, vacuum or episiotomy had been performed during labor; and the baby's Apgar score in the fifth minute.

Bologna score: This is an instrument that was developed by Chalmers and Porter[15] for the purpose of assessing the quality of care given to women during the process of labor, based on the intrapartum care recommendations of the WHO[21]. The researchers first translated the Bologna score into the Turkish language. To verify the comprehensibility and the applicability of both the questionnaire and the Bologna score, a pilot study was conducted with 10 individuals, after which sections that were difficult to understand or apply were revised.

Women who were admitted to the maternity unit and were expected to have a vaginal delivery were invited into the study. The women were first informed about the study and their verbal and written consent was obtained. Later, the researchers completed the questionnaires based on the results obtained from face-to-face interviews held with the mothers. Other parts of the research data were obtained from patient files and through observations. All of the questions in the data collection instrument contained concrete data and therefore no differences stemming from observations existed.

Statistical Analysis

The Statistical Package for the Social Sciences Version 18 (PASW Inc, Chicago, IL, USA) was used in the data analysis. All of the variables in the study were analyzed using descriptive statistics.

Results

The study was conducted with 303 women giving vaginal birth whose mean age was 25.14±5.37 years (range, 14-41 years). Data on the women's age groups, their educational level and employment status, perceived income level, social security status, civil status, obstetric characteristics, body mass index (BMI) before pregnancy, and weight gained during pregnancy can be found in Table 1.

Of the women in the study, 35.7% (n=108) had experienced one, 29.1% (n=88) two, 20.1% (n=61) three, and 15.1% (n=61) had experienced 4-13 pregnancies; 40.5% (n=123) had gone through one live birth and had one living child. Some 17.5% (n=53) of the women had experienced one and 3.9% (n=12) 2-4 spontaneous abortions, and 3.3% (n=10) had experienced one and 1.3% (n=4) 2-3 curettages.

It was found that 24.4% (n=74) of the women had not planned the pregnancy and 8.3% (n=25) had not wanted the pregnancy, 1.3% (n=4) had not received prenatal care, and 7.2% (n=22) received prenatal care after the 13th week of pregnancy. It was observed that the women's pre-pregnancy mean BMI score was 23.14±3.41 kg/m^2 (range, 15.99-34.67 kg/m^2) and their average weight gain over the course of the pregnancy was 10±21 kg (range, 0-33 kg). Smoking prior to pregnancy was reported by 20.8% of the women and 13.2% said they smoked during pregnancy (Table 1).

Table 2 reveals data on the women's deliveries and their status of being at high risk. Four percent (n=12) of the women had not reached term when they were admitted to the maternity unit, the babies were not in the vertex presentation in 3.3% (n=10), and 7.3% (n=22) did not undergo a spontaneous onset of labor. The fetal heart rate of two fetuses (0.7%) were not within normal boundaries (120-160 bpm). There was some kind of obstetric complication in previous births in 5.0% (n=15) of the women, and 11.2% (n=34) had complications in the present birth; 1.7% (n=5) had a medical condition that needed special care.

The following risk factors were observed in some women in the study: preterm labor (n=16), presentation anomaly (n=10), induced labor (n=22), fetal distress (n=2), meconium amniotic fluid (n=5), oligohydramnios (n=2), intrauterine exitus (n=1), placenta previa (n=1), gestational diabetes (n=1), and gestational hypertension (n=1). Furthermore, bleeding occurred in 4 women after birth and 1 woman developed a deep vaginal tear, and 2 women's infants had Apgar scores below 7 in the fifth minute.

Some 45.2% (n=137) of the women were admitted to hospital with a cervical dilation of 1-3 cm, 76.6% (n=232) were administered enemas, 3.3% (n=10) had epidural anesthesia, vacuum extraction was performed on 2.6% (n=8), and an episiotomy was performed on 54.1% (n=164). Spontaneous lacerations that needed suturing were experienced by 23.8% (n=72) women. Twelve (4.0%) women gave birth to babies who had Apgar scores below 7 in the first minute, and two women's babies (0.6%) had Apgar scores below 7 in the fifth minute (Table 2).

When the quality of the care given to the women was evaluated using the Bologna score, it was found that 92.7% (n=281) went into spontaneous labor and all of the births were assisted by midwives or doctors. Only 7 (2.3%) women had a supporting individual by her side and only 1 (0.3%) gave birth in a nonsupine position. A partogram was used to follow up on the birth process in 72.6% (n=220) women, and 82.5% (n=250) achieved contact with their babies within the first hour after birth. Induction was used in 76.6% (n=232) of women and fundal pressure was applied to 27.4% (n=83) (Table 3).

Discussion

This study examined the content and quality of intrapartum care provided at a state hospital in Turkey using the Bologna score. From the observations of current practices of intrapartum care at the hospital, it could be seen that the use of a partogram,

fundal pressure, and the nonsupine position, as well as having a supporting person present at the birth were not in compliance with the international standards recommended by the WHO nor with evidence-based practices. The data obtained are important in that they reveal the current status through the example of a hospital in Turkey.

It was seen that high-risk factors were at play in the case of some of the women in the study. This may have increased the probability that certain interventions such as induction would be performed.

A small percentage of the women (4.0%) were not at term (37+0-41+6 weeks) when they were admitted to the maternity unit for

Table 1. Sociodemographic characteristics of the women and variables related to pregnancy (n=303)

Variables	
Mean age ± SD* (min-max)	25.14±5.37 (14-41)
Age group (years), n (%)	
14-17	9 (3.0)
18-35	279 (92.0)
36-41	15 (5.0)
Educational status, n (%)	
Literate and illiterate†	37 (12.3)
Elementary school	120 (39.6)
Middle school	86 (28.4)
High school	42 (13.9)
University and graduate school	18 (5.9)
Working at a paying job, n (%)	
Housewife	264 (87.1)
Employed	39 (12.9)
Health insurance, n (%)	
Yes	270 (89.1)
None	33 (10.9)
Marital status, n (%)	
Officially married	282 (93.1)
Not officially married	16 (5.3)
Divorced/widowed‡	5 (1.6)
Perceived income status, n (%)	
Income less than expenditure	58 (19.1)
Income equal to or more than expenditure	245 (80.9)
Number of pregnancies mean ± SD* (min-max)	2.30±1.52 (1-13)
Number of live births mean ± SD* (min-max)	1.93±1.02 (1-7)
Number of living children mean ± SD* (min-max)	1.93±1.01 (1-7)
Abortions, n (%)	14 (4.6)
Spontaneous abortions, n (%)	65 (21.5)
Stillbirths, n (%)	9 (2.9)
Unplanned pregnancy, n (%)	74 (24.4)
Undesired pregnancies, n (%)	25 (8.3)
Not benefiting from prenatal care services, n (%)	4 (1.3)
Body mass index before pregnancy (mean ± SD)	23.14±3.41 (15.99-34.67)
Weight gain in pregnancy, (mean ± SD)	10.21±4.86 (0-33)
Smoking before the pregnancy	63 (20.8)
Smoking during pregnancy	40 (13.2)

*SD: Standard deviation, Min: Minimum, Max: Maximum, †Twenty-two women were illiterate, ‡One woman in this group was a single parent

vaginal labor. A study conducted in Switzerland similarly noted that only 6.0% of pregnant women were admitted for delivery before their 37th gestational week[18]. These outcomes may be associated with early delivery risk or with early membrane rupture.

A significant percentage woman (45.2%) was admitted to hospital in the latent phase. It is reported, however, that women should be admitted to the maternity unit at a later stage, that is, in the active phase of labor (when cervical dilation is 4 cm or more)[22]. It has also been asserted that early admittance to

Table 2. Risk status related to childbirth (n=303)

Childbirth-related risks	No n (%)	Yes n (%)
Gestational week between 37+0 - 41+6	12 (4.0)	291 (96.0)
Vertex presentation	10 (3.3)	293 (96.7)
FHR within normal limits (120-160)	2 (0.7)	301 (99.3)
Labor began spontaneously	22 (7.3)	281 (92.7)
No obstetric complications before	288 (95.0)	15 (5.0)
No obstetric complications at this time	269 (88.8)	34 (11.2)
History of any medical condition requiring special care	298 (98.3)	5 (1.7)
Childbirth-related data		
Cervical dilation upon admittance to hospital is 4-10 cm	137 (45.2)	166 (54.8)
Epidural anesthesia used	293 (96.7)	10 (3.3)
Vacuum extraction during delivery	295 (97.4)	8 (2.6)
Episiotomy	139 (45.9)	164 (54.1)
Spontaneous lacerations requiring sutures	231 (76.2)	72 (23.8)
Enema	71 (23.4)	232 (76.6)
Apgar score 7 or above in the 1st minute	12 (4.0)	291 (96.0)
Apgar score 7 or above in the 5th minute	2 (0.6)	301 (99.4)

FHR: Fetal heart rate

Table 3. The items in the Bologna score (indicators of the effectiveness of care during labor) (n=303)

Indicators	Items	No n (%)	Yes n (%)
A	Planned (elective) cesarean*	---	---
	Inducing labor	281 (92.7)	22 (7.3)
B	Trained healthcare professionals present at birth	-	303 (100.0)
C	Presence of a supportive individual (spouse, relative, friend)	296 (97.7)	7 (2.3)
	Use of partogram	83 (27.4)	220 (72.6)
	Use of induction (oxytocin)	71 (23.4)	232 (76.6)
	Applying fundal pressure	220 (72.6)	83 (27.4)
	Emergency cesarean*	---	---
	Use of nonsupine position during labor	302 (99.7)	1 (0.3)
	Skin contact between mother and baby within the first hour after birth for at least 30 minutes (skin contact should last for at least a half-hour/30 minutes)	53 (17.5)	250 (82.5)

*The planned and emergency cesarean rates of the women in the study were not evaluated. However, the primary cesarean rate in the hospital during the period of the research was 15.63% (n=1397/8937) and the total cesarean rate was 31.08% (n=2778/8937)

the maternity unit may be associated with increased rates of oxytocin and analgesic use[22].

Our results could be associated with the traditional approach adopted by healthcare professionals and the general public in Turkey. Women are unable to distinguish between real and false labor, are unaware of the course of labor, and rush to the hospital as soon as they feel the first contractions because of the current inadequacy of prenatal education in Turkey. When this happens, healthcare professionals admit them to the hospital against the probability of risk, which occurred with most women (76.6%) in the present study. This rate is considerably higher than what was reported in Switzerland[17] and Canada[23], where rates were 39% and 5.4%, respectively. This might be a consequence of the country's prevailing general health practices related to this matter. This is the case even though it is known in Turkey, however, that evidence-based research has shown that enemas and other applications that are not mother-friendly should be avoided under all circumstances.

It was observed in this study that epidural anesthesia was administered to only a few women (3.3%). This rate is much lower than reported by Sandin-Bojö et al.[17,18], Chalmers et al.[24], and Li et al.[25] (57%, 48.7%, 57.3%, and 18.3%, respectively). This finding may be connected to the fact that techniques of coping with labor pains are not widely used in Turkey.

The vacuum technique is generally used as a birthing instrument in Turkey. The use of vacuum extraction in this study was 2.6%, lower than reported by Li et al.[25] and Sandin-Bojö and Kvist[18] (10.5% and 8.1%, respectively). In a study conducted in Canada, Chalmers et al.[23] reported a vacuum extraction utilization rate of 10.0% and a rate of 14.3% for all instrumental deliveries. In another study performed at the same location as the present study, the vacuum extraction rate was similar (3.74%), significantly lower than reported in studies conducted in other countries[11]. Although the low rate of births with intervention reported in the literature in Turkey is a positive finding, this may be associated with the high rate of cesarean deliveries.

It was observed in the study that episiotomies are still widely implemented (54.1%). Similar results were reported in studies previously conducted in Aydın (59.21%) and Ankara (64.0%) [11,12]. These rates are much higher than reported in the United Kingdom (UK)[25] and Canada[24] (11.2% and 20.7%, respectively). This finding is important because it reflects the traditional approach of clinical personnel to performing episiotomies.

A significant percentage of women (23.8%) experienced spontaneous lacerations that needed suturing. In another study that was carried out previously at the same hospital, spontaneous lacerations requiring repair with sutures were reported as 8.98%[11]. This rate was reported as 64% in a study in Canada[24] and 15.7% in the UK[25]. The differences in these results may be associated with birth assistance techniques used by health professionals (e.g., birth position, perineal massage, management of the second phase).

When intrapartum care was evaluated in this study using the Bologna score, it was found that most women (92.7%) experienced spontaneous onset of labor. The study encompassed all births in the hospital and all of these births were attended to by midwives or doctors. On the other hand, the Turkish Ministry of Health encourages hospital births in the presence of health professionals. The Turkish Population Health Research Survey results of the last five years show that 97% of the births taking place in the country occurred under the supervision of health professionals[8]. Similarly, studies conducted in Brazil[26] and Switzerland[18] reported that all births occurred with the help of health professionals. These findings are positive and gratifying when considered in terms of maternal and infant health.

Studies on the provision support during childbirth in Turkey are still controversial and all intrapartum care is handled by midwives. The results of the present study confirmed that only 7 women were able to receive supportive intrapartum care. The WHO[1], on the other hand, strongly recommends in its "Coalition for Improving Maternity Services"[10] that among the mother-friendly care that can be provided, mothers in childbirth should have, besides midwives, nurses, and doctors on hand, a doula (a woman assisting the mother in labor) or other individuals (spouse, partner, family member, friend) to provide support during labor. In their study in Switzerland, Sandin-Bojö and Kvist[18] reported that 98.7% of mothers in labor received this kind of support. This brings the matter of intrapartum care services in Turkey to the forefront and points to the need for reviewing and developing the system.

Similar to other Turkish studies[11,12], the present study observed that almost all births occurred with women in the supine position and her legs in stirrups. This high percentage is pronounced when compared with the rate of 35% reported in Switzerland[18] and the rate of 57% reported in Canada for placing women's legs in stirrups and the rate of 48% for the use of the supine position[24]. In other studies, it is reported that even though placing the mother in vertical positions during labor and childbirth positively affects the mother's control and satisfaction in terms of the length of the second stage, the performance of an episiotomy, instrumental birth, severe pain, and the fetal heartbeat[27], it is the attitudes of health professions that play a decisive role in choosing a position for the mother[28]. Nieuwenhuijze et al.[29] stressed that making a joint decision is important in terms of increasing women's sense of control and satisfaction.

In this study, most births (73%) were monitored using a partogram. Rani et al.[30] and Sandin-Bojö and Kvist[18] reported similar findings (72% and 93%, respectively). Giglio et al.[26], however, reported a considerably lower percentage (29%). According to these results, it may be said that the use of

the partogram varies depending upon the individual working protocols of institutions.

In most births (83%), contact between mother and child took place in the first hour after birth. Similar results were reported in other studies conducted in Turkey[13,31]. This rate was 92% in a study conducted in Switzerland[18]. These findings show that healthcare practices are satisfactory in terms of ensuring early contact between mother and child.

In this study, the rate of inducing labor was significantly high (76.6%). Similar results have been reported in other studies conducted in Turkey[11]. In studies carried out in many other countries, lower rates for using oxytocin or labor augmentation were reported[17,18,23-26]. Moreover, the WHO[1] suggests as part of its description of mother-friendly hospital applications that the practice of induced labor must be used to a limited extent and not for more than 10% of births. These findings indicate that there is a need to carry out studies that will help to reduce the use of induction methods in Turkey.

The WHO[32] reports a very low quality of evidence regarding the routine use of amniotomy and induction and offers a weak recommendation regarding these procedures. Smyth et al.[33] also asserted that amniotomy was not recommended as a standard part of intrapartum care and management. In the present study, however, and similar to the results of other studies conducted in Turkey[11], it was observed that amniotomy (67%) and induction (60%) were widely used. Matsuo et al.[34] and Sartore et al.[35] reported lower rates of induction in their studies (49% and 22%, respectively). These findings are important in that they show that amniotomies and induction are in fact routine in Turkey.

It was seen in the study that fundal pressure was applied to a significant percentage (27.4%) of women. This rate is lower than previously reported in other studies conducted in Turkey[11,36]. On the other hand, it is higher than reported in other countries[18,23]. This finding is significant because it points to the dimension of the wide use of fundal pressure in intrapartum care in Turkey despite the recommendation that this is not made a routine part of care given in this period.

Study Limitations

There are some limitations to this study. The first is that the study was based on a nonrandom sampling. Accordingly, the results obtained represent the women taken into the study and cannot be generalized. Secondly, the study data were collected through face-to-face interviews and observations from patient files. The different sources may have affected the reliability of the data obtained. Only concrete and uncomplicated data may increase the reliability of research. Thirdly, at the hospital where the study was carried out, all cases of spontaneous lacerations were sutured. This may have explained the higher percentage of sutured lacerations compared with that reported in the international literature. Fourthly, the difficulty in collecting data in the study for cases of emergency and planned cesareans made it necessary to include only women who were having their babies through vaginal delivery. Accordingly, there is a need for studies that include emergency and planned cesarean births. This study does, however, include the ratios of primary and total cesarean deliveries that took place over the period the research was conducted.

Conclusion

This study revealed that the intrapartum care provided at a state hospital in Turkey was in compliance with international standards and evidence-based practices recommended by the WHO in terms of the presence of trained health professionals during labor and that early bonding was achieved between mother and child. However, the care was not in compliance in terms of factors related with admittance to hospital, performing episiotomies, enema, the use of partograms, induction, fundal pressure, and the nonsupine position, or in terms of receiving the assistance of a supportive individual during labor. According to the findings, recommendations might be: (1) Administrators should reformulate intrapartum care services to comply with the recommendations of the WHO, international standards and evidence-based practices. (2) The curriculums of programs of formal and widespread education should be reviewed and adjusted in concordance with standards and health professionals should thus be encouraged to update their knowledge and practices in this context. (3) Health administrators should create institutional and national policies that will raise the quality of current healthcare services and bring them up to par with international standards. (4) Studies on this matter should be conducted at different hospitals, with the inclusion of emergency and planned cesarean cases and with different sample groups. (5) More experimental, qualitative and quantitative research should be undertaken to explore specific problems at different hospitals to reveal the attitudes and experiences of healthcare professionals, and to suggest solutions.

Ethics

Ethics Committee Approval: Regulatory permission for the collection of data for the research was obtained from the Turkish Ministry of Health Aydın State Hospitals Association General Secretariat. The study protocol was approved by the Adnan Menderes University, Faculty of Medicine Ethics Committee (Approval number: 2012/111), Informed Consent: The women recruited into the research were informed about the study and their verbal consent was obtained.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Obstetrics and Gynaecology Practice: Z.K., D.A.K., G.G., Concept: Z.K., D.A.K., G.G., Design: Z.K., D.A.K., G.G., Data Collection or Processing: D.A.K., G.G., Analysis or Interpretation: Z.K., D.A.K., G.G., Literature Search: Z.K., G.G., Writing: Z.K., G.G.

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Prevalence of gestational diabetes mellitus according to the different criterias

Farklı kriterlere göre gestasyonel diyabet prevalansı

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Abstract

Objective: The two-step approach recommended by the National Diabetes Data Group (NDDG), Carpenter and Coustan (C&C), and O'Sullivan, and the single-step approach recommended by the International Association of Diabetes and Pregnancy Study Group (IADPSG) are used to diagnose gestational diabetes mellitus (GDM). We aimed to determine GDM prevalence and to compare the two-step and single-step approaches used in the southeastern region of Turkey.

Materials and Methods: In total, 3048 records of pregnant women screened for GDM between 2008 and 2014 were retrospectively extracted from our laboratory information system. GDM was defined according to the criteria of NDDG, C&C, and O'Sullivan between in 2008 and 2011, and according to those of the IADPSG between 2012 and 2014. Demographic variables were compared using student's t-test. The linear trends in GDM prevalence with age were calculated using logistic regression.

Results: GDM prevalence was found as 4.8%, 8%, and 13.4% using the NDDG, C&C, and O'Sullivan two-step approach, respectively, and 22.3% with the IADPSG single-step approach. GDM prevalence increased with increasing age in both approaches.

Conclusion: GDM prevalence was higher using the single-step approach than with the two-step approach. There was a significant increase in GDM prevalence using the IADPSG criteria.

Keywords: Gestational diabetes mellitus, oral glucose tolerance test, diagnostic criteria, prevalence

Öz

Amaç: Gestasyonel diabetes mellitus (GDM) tanısı için Ulusal Diyabet Veri Grubu (NDDG), Carpenter ve Coustan (C&C), O'Sullivan tarafından iki basamaklı yaklaşımlar önerirken, Uluslararası Diyabet ve Gebelik Çalışma Grupları Birliği (IADPSG) tek basamaklı yaklaşımı önermektedir. Çalışmamızın amacı Güneydoğu bölgesinde iki basamaklı yaklaşımlar ile tek basamaklı yaklaşımları karşılaştırarak GDM prevalansını belirlemektir.

Gereç ve Yöntemler: 2008 ile 2014 yılları arasındaki 3048 gebe kadının kayıtları laboratuvar bilgi sisteminden alındı. GDM tanısı 2008-2011 yılları arasında NDDG, C&C ve O'Sullivan kriterlerine göre, 2012-2014 yılları arasında IADPSG kriterlerine göre belirlendi. Demografik veriler student's t-testi kullanılarak karşılaştırıldı. Gestasyonel diyabet prevalansının yaşla ilişkisini saptamak için lojistik regresyon testi yapıldı.

Bulgular: Gestasyonel diyabet prevalansı NDDG, C&C ve O'Sullivan kriterlerine göre sırasıyla %4,8, %8 ve %13,4 olarak; IADPSG kriterine göre %22,3 olarak bulundu. GDM prevalansının tüm kriterlerde yaşla arttığı saptandı.

Sonuç: GDM prevalansı tek basamaklı yaklaşım kullanıldığında iki basamaklı yaklaşımlara göre daha yüksektir. IADPSG kriterleri kullanıldığında GDM prevalansında anlamlı yükselme olmaktadır.

Anahtar Kelimeler: Gestasyonel diabetes mellitus, oral glukoz tolerans testi, tanı kriteri, prevalans

Introduction

Gestational diabetes mellitus (GDM) is one of the most common medical complications of pregnancy. GDM is defined as glucose intolerance with onset or first recognition during pregnancy and is a well-established risk factor for adverse infant health outcomes, including fetal macrosomia, birth trauma, neonatal hypoglycemia, and fetal death[1,2].

The initial criteria for GDM were established by O'Sullivan and Mahan in 1964. In this criteria, two or more abnormal glucose values in the 3-h, 100-g oral glucose tolerance test (OGTT) were considered pathological[3]. In 1979 and 1982, the National Diabetes Data Group (NDDG) and Carpenter and Coustan (C&C), respectively, recommended new diagnostic thresholds for the 100-g OGTT. These approaches are still used for pregnant women who have a high glucose challenge

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test (GCT) result[4,5]. More recently, after an extensive analyses of the Hyperglycemia and Adverse Pregnancy Outcomes study, the International Association of Diabetes and Pregnancy Study Group (IADPSG) recommended a single-step approach and new diagnostic criteria for GDM that was based on a 2-h, 75-g OGTT[6,7]. However, in general practice, this approach is still controversial. The American Diabetes Association and World Health Organization have adopted the IADPSG recommendation, whereas the American College of Obstetricians and Gynecologists advises continuing with the two-step screening strategy[8-10].

GDM prevalence varies widely depending on the population studied, age, and the diagnostic test employed. In Turkey, the prevalence ranges from 1.2% to 4.48% according to the criteria of NDDG and C&C. However, there are no data on GDM prevalence using the new, single-step approach.

Our aim was to determine GDM prevalence and to compare the two-step approach with the single-step approach among a population from the southeastern region of Turkey.

Materials and Methods

This study was approved by the Ethics Committee of Selçuk University Faculty of Medicine on September 8th, 2015 (approval number: 2015/267).

This retrospective study was conducted between January 2008 and December 2014 in the Birecik State Hospital, Şanlıurfa, which is located in the southeastern region of Turkey and provides service to approximately 150000 people. All women who were non-diabetic, between 24 and 28 weeks' pregnancy, and aged between 15 and 49 years were screened for GDM using a two-step approach between January 2008 and December 2011, and the single-step approach between January 2012 and December 2014. During the two-step approach, all pregnant women were screened for GDM with the 50-g, 1-h GCT. A positive GCT result was defined as a serum glucose level of ≥140 mg/dL. Patients with a positive GCT underwent a 3-h, 100-g diagnostic OGTT. Patients with two or more elevated glucose results from the diagnostic OGTT were diagnosed as having GDM according to the criteria of O'Sullivan [i.e. fasting plasma glucose (FPG) level: ≥90 mg/dL, 1 h: ≥165 mg/dL, 2 h: ≥145 mg/dL, and 3 h: ≥125 mg/dL], NDDG (FPG: ≥105 mg/dL, 1 h: ≥190 mg/dL, 2 h: ≥165 mg/dL, and 3 h: ≥145 mg/dL), and C&C (FPG: ≥95 mg/dL, 1 h: ≥180 mg/dL, 2 h: ≥155 mg/dL, and 3 h: ≥140 mg/dL). In the single step approach, patients were screened for GDM with a 2-h, 75-g OGTT. GDM was diagnosed by a single elevated 2-h, 75-g glucose tolerance test (FPG: ≥92 mg/dL, 1 h: ≥180 mg/dL and 2 h: ≥153 mg/dL) as defined by the IADPSG.

Statistical Analysis

The records of pregnant women screened for GDM were extracted from the laboratory information system. All glucose measurements in patient samples were performed using the hexokinase method. Demographic variables were compared using student's t-test. Linear trends with age and GDM prevalence were calculated using logistic regression. Statistical analyses were performed using SPSS v16. A p-value <0.05 was considered significant.

Results

A total of 1385 pregnant women were screened for GDM with a two-step approach between January 2008 and December 2011. Of these women, 501 (36.2%) were found at risk for GDM during GCT and were included in the 3-h, 100-g diagnostic OGTT. During the diagnostic OGTT, 66 of the 501 patients were diagnosed as having GDM according to the criteria of NDDG and 111 and 185 of 501 patients were diagnosed as having GDM according to the criteria of C&C and O'Sullivan, respectively. GDM prevalence was found as 4.8%, 8%, and 13.4% based on the criteria of NDDG, C&C, and O'Sullivan, respectively, during the two-step approach. GDM prevalence for each year is presented in Table 1. A total of 1663 pregnant women were screened for GDM using the single-step approach between January 2012 and December 2014, and 371 were diagnosed as having GDM. The GDM prevalence rate was found as 22.3% according to the criteria of IADPSG. The prevalence rates for each year are presented in Table 2.

In our study, patients who were diagnosed as having GDM were significantly older than healthy patients (Table 3). GDM prevalence increased with increasing age with both approaches (Table 4).

Table 1. Gestational diabetes mellitus prevalence according to the two-step approaches by year

Years	GCT		100-g OGTT (NDDG)			100-g OGTT (C&C)			100-g OGTT (O'Sullivan)		
	n	Positive	n	Positive	Prevalence (%)	n	Positive	Prevalence (%)	n	Positive	Prevalence (%)
2008	241	87	87	5	2.1	87	13	5.4	87	31	12.9
2009	156	55	55	7	4.5	55	10	6.4	55	16	10.3
2010	390	151	151	29	7.4	151	41	10.5	151	68	17.4
2011	598	208	208	25	4.2	208	47	7.9	208	70	11.7
Total	1385	501	501	66	4.8	501	111	8.0	501	185	13.4

GCT: Glucose challenge test, OGTT: Oral glucose tolerance test, NDDG: National Diabetes Data Group, C&C: Carpenter and Coustan

Discussion

GDM prevalence may differ depending on the population being screened and the diagnostic test being performed. GDM prevalence was reported as 8.8% using the NDDG criteria and 10.6% using the C&C criteria in Spain[11,12]. GDM prevalence was also determined as 5.5% in the United States of America (USA), 8.4% in China, and 7.7% in Morocco according to the C&C criteria[13-15].

In studies conducted in different regions of Turkey, GDM prevalence was found between 1.23% and 4.2% according to the criteria of the NDDG, and between 2% and 4.48% according to the C&C criteria[16-20]. In our study, GDM prevalence was found as 4.8% and 8% using the NDDG and C&C criteria, respectively, which is higher than that those reported in previous Turkish studies. The higher GDM prevalence is probably due to regional dietary habits. GDM was higher using the criteria of C&C than with the NDDG criteria. This increase may result from the increased sensitivity of the test when using the C&C criteria because its glucose value for a diagnosis of GDM is lower than in the NDDG criteria.

After IADPSG issued a consensus statement on the new criteria for the diagnosis of GDM, GDM prevalence significantly increased when the new criteria were adopted[12,21,22]. GDM prevalence increased 3.3 times in Spain (10.6% to 35.5%), 2.8 times in the USA (5.5% to 15.6%) and 2.25 times in China (8.4% to 18.9%) using the new IADPSG criteria[12-14].

In Turkey, our study is the first to determine GDM prevalence using the new, single-step approach. Similar to other studies, we found that GDM prevalence using the IADPSG single-step approach increased the positivity rate as much as 4.5 times than that of the two-step NDDG approach, 3 times more than the two-step C&C approach, and 1.7 times more than the two-step O'Sullivan approach. This significant increase results from the fact that only one elevated result is sufficient to make the diagnosis, not two. In our study, the increase in GDM prevalence with IADPSG was 2 times higher in a subgroup of women aged <30 years.

In our study, GDM prevalence increased significantly with increasing age, regardless of the criteria used. A similar association has been observed in various studies[16,23,24]. GDM prevalence in women aged >30 years was 4.2 times greater than that of women aged ≤30 years using the C&C and NDDG criteria, 2.5 times greater using the criteria of O'Sullivan, and 2 times greater using the IADPSG criteria. This means that the criteria of O'Sullivan and IADPSG diagnose more younger women (i.e. women <30 years) as having GDM.

Table 2. Gestational diabetes mellitus prevalence according to the single-step approach by year

Years	75-g OGTT (IADPSG)		
	n	Positive	Prevalence %
2012	434	96	22.1
2013	455	102	22.4
2014	774	173	22.4
Total	1663	371	22.3

OGTT: Oral glucose tolerance test, IADPSG: International Association of the Diabetes and Pregnancy Study Group

Conclusion

Therefore, the new IADPSG criteria provide a higher GDM prevalence and diagnose more young women. This may also be effective in decreasing the medical disbursement for the treatment of the disease; however, the benefits of these findings are still unclear. New prospective studies may highlight the outcomes of new approaches by the criteria of IADPSG.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of Selçuk University Faculty of Medicine on

Table 3. Age characteristics of healthy patients and patients with gestational diabetes mellitus

Test	Ages of patients			
	Total	Negative	Positive	p
GCT	29.77±6.14 n=1385	28.59±5.75 n=884	31.87±5.90 n=501	<0.001
100-g OGTT according to NDDG	31.87±5.90 n=501	31.65±6.01 n=435	33.32±4.89 n=66	0.032
100-g OGTT according to C&C	31.87±5.90 n=501	31.35±5.98 n=390	33.70±5.26 n=111	<0.001
100-g OGTT according to O'Sullivan	31.87±5.90 n=501	31.08±6.02 n=316	33.21±5.45 n=185	<0.001
75-g OGTT according to IADPSG	27.5±6.07 n=1663	26.74±5.84 n=1292	30.13±6.12 n=371	<0.001

GCT: Glucose challenge test, OGTT: Oral glucose tolerance test, NDDG: National Diabetes Data Group, C&C: Carpenter and Coustan, IADPSG: International Association of the Diabetes and Pregnancy Study Group

Table 4. The trends in the prevalence of gestational diabetes mellitus with age

Age (years)	GCT			100 gr. OGTT (NDDG)			100 gr. OGTT (C&C)			100 gr. OGTT (O'Sullivan)			75 gr. OGTT (IADPSG)		
	n	Positive	Prevalence %	n	Positive	Prevalence %	n	Positive	Prevalence %	n	Positive	Prevalence %	n	Positive	Prevalence %
<25	316	75	23.7	75	5	1.6	75	9	2.8	75	17	5.4	593	82	13.8
25-29	394	118	29.9	118	8	2.0	118	13	3.3	118	37	9.4	465	88	18.9
30-34	365	135	37.0	135	23	6.3	135	35	9.6	135	49	13.4	370	108	29.2
35-39	215	113	52.6	113	20	9.3	113	36	16.7	113	56	26.0	178	68	38.2
>39	95	60	63.2	60	10	10.5	60	18	18.9	60	26	27.4	57	25	43.9
p=0.002 [95% CI: (0.065-0.126)]				p=0.005 [95% CI: (0.212-0.542)]			p=0.006 [95% CI: (0.113-0.301)]			p=0.007 [95% CI: (0.081-0.208)]			p=0.001 [95% CI: (0.099-0.149)]		

GCT: Glucose challenge test, OGTT: Oral glucose tolerance test, NDDG: National Diabetes Data Group, C&C: Carpenter and Coustan, IADPSG: International Association of the Diabetes and Pregnancy Study Group, CI: Confidence interval

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Surgical and Medical Practices: E.A., F.D.G., Concept: E.A., A.Ü., Design: E.A., S.A., Data Collection or Processing: E.A., F.D.G., Analysis or Interpretation: E.A., S.A., Literature Search: E.A., Writing: E.A., S.A.

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The significance of reverse flow in ductus venosus between sixteen and twenty weeks' gestation

On altıncı ve yirminci gebelik haftaları arasında değerlendirilen duktus venozus ters akımının önemi

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Abstract

Objective: To evaluate the correlation between reversed a-wave in ductus venosus at 16-20 weeks' gestation and trisomy 21 and adverse perinatal outcomes.
Materials and Methods: Our study included 174 pregnant women who were under follow-up at a tertiary center between May and September 2010. Ductus venosus Doppler (DVD) measurements were obtained throughout the 6-month period from women who underwent amniocentesis procedures due to increased risk for trisomy 21 in terms of first or second trimester screening test results. These women were followed up for enrollment of subsequent data about perinatal outcomes.
Results: In 13 of 174 cases, Doppler studies indicated a reversed a-wave in the ductus venosus. Of these fetuses, 3 were diagnosed as having trisomy 21 after amniocentesis, which related to 60% (3 of 5 fetuses) of all fetuses with trisomy 21. The pregnant women with reversed a-wave in DVD also had an increased rate of preeclampsia (15%) and gestational diabetes mellitus (GDM) (23%) in late pregnancy.
Conclusion: Reversed a-wave in ductus venosus between 16-20 weeks' gestation is associated with increased risk of trisomy 21, preeclampsia, and GDM. If further prospective studies confirm its utility, DVD interrogation for trisomy 21 may be extended until 20 weeks' gestation.
Keywords: Ductus venosus Doppler, gestational hypertension, gestational diabetes mellitus, second trimester, trisomy

Öz

Amaç: Gebeliğin 16.-20. haftasında saptanan duktus venozus ters a-dalgası ile trizomi 21 ve advers perinatal sonuçlar arasındaki korelasyonun değerlendirilmesidir.
Gereç ve Yöntemler: Çalışmamız, Mayıs-Eylül 2010 tarihleri arasında üçüncül bir merkezde takip altında olan 174 gebeyi içermektedir. Birinci veya ikinci trimester tarama testi sonuçları açısından artmış trizomi riski nedeniyle amniyosentez uygulanan kadınlardan 6 ay boyunca duktus venozus Doppler (DVD) ölçümü elde edildi. Bu kadınlar, perinatal sonuçla ilgili daha sonraki verileri kaydetmek için takip edildi.
Bulgular: Yüz yetmiş dört olgunun 13'ünde, DVD'de ters a-dalgası izlendi. Bu fetusların 3'ünde, amniyosentez sonrası trizomi 21 teşhisi kondu. Trizomi 21 olan tüm fetusların %60'ı (5 fetustan 3'ü) ters a-dalgası varlığı ile ilişkiliydi. DVD'de a-dalgası tersine çevrilen olguların gebeliğin ilerleyen aşamalarında preeklampsi (%15) ve gestasyonel diabetes mellitus (GDM) oranı da artmış olarak izlendi (%23).
Sonuç: On altı-20 haftalık gestasyonda duktus venozusta saptanan ters a-dalgası, trizomi 21, preeklampsi ve GDM riskinde artış ile ilişkilidir. Daha ileri prospektif çalışmalar yararını teyit ederse, trizomi 21 için DVD sorgulaması gebeliğin 20. haftasına kadar uzatılabilir.
Anahtar Kelimeler: Duktus venozus Doppler, gestasyonal hipertansiyon, gestasyonal diabetes mellitus, ikinci trimester, trizomi

Introduction

The primary purpose of prenatal aneuploidy screening tests is early detection of pregnancies at high risk for Down syndrome, which is the most common autosomal trisomy among live births[1]. First trimester combined screening tests can detect approximately 84% of trisomy cases with a false positive rate (FPR) of 5 percent[2]. Incorporation of assessment of nasal bone, tricuspid blood flow, and ductus venosus (DV) waveform to the combined test increases the detection rate to approximately 93-96% with a FPR of 2.5 percent. In the second trimester, by combining classic ultrasonographic markers for Down syndrome (hyperechogenic intestines, an echogenic

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cardiac focus, pyelectasis, and short femur or humerus) with maternal age can diagnose 70% of trisomy 21 cases, but it may also record a false positive diagnosis in 10-15% of cases[3].

DV is a special shunt that directs oxygen rich blood from the umbilical vein to the heart[4]. The characteristic properties of ductal blood flow include a high flow rate during ventricular systole (S wave) and diastole (D wave), and a continuous forward flow during atrial systole (A wave). A-wave negativity is regarded as a reflection of fetal cardiac dysfunction[5].

Abnormal DV waveforms between 10 to 13^{+6} weeks have shown a relationship with chromosomal defects, cardiac anomalies, and poor gestational prognosis[5]. Following the demonstration of a correlation between abnormal ductal flow and nuchal translucency (NT), it has been proposed that a combined assessment of DV and NT thickness may increase the efficacy of early sonographic screening of trisomy 21. Ultrasonographic evaluations in the first trimester have shown that this abnormality is present in 66.3% to 80% of trisomy 21 cases[6]. Additionally, DV flow abnormality is a common finding in the presence of a cardiac defect in fetal Doppler examination in the first trimester[7,8]. Furthermore, some abnormalities have been found in DVD ultrasonography during pregnancies with gestational hypertension (GHT), preeclampsia, and gestational diabetes mellitus (GDM)[9-11].

Although analysis of free fetal DNA in maternal blood flow for screening is a promising method, its widespread use is still restricted due to high costs. Thus, parameters that aid increased detection rates of routine screening tests are still substantial. The aim of our study was to determine whether DV waveform abnormality in Doppler ultrasonography would aid in second trimester screening when the detection rate is relatively low, and whether it was correlated with maternal complications.

Materials and Methods

Our study included 174 pregnant women aged 20 to 45 years who were followed up at Zekai Tahir Burak Women's Health Training and Research Hospital between May 2010 and September 2010. The study design was approved by the local institutional ethics committee and review board (approval number: 04/2009-16). Written consent for participation was obtained prior to recruitment into the study. The subjects were referred for high risk for Down syndrome and scheduled for amniocentesis as a result of a risk assessment based on maternal age and/or the results of double test [NT, nasal bone hypoplasia, and beta human chorionic gonadotropin (βhCG) and pregnancy-associated plasma protein A measurements between 11 and 13^{+6} gestational weeks] or triple test (βhCG, unconjugated estriol, and alpha-fetoprotein measurements between 16 and 19 gestational weeks). All pregnancies were between 16 and 20 gestational weeks. High-risk pregnancies including multiple pregnancies, maternal diabetes, and hypertension were excluded.

DVD was performed to all subjects prior to the amniocentesis procedure. Ultrasonographic examination and measurements were conducted by two sonographers (G.K. and A.Y.) using a Voluson 730 Expert color Doppler ultrasonography device. A 4 MHz convex transducer was used in all examinations. Doppler ultrasonography was performed in the right ventral part of the fetal body on the mid-sagittal plane. Pulsed Doppler was used for measurements from the mid-section of ductus venosus. After adjustment of the insonation angle to <30 °C, DV was easily visualized using the aliasing phenomenon. Abnormal DV blood flow was defined as reversed velocities during atrial contraction (A-wave). The demographic data of the patients, and results of amniocentesis and detailed ultrasonography were recorded. The women were followed up throughout pregnancy and gestational complications were investigated. Neonatal records were inspected after birth. All study data were digitally recorded and analyzed using Statistical Packages for the Social Science (SPSS) version 11.5. All variables are expressed as mean ± standard deviation, frequency, and percentage. All comparisons were performed using the Mann-Whitney U test. Nominal and ordinal variables were analyzed using one of the chi-square tests suitable for expected values and frequencies of the variables (Fisher's exact, and Yates's chi-square tests). Statistical significance was set at $p<0.05$.

Results

One hundred seventy-four women were enrolled in the study. The mean maternal age was 32.15 years; the mean number of previous pregnancies was 3.06; the mean number of previous deliveries was 2.24; and the mean number of previous abortions was 0.75. The demographic data of patients are shown in Table 1. Amniocentesis was scheduled according to the results of first trimester screening in 66 patients and the results of second trimester screening in 98 patients. Twenty-four (13.8%) subjects were aged more than 35 years. Of these, six women had detected risk in the first screening test and eight had risk in the second trimester screening test. The remaining 10 women were offered amniocentesis due to maternal anxiety.

In the later stages of pregnancy, 6 (3.4%) women developed GDM, 4 (2.3%) developed GHT, 4 (2.3%) developed preeclampsia, and 2 (1.1%) developed abortus. Eleven (68.8%)

Table 1. The demographic data of the patients

	Mean	SD	Minimum	Maximum
Maternal age (years)	32.15	5.56	20	45
Paternal age (years)	35.46	5.95	23	52
Gravida (n)	3.06	1.7	1	8
Parity (n)	2.24	1.04	0	5
Previous abortus (n)	0.75	1.05	0	5

SD: Standard deviation

of 16 pregnancies with maternal complications had normal DVD and 5 (31.2%) had abnormal DVD. Three (50%) of these women had GDM and 2 (50%) had preeclampsia. The presence of reversed a-wave in DV was a significant predictor of maternal complications in later weeks of pregnancy (p=0.003, Fisher's exact test) (Table 2).

Among the pregnant women without fetal problems (spontaneous abortus, trisomy, cardiac defect), 157 (95.7%) had normal DVD and 7 (4.3%) had reversed a-wave in DV. A total of 10 fetuses had problems, 2 of which were lost to spontaneous abortion (post-amniocentesis abortus), 4 had cardiac anomalies, and 5 had trisomy 21 (1 fetus had both trisomy 21 and ventricular septal defect).

In 13 of 174 cases, Doppler studies indicated a reversed a-wave in the ductus venosus. Of those, 3 fetuses had trisomy 21, which related to 60% (3 of 5 fetuses) of all fetuses with trisomy 21. In the euploid group, reversed flow in the DV was observed in 5.9% of the cases. The rate of reversed a-wave in DV was significantly higher than in normal DVD in fetuses with trisomy 21 (p=0.003, Fisher's exact test) (Table 3).

Discussion

The diagnostic accuracy and false positivity rates of the available screening methods for trisomy 21 have not reached an ideal level[12,13]. Recently, a novel screening method called non-invasive prenatal test based on free fetal DNA analysis in maternal blood was developed[14,15]. However, such tests cannot be included in routine screening tests owing to their high costs in developing countries.

Based on fetal ultrasonographic examinations of cases of trisomy 21, former studies reported that DV showed an abnormal flow pattern in these cases[16-18]. In a study on over 5000 pregnant women, 281 cases of trisomy 21 were diagnosed. An abnormal flow pattern in DVD was observed in 80% of trisomy 21 cases and 5% of euploid fetuses[12]. Another study detected a DV flow pattern abnormality in the first trimester in 66.3% of trisomy 21 cases[6]. In most studies where DV was assessed with Doppler ultrasonography, the assessment was made in the first trimester. Geipel et al.[16] evaluated women with 808 euploid fetuses and 37 fetuses with Down syndrome between the 14th and 18th weeks of gestation. These women were investigated for the presence of abnormal DV waveform, tricuspid regurgitation, and nasal bone hypoplasia/aplasia. The trisomy 21 group had reversed a-wave in DVD at a rate of 23.3%, tricuspid regurgitation 27%, and nasal bone hypoplasia/aplasia 45.9%, and the euploid group had a rate of 1.6% for reversed a-wave in DVD, 4.6% for tricuspid regurgitation, and 3.2% for nasal bone hypoplasia/aplasia. The authors concluded that the presence of these ultrasonographic markers in the second trimester increased the risk of Down syndrome by 6-15-fold. Combining maternal age, nuchal fold, nasal bone, tricuspid regurgitation with DVD, they accurately diagnosed 90% of all trisomy 21 cases[16]. A large-scale study conducted in 2011 that involved 20,000 euploid fetuses and 20,000 cases of trisomy 21 showed that tests including DV, tricuspid blood flow, and nasal bone at 15-18 gestational weeks improved trisomy 21 screening performance when used in conjunction with maternal age. That study revealed rates of 1.7% and 14.3% for abnormal DV flow in the euploid and trisomy 21 groups, respectively[17].

We detected DV waveform abnormalities in 3 (60%) of 5 cases of trisomy 21. Our study indicated that DVD evaluation at 16-20 gestational weeks was significantly beneficial for predicting trisomy 21, in accordance with the above-mentioned studies. The strengths of our study over other studies include its prospective design and the more homogenous nature of its sample.

Table 2. Correlation between maternal complications and ductus venosus Doppler

Ductus venosus Doppler	Pregnancies with maternal complication (n=16)				Pregnancies without maternal complication (n=158)	p
	GDM	GHT	Preeclampsia	Abortus		
Normal (n=161)	3 (1.8)	4 (2.4)	2 (1.2)	2 (1.2)	150 (93.1)	0.003
Abnormal (n=13)	3 (23)	-	2 (15)	-	8 (61.5)	

Data are given as numbers with frequencies within parentheses, GDM: Gestational diabetes mellitus, GHT: Gestational hypertension

Table 3. Distribution of normal and abnormal ductus venosus flow rate waveforms based on the presence of Down syndrome

Ductus venosus Doppler		Trisomy 21		p
		Absent	Present	
Normal (n=161)	Number	159	2	0.003
	%	94.1	40	
Abnormal (n=13)	Number	10	3	
	%	5.9	60	

Study Limitations

Our limitation is the small sample size. It has been shown previously that among cases proven to be free of chromosomal anomalies in first trimester fetal Doppler ultrasonography examination, abnormal DV flow pattern was present in 0-40% of those without cardiac defects, but 75-100% of those with cardiac defects[7,8]. We found that 3 of 4 fetuses with cardiac problems had abnormal DV waveform. This rate appears to be in accordance with previously reported studies.

It has been reported that women with GHT and preeclampsia had altered DV waveforms in fetal Doppler ultrasonographic examination performed after the index of disorder due to placental dysfunction[9]. A recent study that aimed to determine the performance of maternal characteristics, Doppler, and a set of biochemical markers for preeclampsia screening in the first and second trimester demonstrated that inclusion of pulsatility index of DV to other parameters could potentially aid patient counseling with regard to early screening for preeclampsia[10]. We demonstrated abnormal DV flow in all 4 cases of preeclampsia. Some studies indicated that the pulsatility index of DV was higher in women with GDM compared with control subjects[11,18]. We found an abnormal DV flow pattern in 3 of 6 women with gestational diabetes. Our results concerning GDM were in agreement with literature reports. In our study, the ratio of DVD abnormality was significantly greater in pregnancies that would later develop maternal complications.

Conclusion

Despite limited safety data due to the small number of fetuses with Down syndrome, we are of the opinion that the addition of DVD to second trimester screening tests will be an inexpensive and beneficial method to increase the rate of Down syndrome detection in women who cannot undergo DVD examinations in the first trimester. DVD examination in the second trimester may also provide information to predict adverse pregnancy outcomes such as preeclampsia and GDM. However, this hypothesis needs to be supported by further research with large sample sizes.

Ethics

Ethics Committee Approval: The study was approved by the Zekai Tahir Burak Women's Health Training and Research Hospital Local Ethics Committee (Approval number: 04/2009-16), Informed Consent: Consent form was filled out by all participants.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.K., A.Y., Concept: G.K., N.D., Design: S.E.Y., M.Ö.A., Data Collection or Processing: G.K., A.Y., Analysis or Interpretation: S.E.Y., M.Ö.A., N.D., Literature Search: G.K., A.Y., S.E.Y., Writing: G.K., A.Y., S.E.Y.

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The incidence, risk factors, and mortality of preterm neonates: A prospective study from Jordan (2012-2013)

Preterm yenidoğan insidansı, risk faktörleri ve mortalitesi: Ürdün'den prospektif bir çalışma (2012-2013)

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Abstract

Objective: To explore the incidence of preterm delivery, maternal risk factors for having a preterm neonate, and preterm neonates' mortality in Jordan.
Materials and Methods: A cross-sectional population-based design was applied. Socio-demographic, perinatal, delivery risk factors, and survival information were gathered in pre- and post-hospital discharge interviews with 21075 women who gave birth to live neonates at ≥20 weeks of gestation in 18 hospitals in Jordan. Women were interviewed between 2012 and 2013. The sample was limited to singleton women who gave birth to live neonates. Women who gave birth to stillborn babies were excluded.
Results: Preterm delivery incidence was 5.8%, of which 85% were in 32-36 gestational weeks. Male sex, primigravidity, hypertension, preeclampsia, and diabetes were significantly associated with an increased risk of preterm delivery. Women aged 20-35 years had the lowest risk of preterm delivery. Mother's weight <50 kg, hospitalization at 24-34 gestational weeks, lack of antenatal care visits or <8 visits during pregnancy, a history of preterm delivery, and a history of stillbirth/neonatal death were associated with increased risks of preterm delivery. The neonatal mortality rate was 4/1000 live births among full-term and 123/1000 live births among preterm babies. Prematurity, congenital anomalies, and maternal diseases were the causes of 84% of preterm neonatal deaths.
Conclusion: The mortality rate was considerably higher among preterm neonates than among term neonates; discrepancies between Jordan and other countries existed. Systematic prenatal risk assessment and quality postnatal health care improvements are required to improve the survival rates of preterm neonates.
Keywords: Preterm, infant, prematurity, obstetric, premature birth

Öz

Amaç: Ürdün'deki preterm doğum insidansı, prematüre yenidoğan için maternal risk faktörleri ve preterm yenidoğan mortalitesinin incelenmesidir.
Gereç ve Yöntemler: Kesitsel, popülasyon temelli bir tasarım uygulanmıştır. Ürdün'deki 18 hastanede ≥20. gebelik haftasında canlı doğum yapan 21075 kadınla hastane öncesi veya sonrası yapılan görüşmelerde sosyo-demografik, perinatal ve doğum sırasındaki risk faktörleri ve sağkalım bilgileri elde edilmiştir. Kadınlarla yapılan görüşmeler 2012 ve 2013 yılları arasında gerçekleştirilmiştir. Çalışmaya tekli gebeliği olup canlı doğum yapanlar dahil edilmiştir, ölü doğum yapanlar çalışmaya alınmamıştır.
Bulgular: Preterm doğum insidansı %5,8 olarak hesaplanmıştır. Bunun %85'i 32-36. gebelik haftasına ait doğumlardan meydana gelmektedir. Erkek cinsiyet, ilk gebelik, hipertansiyon, preeklampsi ve diyabet belirgin olarak artmış preterm doğum riski ile ilişkili bulunmuştur. Yirmi-35 yaş arasındaki kadınların preterm doğum için en az riski taşıdığı görülmüştür. Anne kilosunun 50 kg altında olması, 24-34. gebelik haftalarında hastaneye yatma, antenatal bakım ziyaretlerinin yokluğu veya gebelik boyunca 8'den az ziyaret, preterm doğum hikayesi ve anamnezde ölü doğum/yenidoğan ölümü olması preterm doğum için artmış riskler olarak belirlenmiştir. Yenidoğan mortalite hızı miyadında doğanlar için 4/1000 canlı doğum olarak hesaplanırken, preterm bebekler için 123/1000 canlı doğum olarak bulunmuştur. Preterm yenidoğan ölümlerinin %84'ünde neden olarak prematürite, konjenital anomaliler ve maternal hastalıklar saptanmıştır.
Sonuç: Preterm yenidoğanlarda, miyadında doğanlara kıyasla, mortalite hızı daha yüksek olarak izlenmiştir. Ürdün ve başka ülkelerin sonuçları arasında farklılıklar olduğu görülmektedir. Preterm yenidoğanların sağkalım oranlarını iyileştirmek için sistematik prenatal risk değerlendirmesi ve postnatal sağlık hizmet kalitesinde iyileştirme çalışmaları gerekmektedir.
Anahtar Kelimeler: Preterm, infant, prematürite, obstetrik, prematüre doğum

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PRECIS: The neonatal mortality rate was 30 times higher in preterm neonates than in term neonates, which indicates a survival gap between the two groups.

Introduction

Prematurity presents a significant challenge to the global community due to the rapid increase in its incidence and its disproportionate contribution to increased infant mortality rates. In 2010, approximately 15 million babies were born preterm, and more than 1 million died due to complications during the first month of life[1]. Globally, among all neonatal deaths in 2013, 35% were caused by preterm birth complications alone[2]. Research that expands our understanding of the causes and risk factors of preterm birth and how to identify women and adolescents at risk is particularly needed to decrease the global neonatal mortality rate[1]. Without accurate, comprehensive background information describing the existing state of preterm neonatal births, risk factors, and national mortality, an international improvement in preterm neonatal care would be extremely challenging to achieve. Population-based studies reporting the outcomes of preterm birth using standardized mortality definitions are highly recommended in low- and middle resource settings[3].

Jordan has a total fertility rate of 3.5 per woman, and a birth rate of 27 per 1000 people (2010-2012)[4]. Corresponding to the global picture, during 2013, half of the 4000 children in Jordan who died under the age of five years were neonates[2]. Jordan ranked 97th globally in under-five mortality rates in 2012[5]. Despite a progressive decline in neonatal mortality rates between 1990 and 2013, the national neonatal mortality rate remains high, at 11 neonatal deaths per 1000 live births in 2013[2]. However, evidence regarding the incidence, geographic distribution, associated factors, and mortality risks of preterm births in Jordan is limited; these are mostly deduced from single settings or confined to data from limited geographic areas[6-14]. This study is part of a larger nation-wide study, conducted in 2012 and 2013, to examine perinatal mortality in Jordan[15]. The purpose of this paper was to report the incidence of preterm birth, its risk factors, and its contribution to neonatal mortality.

Materials and Methods

Study design

This was a national, prospective, hospital-based study.

Setting

The study was conducted at 18 maternity hospitals that were carefully selected based on criteria determined by the study's technical committee, which consisted of representatives from the United Nations International Children's Emergency Fund (UNICEF), the World Health Organization (WHO), and the Jordanian health sectors. These criteria reflected the diverse socioeconomic status of the participants and the quality levels of services provided to them. The hospital selection criteria also considered the workload of the hospitals in terms of the number of deliveries.

Accordingly, the 18 hospitals were distributed over the three regions of the country: seven hospitals in the middle, six in the north, and five in the south. The hospitals represented all health care delivery sectors in the three geographic regions of Jordan, including urban and rural areas. The number of births selected from each hospital was proportional to the number of births in each health sector and region. The Institutional Review Boards at the Ministry of Health and selected hospitals approved the study (approval number: 2012/035).

Participants

All women who gave birth to dead or live neonates at 20 or more weeks of gestation in each of the selected hospitals were eligible for inclusion and were interviewed before discharge from the hospital. The sampling criteria and size of the larger study are described in detail elsewhere[15]. In the current analysis, the sample was limited to singleton women who gave birth to live neonates. Women who gave birth to stillborn babies were excluded. Written informed consent was obtained for each participant prior to commencing the interviews.

Data source and measurements

A number of questionnaires and forms were developed, revised, and finalized by the study team to facilitate the gathering and recording of research data. The questionnaires had specific instructions, and the content was organized to increase clarity and enhance the accuracy of the obtained data. A team of 3-6 midwives/nurses, led by an obstetrician and a neonatologist or pediatrician, was assigned to collect data at each selected hospital. Qualified local trainers conducted a two-day training workshop for researchers working in each region. The study questionnaires and forms were pre-tested in the field on a sample of women similar to those who were actually included in the study.

The pre-discharge interview questionnaire contained information about the socio-demographic, maternal, and clinical characteristics of the women; information about pregnancy, labor, and delivery; relevant information about the neonates; and perinatal and neonatal deaths. Information was also gathered from the participating women's medical records pre-discharge. Woman whose neonates died before discharge were asked further questions about the circumstances and causes of death.

For those women who did not experience perinatal or neonatal death before discharge, consent to follow-up with them postpartum was obtained, and their phone number was noted. The women who agreed to be contacted were called 30 days postpartum to participate in a phone interview; questions were asked about whether the neonate was alive, the health of the neonate, and details of visits to health facilities for both

the mother and her neonate. If, through this screening call, it was discovered that a neonate had died, plans were made for a follow-up interview at the woman's home for a "verbal autopsy". Neonatal gestational ages were recorded in the women's medical records by practicing physicians. The gestational age was based on both ultrasound and the last menstrual period (the interval between the first day of the mother's last normal menstrual period and the date of delivery of the fetus or newborn). A preterm neonate was defined as a neonate that was born before 37 completed weeks of pregnancy. Based on the gestational age, preterm babies were further classified as born between 32-36 weeks of gestation and born at <32 weeks. A birth weight less than 2500 grams (5 pounds, 8 ounces) was considered as low birth weight and a birth weight of 2500 grams and above was considered as normal weight. The neonatal mortality rate was defined as the number of deaths during the first 28 completed days of life per 1000 live births that occurred during the study period. Neonatal deaths were subdivided according to the time of death into early neonatal deaths at 0-6 days after live birth and late neonatal deaths at 7-27 days after live birth. Both were expressed as per 1000 live births.

The hospital diagnosis of the causes of neonatal deaths was based on standard obstetric and neonatal guidelines. The deaths were classified according to the National Institute for Heath and Care Excellence (NICE) system, a standard classification system that is based on the modified Wigglesworth classification[16], together with information on the calculation of birth weight in relation to gestational length. The NICE classification program classifies neonatal death into one of a range of specific, mutually exclusive, cause-of-death subgroups. The order of the subgroups is strictly hierarchical.

Statistical Analysis

Data were described using means (standard deviation) for continuous variables, and frequencies and percentages were used for categorical variables. The differences between proportions were tested using chi-square tests. Risk factors were analyzed using generalized, linear-mixed multilevel models, and traditional logistic regression analysis was used to measure the hierarchical complexity of predictor variables. The Akaike information criterion (AIC) and the Bayesian information criterion were used to select and compare models based on the -2 log likelihood. Based on the information criteria, we preferred the final binary logistic regression model predicting prematurity over the final generalized linear mixed model with one random intercept, because it had smaller AIC values. Based on a likelihood ratio test, the binary logistic regression (no random effect) was still preferred. The variables were included in the model systematically, and those with $p<0.10$ in the univariate analysis were included in the model. The possible associated factors were examined for evidence of multicollinearity, which was reflected by either the changes in the direction of effect between the univariate and multivariable analysis or implausible standard errors for a particular variable. A p-value of <0.05 was considered statistically significant. Traditional and multilevel analyses were performed using IBM SPSS 20 (SPSS Inc., Chicago, IL, USA).

Results

Participants' characteristics

During the study period, 21 075 women gave birth in the selected hospitals. Approximately one third of deliveries (34.2%) occurred in the northern region, 55.0% in the middle region, and 10.8% in the southern region. About 30.5% of women gave birth in private hospitals, 46.9% in public hospitals, 18.7% in military hospitals, and 3.8% in teaching hospitals. Almost all women (99%) sought antennal care, with 70.1% seeking antennal care >8 times. Less than one-third (32%) of women had an education level that was lower than high school, and 41.5% had an income of >350 Jordanian dinar (JD) per month (1 $= 0.71 JD). About 8.0% of women had a history of preterm or low-birth-weight delivery, 3.2% were smokers, 1.2% had preeclampsia, 1.2% had gestational diabetes, 0.5% had pre-gestational diabetes, and 4.8% had pre-gestational high blood pressure.

Incidence of preterm birth

Among the participants, 5.8% delivered before 37 completed weeks of gestation. The majority of preterm deliveries (85%) occurred between 32 and 36 weeks, and 15% reached <32 weeks of gestation. The preterm birth rate, according to the socio-demographic and clinical characteristics of the mothers and their babies, is shown in Table 1. The preterm birth rate was the lowest among women aged 20-35 years (7.8% for women aged <20 years, 5.4% for women aged 20-35 years, and 7.7% for women aged >35 years). The rate was extremely high among women who did not use antenatal care services (13.8%). The rate was also higher among women who had a history of preterm/low-birth-weight delivery (14.4%), hypertension (12.6%), preeclampsia (24.7%), gestational diabetes (10.3%), pre-gestational diabetes (25.7%), and women who were hospitalized between 24 and 34 gestational weeks. The rate of cesarean section births (46.4%), both planned and emergency, among the preterm neonates was almost equal to that by vaginal delivery (50.7%).

The main characteristics of the full-term and preterm deliveries are shown in Table 2. Presentation at delivery was cephalic in 95.4% of full-term deliveries and 86.9% of preterm deliveries. About 27% of full-term deliveries and 46.4% of preterm deliveries were performed via cesarean section. Neonatal resuscitation was necessary for 9.6% of full-term babies and 29.2% of preterm babies. Preterm babies were more likely to have poor Apgar scores at 1 and 5 minutes compared with full-term babies.

Risk factors of preterm delivery

In multivariable analysis (Table 3), male sex [odds ratio (OR)=1.2], primigravid (OR=1.6), hypertension (OR=1.5),

Table 1. The rate of preterm birth according to socio-demographic and clinical characteristics of mothers and their babies

	Gestational age				
	Full term (GA≥37)		Preterm (GA<37)		p
	n	%	n	%	
Mother's age					
<20	1201	92.2	101	7.8	<0.001
20-35	16250	94.6	934	5.4	
>35	2360	92.3	197	7.7	
Mother's education					
<12	6276	93.5	434	6.5	0.016
12-14	9025	94.2	551	5.8	
>14	4441	94.8	244	5.2	
Income (JD)					
≤350	11581	94.3	701	5.7	0.270
>350	8170	93.9	528	6.1	
Region					
North	6821	94.6	387	5.4	0.012
Middle	10866	93.7	728	6.3	
South	2147	94.8	117	5.2	
Health sector					
Private	6087	94.6	345	5.4	<0.001
Public	9341	94.4	549	5.6	
Military	3654	92.9	280	7.1	
Teaching	752	92.8	58	7.2	
Nationality					
Jordanian	18688	94.2	1156	5.8	0.569
Others	1146	93.8	76	6.2	
Baby sex					
Male	10 174	93.8	671	6.2	0.032
Female	9650	94.5	561	5.5	
Number of antenatal care visits					
None	187	86.2	30	13.8	<0.001
1-8	5558	92.3	464	7.7	
>8	13906	95.0	727	5.0	
Inter-delivery interval					
First delivery	5531	93.6	377	6.4	0.007
<2 years	4912	93.8	326	6.2	
>2 years	8397	94.7	467	5.3	
Smoking					
Yes	636	93.4	45	6.6	0.392
No	19188	94.2	1187	5.8	

GA: Gestational age, JD: Jordanian dinar

preeclampsia (OR=3.1), and diabetes (OR=1.6) were significantly associated with an increased risk of preterm delivery. Women aged between 20 and 35 years had the lowest risk of giving birth to a preterm neonate compared with older or younger women. A mother's weight <50 kg, hospitalization at 24-34 gestational weeks, no antenatal care visits or <8 visits during pregnancy, and a history of preterm or low-birth-weight delivery or stillbirth/neonatal death were all associated with an increased risk of preterm delivery.

Rates and causes of neonatal mortality among preterm and full-term babies

The neonatal mortality rate was four per 1000 live births among full-term (early neonatal death=three per 1000 live births, and late neonatal death=one per 1000 live births). The neonatal mortality rate was 123 per 1000 live births among preterm babies (early neonatal death=99 per 1000 live births, and late neonatal death=24 per 1000 live births). Among normal birth weight babies, the neonatal mortality rate was 3 per 1000 live births for full-term and 22 per 1000 live births for preterm babies. Among low-birth-weight babies, the rate was 32 per 1000 live births for full-term, and 116 per 1000 live births for preterm babies. The causes of death for full-term and preterm babies are shown in Table 4.

Discussion

The incidence of preterm births in the current study was 5.8%, comparable to that reported in developed countries such as Finland, Ireland, and Sweden[17]. The preterm birth rate in this study compares positively with that observed in the United States and in most low- and middle-income countries[17-20]. The relatively lower incidence rate in this study may be due to the larger number of participants aged 20-35 years and educated participants. Evidence from previous studies indicated that young (<20 years) and advanced (≥40 years) maternal ages are strong risk factors of preterm births[9,21,22]. Similarly, increased risks of mothers having a preterm birth were associated with low or no education levels[21].

Table 2. The main characteristics of full and preterm deliveries

	Gestational age				
	Full term (GA≥37)		Preterm (GA<37)		Total
	n	%	n	%	
Presentation at delivery					
Cephalic	18898	95.4	1069	86.9	19967
Breech	628	3.2	114	9.3	742
Other	285	1.4	47	3.8	332
Mode of delivery					
Vaginal delivery	13367	67.7	620	50.7	13987
Forceps/vacuum delivery	1045	5.3	36	2.9	1081
Emergency cesarean	2451	12.4	287	23.5	2738
Planned cesarean	2872	14.6	280	22.9	3152
Neonatal resuscitation					
Not necessary	17661	90.4	837	70.8	18498
Necessary/not performed	766	3.9	41	3.5	807
Necessary/performed	1112	5.7	304	25.7	1416
Apgar score at 1 minute					
Poor (0-3)	73	0.4	47	4.1	120
Intermediate (4-7)	8251	42.3	731	63.1	8982
Normal (8-10)	11199	57.4	380	32.8	11579
Apgar score at 5 minutes					
Poor (0-3)	18	0.1	14	1.2	32
Intermediate (4-7)	836	4.3	214	18.5	1050
Normal (8-10)	18661	95.6	926	80.2	19587

GA: Gestational age

The incidence rate of preterm birth noted in this study was also lower than that reported in earlier studies in Jordan[7,9,10]. The proportion of preterm births, as reported by single-setting studies conducted in Jordan, ranged between 10.7%[7] and 12.8%[10] out of the total births in each setting, and the highest mortality in the neonatal intensive care unit was among preterm and low-birth-weight admissions[12]. The discrepancy in the incidence of preterm births between the current study and previous studies in Jordan could be due to the small samples and geographic areas studied previously. The lower preterm birth rate in our study could indicate the positive progress that has been made recently in the quality of maternal-fetal health care in Jordan. The high number of women in the current study who attended antenatal clinics supports this supposition.

However, the high attendance rate of antenatal care in this study did not reflect positively on the preterm neonatal mortality rate. The mortality rate of 123/1000 was relatively high. The neonatal mortality rate was 30 times higher among preterm neonates than among full-term neonates, indicating a survival gap between the groups; this disparity may be perceived as an urgent call for the systematic improvement of postnatal and neonatal intensive health care in Jordan. The best intervention for prevention of spontaneous preterm birth in women with risk factors is still unclear[23]. However, simple cost-effective and research-

Table 3. Multivariable analysis of factors associated with preterm delivery

	OR (95% Confidence interval)	p
Region		
North	1.0	
Middle	1.2 (1.0, 1.4)	0.024
South	0.8 (0.6, 1.0)	0.021
Neonate gender (male vs. females)	1.2 (1.1, 1.4)	0.001
Number of deliveries		
1	1.6 (1.3, 2.0)	<0.001
2	1.2 (1.0, 1.5)	0.120
3-4	1.0 (0.8, 1.2)	0.700
≥5	1.0	
Hypertension	1.5 (1.2, 1.9)	0.002
Preeclampsia	3.1 (2.2, 4.5)	<0.005
Diabetes	1.6 (1.1, 2.3)	0.021
Age (year)		
<20	1.3 (1.2, 1.5)	0.043
20-35	1.0	
>35	1.4 (1.1, 1.7)	0.046
Hospitalization at 24-34 gestational weeks		
Not hospitalized	1.0	
Hospitalized/no prophylaxis	4.2 (3.0, 5.8)	<0.005
Hospitalized/with prophylaxis	7.6 (6.1, 9.5)	<0.005
Number of antenatal care visits		
None	3.8 (2.4, 6.1)	<0.005
1-8	1.7 (1.5, 1.9)	<0.005
>8	1.0	
Mother's weight (<50 vs. ≥50 kg)	1.3 (1.0, 1.6)	0.033
History of preterm/low-birth-weight delivery	2.7 (2.3, 3.3)	<0.005
History of neonatal death/stillbirth	1.6 (1.2, 2.0)	<0.005

OR: Odds ratio

supported interventions are available to reduce deaths among premature babies; for example, the promotion of early and exclusive breastfeeding, handwashing, and innovative skin-to-skin care[24,25]. The prevention of hypothermia and management of respiratory distress syndrome, neonatal pneumonia, sepsis, and hyperbilirubinemia are evidence-based interventions that can greatly increase the survival of small and sick neonates[24].

Globally, 4 out of 5 newborn deaths result from three preventable and treatable conditions, primarily prematurity[25,26]. Prematurity alone was the direct cause of almost 50% of neonatal deaths in the current study, followed by congenital anomalies and maternal medical conditions. Prematurity is often complicated by infections and respiratory complications, which commonly leads to the death of preterm infants[19,27]. These complications can be prevented and treated by skilful and high-quality postnatal care of preterm neonates, especially during the first week of life. Our findings indicate that preterm neonates were four times more likely to die postnatally during the first week of life, compared with later times after birth. Nevertheless, high-quality antenatal screening and care are still key components in efforts to identify preterm birth risk factors early, prevent preterm births, and reduce infant mortality.

This research showed that the incidence of preterm birth was significantly reduced when mothers received health care in antenatal clinics during pregnancy. The more antenatal visits mothers attended during pregnancy, the lower was the risk of preterm births. Previous studies have shown that preterm births were significantly more common among women who had no or only occasional visits to antenatal care[27-30]. In this study, the risk of preterm birth was almost four times greater in women who did not attend antenatal care, a risk ratio that is consistent with a study in Thailand[29].

Globally, the proportion of women receiving antenatal care at least once during pregnancy was 83% between 2007 and 2014. However, only 64% of pregnant women attended the WHO-recommended minimum of four or more antenatal care visits[31]. Correspondingly, in this study, almost all of the women had received antenatal care at least once. However, nationally, this is not sufficient, because more than one quarter of the sample received less than the national goal of a minimum of eight visits; this indicates a need to improve women's access to and compliance with antenatal health services. These results may influence health policies in Jordan and globally.

The identification of warning signs during pregnancy is an important goal of antenatal care[31]. Preeclampsia, diabetes, and hypertension, whether pre-existing or gestational, are maternal medical conditions that commonly predict preterm birth[20,32], a finding that is similar to those of this study. For women with preeclampsia, the risk of preterm delivery was three times greater than it was for women who were not affected. This highlights that screening and medical management during antenatal care are clinically important to decrease the risk of preterm birth. Madan et al.[33] found that the risk of preterm birth was augmented for obese and overweight mothers if they experienced one or more of the conditions listed above. Their conclusion highlights the importance of including weight indices in the assessment of preterm birth risk factors. The evidence suggests an increase in the likelihood of preterm birth when body mass index (BMI) decreases below or increases above

Table 4. The leading causes of neonatal deaths among full term and preterm babies, based on the National Institute for Heath and Care Excellence classification

Cause of death	Gestational age				Total
	Full term (GA≥37)		Preterm (GA<37)		
	n	%	n	%	n
Congenital anomalies	44	52.4	37	24.8	81
Unexplained immaturity	0	0.0	71	47.7	71
Maternal disease	4	4.8	17	11.4	21
Specific infant conditions	15	17.9	5	3.4	20
Unexplained asphyxia	13	15.5	3	2.0	16
Obstetric complications	3	3.6	6	4.0	9
Unclassifiable cases	5	6.0	1	0.7	6
Unexplained small-for-dates infants	0	0.0	3	2.0	3
Placental abruption	0	0.0	4	2.7	4
Multiple births	0	0.0	1	0.7	1
Specific fetal conditions	0	0.0	1	0.7	1

GA: Gestational age

normal[29,33]. Due to too many missing data, the researchers were unable to include BMI in the statistical analysis of their study; however, their results provide additional evidence of the role of underweight mothers on the increased risk of preterm birth.

Multiparous women with a history of preterm birth are also at risk for further preterm birth[21,29,33]. In the current study, the likelihood of having a preterm birth at least doubled when there was a history of preterm or low-birth-weight delivery in previous pregnancies; a rate similar to that reported in a Canadian study[21]. Likewise, primigravida was associated with a 1.6 increase in the likelihood of giving birth to a preterm neonate, which is approximate to the findings of similar studies[21,29]. The rate of caesarian section births, both planned and emergency, among the preterm neonates was remarkably high (46.4%) and is worth further investigation.

Maternal hospitalization during 24-34 weeks of gestation was associated with a very high likelihood of preterm delivery. This finding is understandable because early maternal hospitalization during pregnancy indicates the existence of maternal or fetal health problems or early identification of a potential problem. The reasons for hospitalization and types of care provided need more investigation because these factors could lead to a better understanding of preterm birth risk factors and hence prevent prematurity complications and preterm neonate mortality. Interventional studies that incorporate the results of this study in preterm delivery risk assessment in maternal and child health centers are also encouraged.

Study Limitations

Although this study had several strengths compared with previous studies, it also had several limitations. Among the strengths of the current research were that it was nation-wide, covered a wide geographic area, and included information from all birth records in all sectors and types of hospital settings. It was not feasible, however, to include information on deliveries that occurred outside formal birth settings, such as private homes, which do occur in Jordan, albeit rarely. Although not all of the results of this study can be generalized to other countries, efforts were made to follow the WHO's recommended definitions of prematurity and international standards of reporting mortality to allow for international comparisons and to enhance generalizing the data. In addition, this study was conducted over a specific period; therefore, replicating this study is highly recommended in future years to compare trends over time and identify changes in preterm birth estimates. Moreover, a longitudinal cohort study is strongly encouraged to follow preterm neonates because it would be highly beneficial to identify the long-term outcomes of preterm births, and the health needs of babies who survive prematurity.

Conclusion

Addressing the major risks associated with the incidence and the mortality of preterm neonates is a priority to reduce the global burden of preterm birth, along with identifying areas that are crucial to improve the health care systems across countries. Regarding risk factors, the limited research carried out in Jordan shows that the rate of preterm and low-birth-weight infants was highest for males and first-born neonates[10] among teenage women[8,13] and women aged 35 years or above[9,10], as well as for women in consanguineous marriages[11]. By adding relevant information from Jordan, this study has contributed evidence to international comparison tables, and to the national as well as the international picture about prematurity.

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Ethics

Ethics Committee Approval: The study was approved by the Institutional Review Boards at the Ministry of Health, Jordan (Approval number: 2012/035), Informed Consent: A written informed consent was obtained from each participating woman.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Concept: Y.S.K., A.M.B., Design: Y.S.K., A.M.B., Data Collection or Processing: Y.S.K., A.M.B., Analysis or Interpretation: N.M.A.R., Y.S.K., A.M.B., Literature Search: N.M.A.R., Y.S.K., A.M.B., Writing: N.M.A.R., Y.S.K., A.M.B.

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The relationship between fecal incontinence and vaginal delivery in the postmenopausal stage

Postmenopozal dönemde görülen fekal inkontinansların vajinal doğumla ilişkisi

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Abstract

Objective: Obstetric anal sphincter injuries are one of the most significant complications of vaginal delivery that give way to fecal incontinence, which is defined as the involuntary leakage of gas, fluid or solid stool. Although sphincter injuries are seen in 0.5-9% of all deliveries. It has been reported that 20-41% of women who had vaginal deliveries had occult anal sphincter injuries as endoanal ultrasonography began to be used by physicians. The aim of our study was to investigate the relationship between fecal incontinence, whose incidence increases dramatically during the postmenopausal stage, and occult anal sphincter injuries.

Materials and Methods: Two hundred healthy female patients with no history of anal sphincter injury, aged between 18 and 70 years were included in the study. The participants were divided into 4 groups according to their menopausal stages and mode of delivery; premenopausal (group 1) and postmenopausal (group 2) vaginal delivery, and premenopausal (group 3) and postmenopausal (group 4) cesarean section. Wexner incontinence scores were determined. The participants' defects were assessed using endoanal ultrasound and their status of fecal incontinence using anorectal manometric measurements.

Results: Anorectal manometric measurement results were found significantly lower in group 1 than in group 3 ($p<0.01$). The Wexner scores of groups 1 and 3 were similar. The anorectal manometric measurement results of group 2 were significantly lower than those of group 4, and the Wexner score of group 2 was significantly higher than other groups ($p=0.03$).

Conclusion: Anal sphincter injuries formed after vaginal delivery may be one of the reasons that increase the incidence of postmenopausal fecal incontinence and cause the formation of fecal incontinence symptoms in women.

Keywords: Fecal incontinence, obstetric sphincter injury, postmenopausal stage

Öz

Amaç: Obstetrik anal sfinkter yaralanmaları vajinal doğumların önemli bir komplikasyonudur ve istemsiz gaz, sıvı veya katı gaita kaçağı olarak tanımlanan fekal inkontinanslara neden olmaktadırlar. Tüm doğumların %0,5-9'unda sfinkter yaralanması görülmesine rağmen endoanal ultrasonografinin kullanıma girmesiyle vajinal doğum yapmış kadınların %20-41'inde okült anal sfinkter yaralanmaları olduğu tespit edilmiştir. Çalışmamızın amacı postmenapozal dönemde insidansı dramatik artan fekal inkontinansların okült anal sfinkter yaralanmaları ile ilişkisinin incelenmesidir.

Gereç ve Yöntemler: Anal sfinkter yaralanması öyküsü olmayan 18-70 yaş arası 200 sağlıklı kadın çalışmaya alındı. Katılımcılar premenapozal ve postmenapozal vajinal doğum; premenapozal ve postmenaozal sezaryenle doğum yapanlar olmak üzere 4 gruba ayrıldı. Katılımcılar menapoz durumu ve doğum türüne göre 4 gruba ayrıldı. Wexner inkontinans skorları belirlendi. Katılımcıların anal sfinkter defektleri endoanal ultrason ile anal sfinkter fonksiyonları ise anorektal manometer ile değerlendirildi.

Bulgular: Grup 1'de anorektal manometre ölçüm değerleri grup 3'ten anlamlı olarak daha düşük bulundu ($p<0,01$). Grup 1 ve grup 3 arasında Wexner skoru benzerdi. Grup 2'nin anorektal manometrik ölçüm değerleri grup 4'ten anlamlı olarak daha düşüktü. Wexner skoru ise grup 2'de anlamlı olarak daha yüksekti ($p=0,03$).

Sonuç: Vajinal doğum sonrası oluşan anal sfinkter yaralanmaları kadınlarda menapoz sonrası fekal inkontinansların insidansının artmasına ve fekal inkontinans semptomların oluşmasına neden olan bir faktör olabilir.

Anahtar Kelimeler: Fekal inkontinans, obstetrik sfinkter yaralanması, postmenapozal durum

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Introduction

Obstetric anal sphincter injuries (OASIS) account for a significant complication of vaginal deliveries and cause fecal incontinence (FI), which is defined as the involuntary leakage of gas, fluid or solid stool[1]. They are seen in 0.5-9% of all deliveries[2]. Post-delivery FI incidence, however, is about 3%[3]. Only 30% of patients with OASIS were observed to have FI symptoms a year after delivery[4]. It has also been reported that rates of fecal emergency and FI in the geriatric population reaches up to 53-80%[5].

As endosonography became more common, occult anal sphincter injuries were detected in most of women with FI. Moreover, it has been shown that 20-41% of women who had normal deliveries but were without FI symptoms had ongoing occult anal sphincter injuries[6]. Although there have been ample studies on occult anal sphincter injuries within the last decade, its clinical significance and natural history are still unclear[7]. Further, it has also been argued that these injuries might become symptomatic at later ages[8]. The reason for the increase seen in FI prevalence in women at later ages is controversial. It has been suggested that the existence of estrogen and progesterone receptors in women led to an increase in FI in the postmenopausal stage because of their hormonal effects on sphincters and pelvic floor muscles[9] but this correlation still proves to be controversial[10,11].

We believe that occult anal sphincter injuries following delivery become symptomatic with changes seen in the postmenopausal stage. Therefore, our aim in this study was to investigate whether occult anal sphincter injuries are among the causes of postmenopausal FIs.

Materials and Methods

Before the study was initiated, the consent of Necmettin Erbakan University, Meram Faculty of Medicine's Board of Ethics for Clinical Trials was obtained (approval number: 2013/79). Healthy women who presented to the gynecology outpatient clinics of Necmettin Erbakan University Meram Faculty of Medicine between May 2013 and November 2013 with a history of delivery but with no previous history of anal sphincter injury were included in the study. Women aged between 18 and 70 years with at least one delivery and a 6-month interval after their latest delivery were covered by the study. Patients who had been clinically diagnosed as having sphincter injuries and subsequently received treatment for these injuries, and women aged over 70 years were excluded from the study because they were thought to be unsuitable for the tests required. All participants who had vaginal deliveries had a mediolateral episiotomy story at the first birth. Participants who underwent multiple episiotomies or did not have episiotomy were not included in the study. The criteria for inclusion and exclusion in the study are shown in Table 1.

Informed consents were obtained from all participants and they were allocated into 4 groups according to their mode of delivery and menopausal status. Each group had 50 participants, a total of 200 for the whole study. Sample size was set at a minimum of 46 participants for each group with a margin of error of α=0.05 and β=0.20 as revealed by the power analysis performed based on study data presented by Donnelly et al.[12].

Groups

Group 1: Premenopausal women with a history of vaginal delivery,

Table 1. The study inclusion and exclusion criteria

Criteria for inclusion	Criteria for exclusion
- Aged between 18 and 70 years	- Previous history of anorectal or vaginal surgical procedure
- At least one delivery at the expected delivery time	- Diabetes
- At least 6-month interval from the latest delivery for subjects with recent history of delivery	- Chronic constipation
	- History of neurologic disease
- Less than one episiotomy at vaginal delivery	- Pelvic organ prolapsus
	- Inflammatory intestinal diseases
	- Stage 3 or 4 sphincter injury during vaginal delivery
	- Complicated delivery
	- Macrosomia
	- Fetal growth retardation
	- Fetal malformation
	- Oligohydramnios
	- Polyhydramnios
	- Existence of malignancy
	- Pregnancy
	- Other major health issues
	- Multiple episiotomies at vaginal delivery
	- No episiotomy at vaginal delivery

Group 2: Postmenopausal women with a history of vaginal delivery,
Group 3: Premenopausal women with a history of c-section (premenopausal control group),
Group 4: Postmenopausal women with a history of c-section (postmenopausal control group).
Premenopausal period: Women aged between 18 and 49 years with at least one delivery and who menstruated at least once in the last 12 months.
Postmenopausal period: Women aged between 49 and 70 years who had no history of menstruation in the last 12 months.

Evaluation of participants

The age, mode of delivery, number of deliveries, history of postpartum clinical anal sphincter, history of anal sphincter repair, and whether the patients had had symptoms of postpartum FI were questioned. FI scoring was conducted according to the 20-point Wexner incontinence scale (WIS), which is based on patients' gas, fluid, solid incontinence status and designed to determine changes in lifestyle and the frequency of the need to use pads.

Anorectal manometric measurement

All subjects received rectum cleansing with a fleet enema before the examination. The subjects were evaluated in the left lateral decubitus position. A Peritron precision perineometer 9300AV (Cardio Design Pty Ltd, Oakleigh, Victoria, Australia) perineometer and 3010 (Cardio Design Pty Ltd, Oakleigh, Victoria, Australia) type anal sensor were used.
The anal probe was 80 mm in length and was produced to have a pressure-sensitive part of 30 mm in the middle. The average figure for serial measurements of 1 minute anal channel resting pressure of the subjects was recorded. The subjects were then told to contract the anal sensor as powerfully as they could and to hold it in contraction. This procedure was repeated 3 times with 10 second intervals and the data were recorded. The values with the most successful contraction were determined to be the manometric values of the subject[13]. Maximum contraction pressure values were taken into consideration in the evaluation of the subjects' external anal sphincter (EAS) contractions. The pressure unit was taken in cm H_20 values in measurements conducted with the perineometer.

Endoanal ultrasonography

The anal endosonography procedure was performed at the imaging laboratory of our hospital's gastroenterology clinic. Imaging was conducted using a Fujinon ITD-01 EUS and a P2612M model flexible radial ultrasonic sonoprobe with 12 MHz frequency. All endoanal ultrasonography (EAUSG) procedures were performed by two physicians experienced in gastroenterology and proctology. The participants' information about their mode of delivery was not shared with the physician performing EAUSG. The locations of all defects [OASIS and/or internal anal sphincter (IAS)] were located.

Statistical Analysis

The mean, standard deviation, lowest, highest median, frequency, and percentage rates were used in the descriptive statistics of the collected data. The distribution of variables was measured using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used for the analysis of quantitative data, and the chi-square test was used for the analysis of qualitative data. The effect level was investigated by univariate and multivariate logistic regression. SPSS 22.0 was used for all analyses.

Results

The demographic data of the premenopausal (group 1 + group 3) and postmenopausal (group 2 + group 4) groups are shown in Table 2. The episiotomies in vaginal deliveries were all mediolateral. There were no statistical differences between the groups regarding the participants' body mass index (BMI), high birth weight, and instrument use ($p>0.51$).
The mean age and the number of deliveries of the patients in group 1 were similar to those of group 3. The endoanal ultrasonography imaging revealed that 20 (40%) and 2 (4%) patients in groups 1 and 3 had occult anal sphincter defects, respectively. Although sphincter defects were mostly seen in the EAS (24%) in group 1, only 2 patients were detected as having IAS defects in group 3 (Table 3). Anorectal manometric measurements showed that the maximum extrusion pressure, mean extrusion duration, and mean extrusion pressure values of group 1 were significantly lower than group 3 [odds ratio (OR): 1.02, 95% confidence interval (CI): 1.01-1.039; OR: 1.04, 95% CI: 1.02-1.05; OR: 1.03, 95% CI: 1.02-1.05; $p<0.01$, respectively). There was no significant difference ($p>0.05$) between group 1 and group 3 regarding WIS and the mean resting pressure values (Table 4).
There was no difference between group 2 and group 4 with regards to the mean age of the patients and the number of deliveries. Twenty-two (44%) patients in group 2 were detected to have occult anal sphincter defects according to endoanal ultrasonography data, and 2 (4%) patients in group 4 had sphincter defects ($p<0.001$). The most common sphincter defect seen in group 2 was EAS (24%). Anorectal manometric measurements showed that the maximum extrusion pressure, mean extrusion duration, mean extrusion pressure values of group 2 were significantly lower than group 4 (1.025 OR, 95% CI:0,46-0,78; $p<0.001$). There was, however, no significant difference between the groups regarding the mean resting pressure. The Wexner score of group 2 was significantly higher than group 4 (0.64 OR, 95% CI:[0.48-0.86]; $p=0.003$). Although 8 (16%) of patients had distinctive FI and 14 (28%) had incontinence symptoms in group 2, 10 (20%) patients had started to have fecal complaints in group 4 (Table 5). When the patients who had had vaginal delivery were compared with regards to their menopausal status, there were no statistical differences between the groups according to EAUSG data with regards to the existence of sphincter defects and the location of defects ($p=0.68$). Anorectal manometric measurements showed that the maximum extrusion pressure, mean extrusion duration,

mean extrusion pressure values of group 2 were significantly lower than group 1 ($p<0.05$). The Wexner scores of the groups were not significantly different (Table 6). Although no obvious FI was observed in group 1, 7 (14%) patients in group 2 had obvious FI. Figure 1 graphically demonstrates maximum contrusion pressures, WIS, mean contrusion durations, and mean contrusion pressure values of all groups.

Discussion

One of the most significant causes of FI in women is vaginal deliveries that result in anal sphincter injuries. Although OASIS is seen in 0.5-9% of all deliveries, it has been reported that 35-44% of women who had vaginal deliveries also had occult anal sphincter injuries when EAUSG began to be used by physicians[6]. However, FI symptoms are observed in only 20% of these women. Therefore, the natural history and significance of occult anal sphincter injuries still proves to be controversial[14]. In our study, we investigated the effects of occult anal sphincter injuries formed after vaginal deliveries on FI seen in the postmenopausal stage. Factors such as the number of deliveries, which increase the risk of FI after vaginal delivery, use of vacuum and forceps during delivery, BMI,

Table 2. Demographic data of the participants according to premenopausal and postmenopausal stages

Demographic data	Premenopausal group (group 1 + group 3) Mean ± SD Min - Max	Postmenopausal group (group 2 + group 4) Mean ± SD Min - Max	p
Age	36.66±6.44 21-48	55.68±5.49 49-70	>0.001
Delivery number	2.52±1.15 1-6	3.18±1.81 1-11	0.060
Wexner score	1.08±1.84	1.14±2.05	0.828
Maximum contraction pressure cm H_2O	187.66±51.30 90.90-290.30	161.70±50.44 56.50-264.90	**<0.001**
Time/second	65.31±39.14 10-194.29	54.80±30.14 5-147.8	**0.035**
Average contraction pressure cm H_2O	120.83±38.11 40.20-211.60	118.17±43.77 25.40-217.20	0.647
Gradient	42.33±47.17 0.70-223.6	40.31±41.75 2.20-220	0.748

SD: Standard deviation, Min: Minimum, Max: Maximum

Table 3. Endoanal ultrasound data of participants that location and size of defect at all groups

	Location	No defect n (%)	<90° n (%)	90-180° n (%)	<180° n (%)
Group 1	IAS		-	2 (4)	-
	EAS	30 (60)	7 (14)	4 (8)	1 (2)
	IAS + EAS		5 (10)	1 (2)	-
Group 2	IAS		2 (4)	1 (2)	1 (2)
	EAS	28 (56)	10 (20)	1 (2)	1 (2)
	IAS + EAS		6 (12)	-	-
Group 3	IAS		2 (4)	-	-
	EAS	48 (56)	-	-	-
	IAS + EAS		-	-	-
Group 4	IAS		2 (4)	-	-
	EAS	48 (56)	-	-	-
	IAS + EAS		-	-	-

IAS: Internal anal sphincter, EAS: External anal sphincter

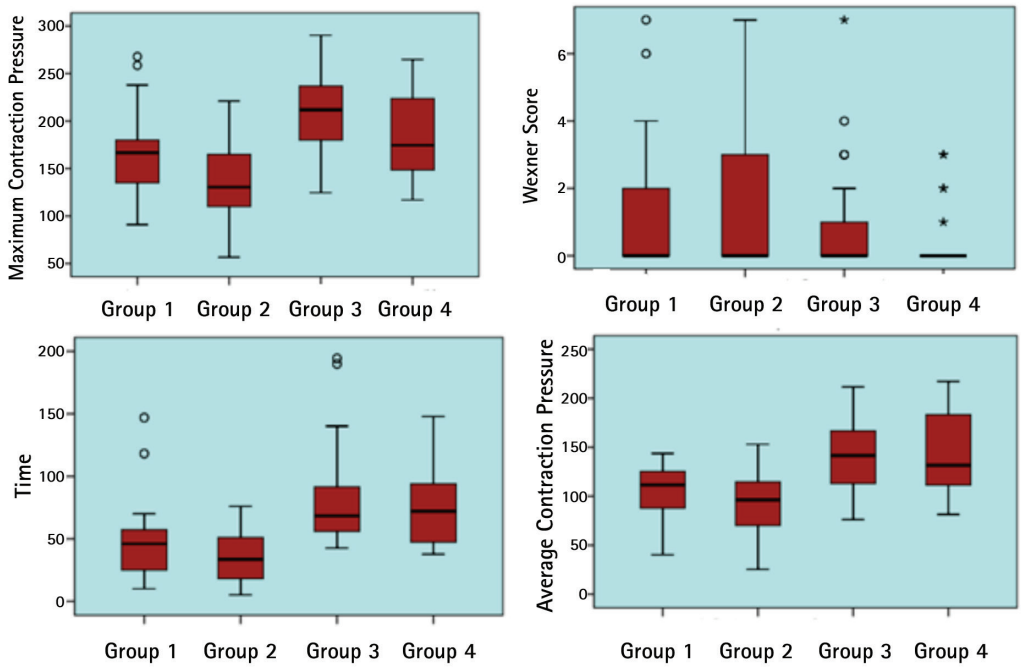

Figure 1. The distribution of maximum contrusion pressure, Wexner incontinence scale, mean contraction duration, and mean contraction pressure values of the participants according to the groups

Table 4. The comparison of demographic data, endoanal ultrasonography, and manometric measurement results of groups 1 and 3

		Group 1				Group 3				p
		Mean ± SD	n (%)	Med	(Min - Max)	Mean ± SD	n (%)	Med	(Min - Max)	
Age		38.0±6.2		38	21-48	37.3±6.4		36	25-48	0.154
Delivery number		2.5±1.4		3	1-6	2.3±0.8		2	1-4	0.064
Wexner score		1.3±2.0		0	0-7	0.8±1.7		0	0-7	0.112
	0	28	56%			36	72%			
	1-3	16	32%			10	20%			
	4-5	2	4%			2	4%			
	> 6	4	8%			2	4%			
RP		53.1±20.7		52	23-95	53.8±12.5		52	33-77	0.912
MCP		163.8±46.6		167	91-268	211.5±44.5		212	125-290	**<0.001**
Time		48.6±30.8		46	10-147	82.0±39.7		68	43-194	**<0.001**
ACP		103.0±29.9		112	40-144	138.6±37.4		141	76-212	**<0.001**
Gradient		33.4±40.1		15	1-153	51.3±52.2		30	3-224	**0.003**
Defect	No	30	60%			48	96%			**<0.001**
	Yes	20	40%			2	4%			
	Defect location									
	IAS	2	4%			2	4%			
	EAS	12	24%			0	0%			
	IAS + EAS	6	12%			0	0%			

RP: Resting pressure, MCP: Maximum contraction pressure, ACP: Average contraction pressure, SD: Standard deviation, Min: Minimum, Max: Maximum, Med: Median, IAS: Internal anal sphincter, EAS: External anal sphincter, Mann-Whitney U test, chi-square test was used

existence and type of episiotomy, and birthweight were regarded as similar to those of the co-control groups. The premenopausal and postmenopausal anorectal manometric measurement data of women with vaginal deliveries were worse than women with c-sections (Table 6). During the course of our study, we observed that anal sphincter functions in post-vaginal delivery life were negatively affected regardless of the existence of FI symptoms. Furthermore, we ascertained that c-section had a protective effect both on OASIS and anal sphincter functions. Similarly, Hannah et al.[15] also reported that c-section proved to be protective for postpartum FI symptoms.

When we compared the results of the premenopausal groups, we saw that 20 (40%) among the patients with vaginal delivery had occult anal sphincter injuries. When patients with vaginal deliveries were compared with the control group, there was no difference between FI symptoms and Wexner incontinence scores, although the former's mean maximum extrusion pressure was lower (p>0.05). Studies in literature have reported that as EAUSG went into effect in medical practice, the rate of sphincter injuries reached 35% in primiparous women and 40% in multiparous women[16]. Moreover, FI symptoms in these patients were observed less than sphincter injuries (13% and 23%, respectively)[17]. Thus, some sphincter injuries formed during vaginal delivery do not result in FI. It is highly likely that remnant sphincter tissue is exposed to hypertrophy and enables the continuation of continence by increasing the amount of collagen in spite of the sphincter injury.

When the postmenopausal groups were compared, 44%(22) of the vaginal delivery group had sphincter injuries. When the vaginal delivery group was compared with the control group, however, it was ascertained that the former had both worse manometric measurement results and significantly higher WIS (p=0.03; Table 5). Based on these data, it can be suggested that anal sphincter injuries that formed after vaginal delivery in the premenopausal stage remained occult but they proved to be a factor, which give way to an increase in FI symptoms in the postmenopausal stage. In contradiction to our results, Mous et al.[18] stated that the increase in FIs in the postmenopausal stage was related to postmenopausal disorders seen in the pelvic floor rather than sphincter injuries formed during vaginal delivery. With increasing age, and especially during the postmenopausal stage when estrogen in the body decreases, type 1 collagen tissue, which has thicker and stronger fibers, is replaced by type 3 collagen tissue, which has thinner, weaker, and isolated fibers. Moreover, IAS sclerosis develops with increasing age and atrophic changes take place in

Table 5. The comparison of demographic data, endoanal ultrasonography, and manometric measurement results of groups 2 and 4

		Group 2				Group 4				p
		Mean ± SD	n (%)	Med	(Min - Max)	Mean ± SD	n (%)	Med	(Min - Max)	
Age		55.3±5.6		54	48-71	55.7±5.5		56	41-64	0.287
Delivery number		4.2±2.0		4	1-11	2.2±0.8		2	1-4	**<0.001**
Wexner score		1.8±2.6		0	0-7	0.4±1.0		0	0-3	**0.003**
	0	28				40	80%			
	1-3	10				10	20%			
	4-5	4				0	0%			
	>6	8				0	0%			
RP		49.2±16.4		45	22-77	53.6±11.1		52	36-83	0.140
MCP		137.0±43.0		131	57-221	186.4±45.2		175	117-265	**<0.001**
Time		36.1±20.8		34	5-76	73.5±26.2		72	38-148	**<0.001**
ACP		91.5±29.0		96	25-153	144.8±39.8		132	81-217	**<0.001**
Gradient		68.8±138.2		28	2-691	42.5±33.0		42	5-112	0.348
Defect	No	28	56%			48	96%			**<0.001**
	Yes	22	44%			2	4%			
	Defect location									
	IAS	4	8%			2	4%			
	EAS	12	24%			0	0%			
	IAS + EAS	6	12%			0	0%			

RP: Resting pressure, MCP: Maximum contraction pressure, ACP: Average contraction pressure, SD: Standard deviation, Min: Minimum, Max: Maximum, Med: Median, IAS: Internal anal sphincter, EAS: External anal sphincter, Mann-Whitney U test, chi-square test was used

the EAS and pelvic floor muscles with the decrease in estrogen as menopause begins[19]. Furthermore, vaginal deliveries cause the pelvic diaphragm to move downward and give way to weakness in the pelvic floor[20]. When all these mechanisms are taken into consideration, it is clear that bodily changes in the postmenopausal stage increase FI. The results of our study revealed that patients with vaginal deliveries had worse results in all anorectal manometric measurements and higher WIS compared with those in the co-control groups when we compared the results of postmenopausal patients with vaginal deliveries and c-sections. Therefore, we believe that occult anal sphincter injuries become symptomatic with pelvic floor disorders formed in the postmenopausal stage, and they bring about a further increase in the incidence of FI. Our results are in parallel with former studies; however, two previous studies that compared more than 15-year follow-up results of patients with FI with or without anal sphincter injury reported contradictory results[21,22]. Nygaard et al.[21] found no significant difference pertaining to FI between women with c-section delivery and those who had OASIS during normal delivery, and Faltin et al.[22] conducted a study with similar groups and the authors reported that OASIS had little contribution to FI. The results of our study revealed that women with vaginal deliveries had a higher rate of anal sphincter injury and had higher WIS and FI symptoms in the postmenopausal stage compared with women with c-section deliveries in the same stage. Previous studies in the literature stated that FI symptoms increased depending on many factors in the postmenopausal stage[20]. The results of our study demonstrated that occult sphincter injury proved to be a significant factor that exacerbated these symptoms.

Study Limitations

One of the limitations of our study is that we did not conduct research on pudendal nerve damage. There is, however, controversy over the effect of pudendal nerve damage formed during vaginal delivery on FI formation[23]. In a study by Sultan et al.[6] the authors found that 16% of primiparous women and 15% of multiparous women had long-term pudendal nerve terminal motor latency (PNTML) 6 weeks after vaginal delivery, but there was no relationship between PNTML change and the development of FI symptoms. Further, abnormal PNTML prolongation had a statistically significant relationship with anal sphincter injuries. The results of another study showed that only one third of prolonged PNTMLs 6 months after delivery

Table 6. Comparison of vaginal delivery groups' demographic, endoanal ultrasonography, and anorectal manometric data according to menopausal status

		Group 1				Group 2				p
		Mean ± SD	n (%)	Med	(Min - Max)	Mean ± SD	n (%)	Med	(Min - Max)	
Age		38.0±6.2		38	21-48	55.3±5.6		54	48-71	**<0.001**
Delivery number		2.8±1.4		3	1-6	4.2±2.0		4	1-11	**<0.001**
Wexner score		1.3±2.0		0	0-7	1.8±2.6		0	0-7	0.584
	0	28	56%			28	56%			
	1-3	16	32%			10	20%			
	4-5	2	4%			4	8%			
	> 6	4	8%			8	16%			
RP		53.1±20.7		52	23-95	49.2±16.4		45	22-77	0.327
MCP		163.8±46.6		167	91-268	137.0±43.0		131	57-221	**0.004**
Time		48.6±30.8		46	10-147	36.1±20.8		34	5-76	**0.037**
ACP		103.0±29.9		112	40-144	91.5±29.0		96	25-153	**0.025**
Gradient		334±40.1		15	1-153	68.8±138.2		28	2-691	0.181
Defect	No	30	60%			28	56%			0.685
	Yes	20	40%			22	44%			
	Defect localization									
	IAS	2	4%			4	8%			
	EAS	12	24%			12	24%			
	IAS + EAS	6	12%			6	12%			

RP: Resting pressure, MCP: Maximum contraction pressure, ACP: Average contraction pressure, SD: Standard deviation, Min: Minimum, Max: Maximum, Med: Median, IAS: Internal anal sphincter, EAS: External anal sphincter, Mann-Whitney U test, chi-square test was used

remained pathological[24]. Thus, we neglected to investigate the effects of pudendal nerve damage on FI in our study.

The other limitation of our study is that the participants in the pre- and postmenopausal groups were composed of different individuals. Pre- and postmenopausal data of participants in the same group could have rendered this study more significant. Instead, we selected participants with FI predisposing factors such as age, number of deliveries, BMI, birthweight, and instrument use to ensure similarity between the groups. This method of selection, in turn, contributed to the reliability of our study.

Conclusion

Vaginal deliveries prove to be one of the most significant causes that increase the rate of anal sphincter injuries. Anal sphincter injury formed subsequent to vaginal delivery can be an important factor which gives way to an increase in the incidence of postmenopausal FIs and the formation of FI symptoms in women.

Ethics

Ethics Committee Approval: The study was approved by the Necmettin Erbakan University, Meram Faculty of Medicine Local Ethics Committee (Approval number: 2013/79), Informed Consent: Consent form was filled out by all participants.
Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.K., S.Ç., A.K., Concept: S.K., H.A., C.K., Design: S.K., M.Ç., Data Collection or Processing: S.K., S.Ç., A.K., Analysis or Interpretation: C.K., Literature Search: A.K., S.Ç., Writing: S.K.
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Management of vesicovaginal fistulas after gynecologic surgery

Jinekolojik cerrahi sonrası oluşan vezikovajinal fistüllerin yönetimi

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Abstract

Objective: In developed nations, surgery, especially gynecologic procedures, is the major cause of vesicovaginal fistulas (VVFs). We retrospectively evaluated our treatment modalities for VVF repair caused by a gynecologic surgery, and discussed the reasons of selecting certain surgical techniques and their outcomes.

Materials and Methods: We compared the surgical procedure preferences of surgeons and their results with patient and surgeon characteristics for the management of VVFs after an inciting gynecologic surgery in Süleyman Demirel University Hospital, Isparta over a 10-year period. The surgical procedures were undertaken in departments of urology and obstetrics and gynecology.

Results: Abdominal repair was chosen for 65%, vaginal repair for 25%, and laparoscopic repair for 10% of patients. For the 75% of the patients that urologists operated, they chose the abdominal route. The mean parity number of patients who underwent abdominal repair was lower than that for vaginal repairs ($p<0.05$). For the patients managed with the vaginal route, 20% had a Martius flap, and 80% had a simple excision and repair. For patients operated via the abdominal route, 18% needed omental flap; no tissue interposition was used for the rest. The mean hospitalization time was less in patients managed with transvaginal repair (3.4 days) compared with transabdominal repair (9.2 days) ($p<0.05$).

Conclusion: The choice of repair method depends on surgeon's training (gynecology vs. urology). The vaginal route should be the first choice because it does not compromise the success rate and the mean hospitalization time is less. For the transvaginal approach, access to the lesion is the most important factor for the success of the procedure. No flap is needed for tissues that appear well vascularized.

Keywords: Vesicovaginal fistula, gynecologic surgery, transvaginal fistula repair, abdominal fistula repair

Öz

Amaç: Gelişmiş ülkelerde, cerrahi ve özellikle jinekolojik prosedürler vezikovajinal fistüllerin (VVF) başlıca nedenidir. Bu yazıda, jinekolojik cerrahi sonrası oluşan VVF'lerin onarımı için üniversitemizde uygulanan tedavi yöntemlerinin neden seçildikleri değerlendirilmiş ve sonuçları tartışılmıştır.

Gereç ve Yöntemler: Süleyman Demirel Üniversitesi Hastanesi, Isparta'da son 10 yılda jinekolojik cerrahi sonrası oluşan VVF'lerin cerrahi olarak yönetimi üroloji ve kadın hastalıkları ve doğum bölümleri tarafından yapılmıştır. Onarım için kullanılan cerrahi yaklaşım tercihleri ve onarım sonuçları, hasta ve cerrah özellikleri göz önünde bulundurularak karşılaştırılmıştır.

Bulgular: Abdominal onarım hastaların %65'inde, vajinal onarım %25'inde ve laparoskopik onarım %10'unda kullanılmıştır. Ürologlar hastaların %75'inde abdominal yolu seçmiştir. Hastaların ortalama parite sayısı abdominal onarım tercih edilenlerde vajinal onarım yapılanlara göre daha düşük olduğu görülmüştür ($p<0,05$). Vajinal yoldan yönetilen hastaların %20'sinde Martius flebi kullanılmış ve %80'inde basit eksizyon ve onarım yeterli olmuştur. Abdominal yolla ameliyat edilen hastalarda, %18 omental flep kullanmış olup, geri kalan hastalarda doku interpozisyonu için flep kullanılmamıştır. Ortalama yatış süresi transabdominal onarım (9,2 gün) ile karşılaştırıldığında transvajinal onarım grubunda (3,4 gün) daha azdır ($p<0,05$).

Sonuç: Tamir yöntemi tercihi cerrahın aldığı eğitime (üroloji ya da jinekoloji) bağlıdır. Başarı olarak abdominal yoldan farkı bulunmayan ve ortalama hastanede kalış süresi daha az olan vajinal yol tamir için ilk seçenek olmalıdır. Transvajinal yaklaşım için lezyona erişim kolaylığı, cerrahinin başarısı için en önemli faktördür. Vaskülarizasyonu iyi görünen dokular için flep kullanımı gerekli değildir.

Anahtar Kelimeler: Vezikovajinal fistül, jinekolojik cerrahi, transvajinal fistül onarımı, abdominal fistül onarımı

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Introduction

Genitourinary fistulas represent significant morbidity, especially in developing nations where obstetric trauma is the major etiologic cause. The true incidence is unknown, and lack of seeking care is a major contribution for this uncertainty[1]. Vesicovaginal fistulas (VVFs) are the most commonly acquired fistulae of the urinary tract. In developed nations, surgery, especially gynecologic procedures, is the major cause[2-4]. The most common symptom in patients with VVF is constant urine leakage from the vagina. Predisposing factors such as chronic illnesses, previous surgery, chemotherapy, infections for postoperative fistulae are blamed, but the majority occur without any of these factors[5].

Diagnosis of genitourinary fistula requires a thorough medical history and careful physical examination. Timing for presentation of symptoms may differ due to the cause and location of the fistula. Most present with leakage of urine from the vagina, immediately following injury. However, fistulae resulting from hysterectomy or cesarean delivery often present later than one or two weeks from the inciting surgery. Radiation-induced fistulas generally occur years after treatment.

The diagnosis can be established based on symptoms and physical examination alone (methylene blue is frequently utilized) or using imaging techniques such as cystoscopy, magnetic resonance imaging, computerized tomography (Figure 1) or ultrasound. Cystoscopy may clarify the exact anatomic origin and it is used frequently.

The type of surgical technique chosen (transvesical, transvaginal, laparoscopic or robotic), depends on surgeon experience, whether the fistula is simple or complex, and patient characteristics. Complex or high fistulas are better treated abdominally with meticulous dissection, and simple ones can be treated easily vaginally by simple excision of the devascularized tissue and multi-layer approximation of healthy tissues. Vaginal operations can be performed according to the Latzko technique as denuding vaginal epithelium and tension free re-suturing, without excision of the entire fistula tract.

In this study, we retrospectively evaluated our treatment modalities for primary VVF repair after a gynecologic surgery, and discussed the feasibility and outcomes of the surgical techniques used in our institution over a 10-year period. The aim of this single-center study was to contribute evidence to the Turkish literature by describing the surgical management of VVF treatment in one university hospital in Turkey. This may aid physicians in the selection of appropriate surgery for their patients.

Materials and Methods

Patient selection

Between 2006 and 2015, a total of 20 patients were admitted to Süleyman Demirel University Hospital, Isparta, for VVF management after an inciting gynecologic surgery. Patient characteristics are outlined in Table 1. The Süleyman Demirel University Ethics Committee and Review Board approved the study (approval number: 01.06.2016/02). The study was performed in accordance with the ethical standards described in an appropriate version of the 1975 Declaration of Helsinki, as revised in 2000.

Methods

Surgical techniques

Transvaginal repair

After positioning the patient in low-lithotomy, we usually start with cystoscopy, especially if there is an uncertainty about involvement of the ureters. A Foley catheter is routinely placed to mark the fistula tract. A cystoscopic identification of the tract is made and ureteral catheterization is performed if the ureteric orifices show close proximity to the fistula.

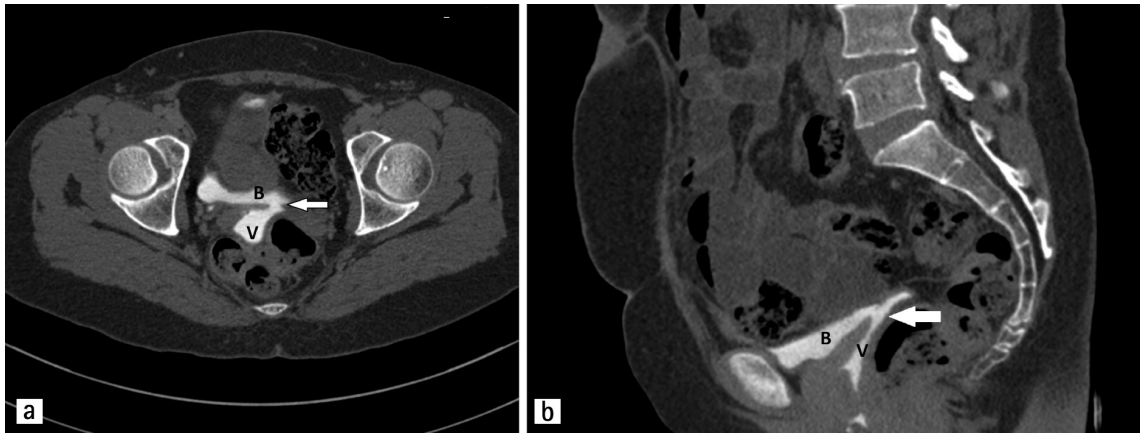

Figure 1. Computerized tomography urogram of a patient who underwent laparoscopic fistula repair in the delayed phase. Arrows indicate the fistula tract a) Axial image b) Sagittal image

B: Bladder, V: Vagina

For transvaginal repair, we prefer excision of the fistula tract and multi-layer closure with or without a Martius flap or fat pad. The excision is accomplished by taking margins with healthy tissue, approximately 1-1.5 cm in diameter. After excising the fistulous tract, the first layer sutured is the bladder mucosa, followed by the detrusor and/or prevesical or endopelvic fascia, and the third or fourth layer incorporates vaginal epithelium. Before the repair of the vaginal epithelium, a leak test is performed using diluted methylene blue. The vaginal epithelium is sutured in a perpendicular fashion with 2-0 Vicryl. For inner layers, 3-0 Vicryl is preferred. A Martius flap is used especially for larger or devascularized tissues managed with the vaginal route. The Martius flap procedure involves the use of a 2-cm wide fat pad dissected along the labium majus and tunneled as a vascular barrier under the vagina in the location of the excised fistula.

Transabdominal repair

For the abdominal approach, after a Pfannenstiel or midline incision and exploration of the pelvis, a cystotomy is made on the dome of the bladder, and if the fistula opening is located near the ureteral orifices, ureteral stents are placed. The fistulous tract is marked by placing a 14-F Foley catheter. The fistulous tract is excised with the catheter inside. An omental or peritoneal flap is attached between the vaginal wall and bladder if necessary. The vagina is closed with 2-0 Vicryl, and the bladder is closed in 2 layers using 3-0 Vicryl.

Laparoscopic repair

Laparoscopic surgery is performed in our institution using one umbilical port for the camera, one suprapubic 10-mm port, and two 5-mm ports bilaterally located medial to the anterior superior iliac spines. We use a 30-degree angled camera for the repair. The vesicovaginal plane is dissected until reaching the fistula tract without making a prior cystotomy. The tract is totally excised and the vagina and bladder are separately sutured using 3-0 Vicryl. A leak test is performed using diluted methylene blue.

Urinary diversion

Urinary diversion is achieved as a part of the pelvic exenteration procedure. The ileal conduit technique is chosen for these patients. A 15-cm ileal segment is isolated using GIA staplers, and a side-to-side anastomosis is performed for the remaining bowel segments using GIA staplers. The left ureter is passed under a tunnel created in the mesentery of the sigmoid colon. A Wallace type 1 anastomosis is performed, as conjoining the distal ends of the ureters together we perform the anastomosis to the proximal end of the ileal segment. Using a Foley catheter to drain the conduit, feeding tubes are passed into each ureter and secured to the distal end of the ileal loop, and a Foley catheter is used to drain the conduit. The stoma is matured to the right side of the patient between the umbilicus and the superior anterior iliac spine.

Statistical Analysis

Statistical analysis of the data was performed using SPSS 15.0 (SPSS Inc. Chicago, IL, USA) and $p<0.05$ was determined as significant. Non-parametric data were compared using Mann-Whitney U test and Pearson's chi-square test.

The effect of age on the preference of the surgical route was calculated using the Mann-Whitney U test.

Results

Abdominal repair was chosen for 11 (55%) patients, vaginal repair for 5 (25%), laparoscopic repair for 2 (10%), and 2 patients underwent ileal conduit urinary diversion (10%). Patient characteristics for each repair type are shown in Table 2. Of the surgeries performed by urologists, 75% were via the abdominal route and 8.3% were vaginal. Laparoscopic repairs were only performed by urologists. All patients treated by gynecologists were operated using the transvaginal route. It is clear that urologists preferred the abdominal or laparoscopic route, whereas gynecologists preferred the vaginal route, and this difference was statistically significant ($p<0.05$). Eighty percent of operations performed both by gynecologists and urologists were performed abdominally.

The most common single symptom was urinary incontinence (80%), followed by constant leakage of urine through the vagina (20%). Cystoscopy was performed for 85% of the patients for confirmation of the diagnosis and to evaluate the exact location of the fistula, and physical examination only sufficed for 15% of the patients.

For patients managed through the vaginal route, 20% were treated with a Martius flap, and 80% with a simple excision and repair. For patients operated via the abdominal route, 18% needed an omental flap; no tissue interposition was used for the remainder. Ureteral catheterization was performed for 5 patients, all of whom were managed via the transabdominal route. Their fistulas had proximity to ureteral orifices, 3 needed bilateral catheterization, and two needed unilateral catheterization (Table 2).

Two VVFs with obstetric etiologies were managed using abdominal excision and repair. The first patient was nulliparous and she had preterm labor at 35 weeks. The second patient had 3 prior vaginal births and had an obstructed labor due to macrosomia. A cesarean section was performed for both obstructed labors and fistulas developed thereafter.

For the patients with malignancies, both had prior history of radiotherapy. The first patient had recurrent endometrial cancer and the other had a cervical cancer and had undergone primary radiotherapy. Both had central recurrence with vesicovaginal fistulas with no evidence of extra-pelvic metastasis. Ileal conduits were performed for both patients as part of a total pelvic exenteration procedure. An infra-levator pelvic exenteration was performed for the patient with cervical cancer, whereas a supralevator procedure sufficed for the patient with endometrial cancer.

Table 1. Patients' characteristics

Case number	Age	Parity number	Surgical treatment	Flap used	Previous surgery	Co-morbidities	Hospitalization time (days)	Recurrence/ follow up (months)
1	51	2	First attempted vaginally to close tract, but due to high location and narrow vaginal orifice, abdominal vesicovaginal fistula repair is done. Bilateral double-J stent inserted	None	TAH + BSO + Burch colposuspension	Hypothyroidism	29	No/10
2	56	2	Abdominal vesicovaginal fistula repair	None	TAH + BSO	Hypertension	15	No/5
3	50	2	Abdominal vesicovaginal fistula repair	None	TAH + BSO	Mitral valve replacement	8	No/6
4	47	3	Vaginal vesicovaginal fistula repair	None	TAH + BSO	None	2	No/2
5	47	2	Abdominal vesicovaginal fistula repair	Omental flap	TAH + BSO	None	8	No/16
6	50	1	Abdominal vesicovaginal fistula repair	Omental flap	TAH + BSO	Diabetes	4	No/12
7	44	2	Abdominal vesicovaginal fistula repair	None	TAH + BSO	Hypertension, diabetes, hypothyroidism	4	No/5
8	42	3	Laparoscopic vesicovaginal fistula repair	None	TAH	None	4	No/6
9	48	3	Abdominal vesicovaginal fistula repair	None	TAH + BSO	None	2	No/4
10	45	1	Abdominal vesicovaginal fistula repair	None	TAH	None	4	No/12
11	47	1	Laparoscopic vesicovaginal fistula repair (recurrence occurred, treated via abdominal way)	None	TAH + BSO	None	5	Yes/13[1]
12	84	4	Vaginal vesicovaginal fistula repair	None	TAH + BSO	None	6	No/9
13	49	3	Abdominal vesicovaginal fistula repair. Bilateral double-J stent inserted	None	Tension-free vaginal tape	None	22	No/18
14	55	2	Supra-levator pelvic exenteratio +- urinary diversion	None	Previous hysterectomy and radiotherapy for endometrial cancer	Hypertension	23	No/16
15	43	3	Infra-levator pelvic exenteration + urinary diversion	None	Radiotherapy for cervical cancer	None	9	No/9
16	44	5	Vaginal vesicovaginal fistula repair	Martius flap	TAH + BSO	Diabetes	5	No/10
17	27	1	Abdominal vesicovaginal fistula repair	None	C/S	None	10	No/6
18	26	2	Abdominal vesicovaginal fistula repair	None	C/S	None	4	No/8
19	47	3	Vaginal vesicovaginal fistula repair	None	TAH + BSO	None	4	No/10
20	55	4	Vaginal vesicovaginal fistula repair	None	TAH + BSO	Hypertension, diabetes	7	No/5

[1]The recurrence occurred after 4 weeks from laparoscopic surgery, managed abdominally. No recurrence thereafter, TAH: Total abdominal hysterectomy, BSO: Bilateral salpingo-oophorectomy, C/S: Cesarean section

Excluding the patients with malignancies who underwent ileal conduit procedures, the mean hospitalization time was less in patients managed with transvaginal repair group (3.4 days) compared with transabdominal repair (7.9 days), and the difference was statistically significant ($p<0.05$). We expected a tendency of more older patients to have undergone surgery through the vaginal route, but we found no difference between the groups, even when we classified the groups by age as 25-45 years, 46-55 years, and >55 years ($p>0.05$). The mean parity number of the patients who underwent abdominal repair was 1.9, for vaginal repairs 3.8, and for laparoscopic repairs 2 ($p<0.05$).

One case was started vaginally and converted to laparotomy, after excision of the fistulous tract. For this patient, the multi-layer closure of tissues was impossible through the vaginal route due to the high location of the fistula. The patient had a recent history of a concomitant abdominal hysterectomy for myoma uteri and Burch colposuspension procedure for urinary incontinence.

One patient developed stress urinary incontinence after the repair. The patient was initially managed via the abdominal route. She was offered various treatment modalities including sub-urethral slings and bulking agents, but she refused treatment.

The only recurrence was noted in a patient who had undergone laparoscopic surgery. A transabdominal repair was successfully performed 4 weeks after the first surgery. No flap was used due to the well-vascularized appearance of the tissues. The etiology of the fistula was abdominal hysterectomy for myoma uteri, which performed 6 weeks earlier than the first repair attempt. No recurrence occurred during her 1-year follow-up.

Discussion

In this retrospective study, we evaluated only the surgical approach for the management of VVFs; therefore, patients who were conservatively treated were out of the scope of this study. There are controversies as to whether the treatment should be conservative or surgical. In the minority of cases, the fistula may close spontaneously after 2-4 weeks of urethral catheterization, especially if the fistula is detected early (no epithelization on the fistula tract) and the diameter is small[6]. Timing of the repair is also important. When identified before 72 hours after iatrogenic cystotomy, VVF can be repaired immediately. If the diagnosis of a small fistula is established late and the fistula is epithelized,

Table 2. Vesicovaginal fistula characteristics stratified by repair type

	Abdominal n (%)	Vaginal n (%)	Laparoscopic n (%)
Presenting symptoms (some patients had multiple symptoms)			
• Urinary incontinence	11	4	2
• Continuous urinary leakage	1	2	1
• Hydronephrosis	1	0	0
• Frequent urinary infection	1	0	0
Hormonal status			
• Premenopausal	9	4	2
• Postmenopausal	3	2	0
Comorbid conditions			
• DM	1	1	0
• HT	2	0	0
• Hypothyroidism	1	1	0
• DM + HT	0	0	1
Age (years)			
• 25-45	4	1	1
• 46-55	8	3	1
• >55	1	1	0
Previous inciting condition			
• TAH +/- BSO	7	4	2
• TAH + BSO + Burch colposuspension	2	0	0
• TVT	0	1	0
• C/S	2	0	0
• RT	2	0	0
Total	13	5	2

DM: Diabetes mellitus, HT: Hypertension, TAH: Total abdominal hysterectomy, BSO: Bilateral salpingo-oophorectomy, TVT: Transvaginal tape, C/S: Cesarean section, RT: Radiation therapy

electrocoagulation of the mucosal layer and catheterization may lead to closure in up to 75% of cases[7].

In a recent report from Turkey, outcomes of 53 cases with VVFs were discussed and none of the fistula closed with conservative management[8]. The use of fibrin sealants for closure of small fistulae has also been reported[9,10]. Fibrin glue has also been successfully used instead of Martius flap in cases when tissue interposition was needed[11]. However, in our clinic, we do not have such experience. As reported in the study of 52 cases by Kapoor et al.[12], the mean blood loss and postoperative pain may be less, and the mean hospital stay may be shorter for transvaginal repair compared with transabdominal repair, especially in non-complicated cases.

For vaginal approach, our clinic prefers simple excision and repair, and the long-term success of this approach seems excellent, because none of the fistula recurred. In the literature, the success of transvaginal repair ranges from 70% to 100%[13-15]. A large prospective cohort study from Africa that compared 1273 abdominal and vaginal genitourinary fistula repairs found that vaginal route repairs were associated with increased risk of failure in closing the fistula compared with the abdominal route. However, the follow-up was 84 to 99 days, nearly 20% of the patients had a degree of genital mutilation; there was extensive scarring in 7.7% of patients operated via vaginal route versus 3.5% of patients operated via the abdominal route, only 3.69% of the patients underwent abdominal surgery, and finally the population comprised VVFs and all types of genitourinary fistulas[16].

Martius flap is used only for 20% of patients, and is chosen for tissues that appear as devascularized. The success of this technique seems more than 90%[2]. The vaginal approach may also be possible for supra-trigonal fistulas, depending on the experience of the surgeon[17].

The abdominal route should be considered for larger, more complex or recurrent fistulas. Large fistulas (>2 cm) and those close to ureteric orifices may be considered as "complicated" or "complex" and there is no consensus as to which fistulas are considered as complicated. The success abdominal repair ranges between 90-100%[14]. Despite the proven long-term results of the vaginal approach for VVFs, there is a tendency in our clinic to perform abdominal repairs, especially for cases that urologists perform. However, that difference may be according to a selection bias; urologists generally deal with more complicated cases. Both patients who received prior radiotherapy underwent surgery with urologists and gynecologists together, and the laparoscopic failure of closure was performed by the urologists. The mean number of births was higher in transvaginal repair group compared with the transabdominal group, and this may be one of the factors for surgeons to consider when choosing either route.

The laparoscopic approach, as an alternative, results in less morbidity and recovery is faster than the transabdominal route. The success of this approach is comparable with open procedures[18]. However, it requires advanced skills such as suturing in non-ergonomic angles.

There are no randomized controlled studies to evaluate whether abdominal, laparoscopic or vaginal approach is superior. We found that the mean hospitalization time was less for vaginal repairs, and avoiding a laparotomy may also reduce the rate of complications, although we did not encounter any. It would be appropriate to repeat classic teaching that if the fistula is large, complex, ureteral involvement is suspected, an abdominal approach may be preferred over a vaginal approach.

No de-novo stress urinary incontinence was reported in the vaginal or laparoscopically managed groups, but there was one in the trans-abdominally managed group. After excluding patients with urinary diversion, the rate was 11%. After fistula surgery, most residual incontinence is thought to be stress urinary incontinence[19]. Nevertheless, there are some data in favor of detrusor instability as a major contributing factor. A report from the United Kingdom mentioned a post-repair stress urinary incontinence rate of about 11%, whereas detrusor instability was documented as 50% in this population[15]. In another report, it was indicated that both stress and urge symptoms occurred in similar numbers in patients after a repaired fistula[20]. A report from Australia indicated a 23.9% rate of urinary incontinence after repair. In developing countries where obstetric fistulas are major contributors, this rate seems much higher[21,22]. A series of 318 consecutive patients from Addis Ababa, where the main inciting factor was obstetric trauma for the fistula, reported an immediate post-operative incontinence rate of 33%[14]. Bladder neck involvement and proximal urethral contribution to fistula can be considered as risk factors for post-closure incontinence[23].

In the current study, abdominal hysterectomies alone contributed to 65% of the fistulas and hysterectomy with Burch colposuspensions caused 10% of the fistulas. These rates are closer to the rates of developed nations as gynecologic surgeries, mainly abdominal hysterectomies, rather than obstetric traumas, are causes of the fistulas[4,12,24]. The effect of colposuspension as a contributing factor could not be analyzed because of concomitant hysterectomies. It is crucial to meticulously dissect the bladder from the cervix and proximal vagina, suturing only vagina without incorporating the detrusor fibers and avoiding excessive use of electrocautery while working in close proximity to the bladder, because usually no cystostomy or urinary tract injury is encountered during hysterectomies causing fistulas.

The incidence of fistulas caused by radiotherapy for malignant conditions such as cervical cancer and endometrial cancer is about 5%[25]. For these circumstances, urinary diversion may be chosen. Simple repair is generally not suitable for these patients because of fibrosis, unhealthy tissue and distorted anatomy may not be amenable to re-approximation. If a repair is to be attempted, an intervening well-vascularized flap is strongly recommended. Successful fistula repair is reported as between 70 and 100% in non-irradiated patients, and between 40% and 100% for patients who had prior radiotherapy[14]. Urinary

diversions are much preferred for patients with cancer who have previously been irradiated. Both ileal conduits performed at our institution were as part of pelvic exenteration procedures for central recurrence of tumors.

Study Limitations

One of the major limitations of the study is that the number of the patients was small for each group to be compared; for example, there were only two cases managed laparoscopically among twenty patients. Also, the retrospective design of our study may be a drawback, but a prospective trial for management of vesicovaginal fistulas is hard due to its rarity. In our opinion, a multi-center trial design is more appropriate for prospective trials related with this problem.

Conclusion

Nearly all VVFs in this series resolved with primary surgery, regardless of the approach. No flap is needed for tissues that appear well vascularized. The mean hospitalization time is less in patients managed with transvaginal repair compared with transabdominal repair, and this difference emphasizes the vaginal route as the first choice without compromising the success rate.

Ethics

Ethics Committee Approval: The study was approved by the Süleyman Demirel University Local Ethics Committee (Approval number: 01.06.2016/02), Informed Consent: Consent form was filled out by all participants.
Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.O., S.S., E.E., Concept: E.E., B.T., Design: F.S.C., B.T., Data Collection or Processing: F.S.C., B.T., Analysis or Interpretation: B.T., Literature Search: B.T., Writing: B.T.
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Prognostic risk factors for lymph node involvement in patients with endometrial cancer

Endometrium kanseri hastalarında lenf nodu tutulumu için prognostik risk faktörleri

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Abstract

Objective: We aimed to analyze variables affecting lymph node (LN) involvement and to assess the need for systematic lymphadenectomy in patients with endometrial cancer (EC).

Materials and Methods: A single centre retrospective analysis was conducted in a total of 128 consecutive patients with EC who underwent systematic pelvic or combined pelvic and paraaortic lymphadenectomy between 2009 and 2012. Mann-Whitney U, chi-square, and Fisher's exact test were used for univariate analyses when appropriate. Variables with a p value <0.05 in the univariate analysis were included into a multivariate logistic regression analysis. The effects of variables on LN involvement are reported using adjusted odds ratios (ORs) and 95% confidence intervals (CI).

Results: In univariate analysis, grade 2-3, tumor size ≥3 cm, deep (≥50%) myometrial invasion, presence of cervical, adnexal or omental involvement, positive peritoneal cytology, open surgical approach (laparotomy), combined pelvic and paraaortic lymphadenectomy and number of total LNs removed (>30) were found associated with LN involvement. However, the number of total LNs removed (>30) was the only independent variable that predict LN involvement in multivariate analysis [OR: 15.08; 95% CI: (1.28-177.59); p=0.03].

Conclusion: This study demonstrates that the more LNs removed during staging of EC, the greater the probability of finding LN metastasis.

Keywords: Endometrium cancer, lymph node dissection, risk factors

Öz

Amaç: Endometrium kanseri olgularında lenf nodu (LN) tutulumunu etkileyen değişkenlerin analizi ve lenfadenektomi gereksiniminin değerlendirilmesidir.

Gereç ve Yöntemler: 2009 ve 2012 yılları arasında sistematik pelvik veya kombine pelvik ve paraaortik lenfadenektomi yapılan ardışık 128 endometrium kanseri olgusunu içeren tek merkezli bir retrospektif analiz yapıldı. Tek değişkenli analiz için Mann-Whitney U testi, ki-kare testi ve Fisher exact testi kullanıldı. Tek değişkenli analizde p değeri 0,05'ten küçük olan değişkenler çok değişkenli lojistik regresyon analizine dahil edildi. Değişkenlerin LN tutulumu üzerine olan etkileri göreceli olasılıklar oranları (OR) ve %95 güven aralığı (GA) ile belirtildi.

Bulgular: Tek değişkenli analizde, grade 2-3, tümör çapının 3 cm'den büyük olması, derin (>%50) miyometriyal invazyon, servikal, adneksal veya omental tutulumun olması, pozitif peritoneal sitoloji, açık cerrahi yaklaşım, kombine pelvik ve paraaortik lenfadenektomi ve toplam çıkarılan LN sayısı (>30) LN tutulumu ile ilişkili olarak bulundu. Ancak çok değişkenli analiz sonucunda sadece toplam çıkarılan LN sayısı (>30) LN tutulumunu öngördüren bağımsız bir değişken olarak kaldı [OR: 15,08; %95 GA: (1,28-177,59); p=0,03].

Sonuç: Bu çalışma endometrium kanserinin evrelenmesi esnasında ne kadar çok LN çıkartılırsa o kadar yüksek olasılıkla LN metastazının saptanabileceğini göstermektedir.

Anahtar Kelimeler: Endometrium kanseri, lenf nodu diseksiyonu, risk faktörleri

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Introduction

Endometrial cancer (EC) is the most common gynecologic malignancy in developed countries. Its age-adjusted incidence is increasing, probably due to increased life expectancy and obesity. However, the mortality rate has increased more rapidly than the incidence over the past three decades[1]. One explanation for this discrepancy is that patients are being diagnosed at an older age, which leads to an increased rate of high-risk histologies and advanced-stage cancers.

EC is staged surgically based on the International Federation of Gynecology and Obstetrics (FIGO) 2009 staging system[2]. Lymph node (LN) metastasis is one of the most important prognostic factors for EC[3]. Although a systematic lymphadenectomy is an essential part of staging surgery, FIGO did not define the optimal limits for lymphadenectomies, nor the adequate number of LNs required for the comprehensiveness of the procedure. On the other hand, it is well known that lymphadenectomy may be associated with increased complications, mainly including lymphedema, vascular, ureteral and visceral injuries, deep vein thrombosis, chylous ascites, and ileus[4].

In the current study, we aimed to analyze variables affecting LN involvement and to assess the need for systematic lymphadenectomy in patients with EC.

Materials and Methods

A single centre retrospective analysis was conducted in a total of 128 consecutive patients with EC who underwent systematic pelvic or combined pelvic and paraaortic lymphadenectomy between 2009 and 2012. Patients were excluded if they had primary synchronous malignancy or if they had no LN dissection. Clinicopathologic data including age, type of surgical procedure, tumor histotype, tumor size, grade, depth of myometrial invasion, lymphovascular space involvement (LVSI), cervical involvement, adnexal involvement, positive peritoneal cytology, number of LNs, and LN involvement were extracted from patient charts and the institutional database following approval of institutional review board of Akdeniz University. Written informed consent was not required for this type of retrospective study. This study has been approved by the Local Ethics Committee of the Akdeniz University (date and approval number: 2012/1205). The study was performed in accordance with the ethical standards described in an appropriate version of the 1975 Declaration of Helsinki, as revised in 2013.

As a routine policy of our institution, patients with newly diagnosed EC were offered treatment with total hysterectomy and bilateral salpingo-oophorectomy with systematic pelvic lymphadenectomy. Paraaortic LN dissection was added to pelvic LN dissection in patients with at least one of the following risk factors: a) non-endometrioid histology, b) grade 2 or 3 endometrioid adenocarcinoma, c) deep (≥50%) myometrial invasion on intraoperative frozen-section examination.

The primary endpoint of the study was determination of independent factors influencing LN metastasis. The Stata software package was used for statistical analyses (Special Edition v11.2 for Macintosh OSX, StataCorp, Texas, USA). Mann-Whitney U, chi-square, and Fisher's exact tests were used for univariate analyses when appropriate. Variables with a p value <0.05 in the univariate analysis were included into a multivariate logistic regression analysis. The effects of variables on LN involvement are reported using adjusted odds ratios (ORs) and 95% confidential intervals (95% CI).

Results

The mean age at surgery was 59.3±11.2 years and the majority of patients (86.7%) had open surgery. Sixty-six patients (51.6%) had pelvic lymphadenectomy alone, and 62 (48.4%) had combined pelvic and paraaortic lymphadenectomy. The median number of pelvic LNs removed, paraaortic LNs removed, and total LNs removed (both pelvic and paraaortic) were 24, 15, and 32, respectively. Most patients had endometrioid histology (75%). LN involvement was detected in 17.9% of the patients, deep myometrial invasion in 45.3%, LVSI in 25%, cervical involvement in 16.4%, adnexal involvement in 11.7%, omental involvement in 4.7%, and positive peritoneal cytology in 8.6% (Table 1).

In the univariate analysis, grade 2-3, tumor size, deep (≥50%) myometrial invasion, presence of cervical, adnexal or omental involvement, positive peritoneal cytology, surgical approach (laparotomy vs. laparoscopy), combined pelvic and paraaortic lymphadenectomy, and the total number of LNs removed were found associated with LN involvement (Table 2). A receiver operating characteristic analysis was performed to determine the tumor size that would be the most significant in predicting LN involvement (Figure 1). The cut-off value was found as 3 cm with an area under the curve of 0.626 [CI: (0.51-0.74); p=0.06].

However, in the multivariate analysis, the total number of LNs removed (>30) remained as the only independent variable

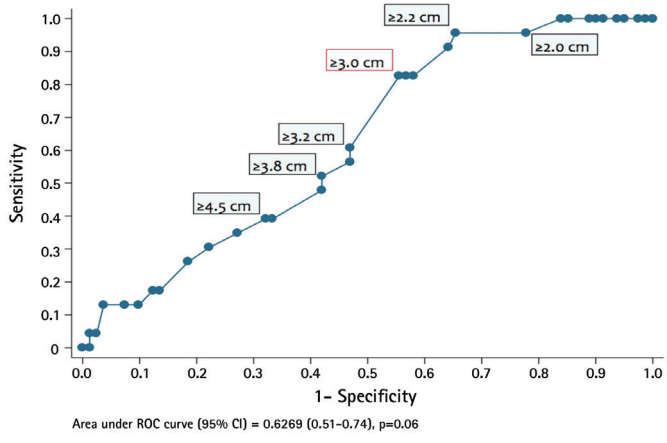

Figure 1. Receiver operating characteristic analysis for calculating cut-off value of tumor size in predicting lymph node metastasis

ROC: Receiver operating characteristic, CI: Confidential interval

that predicted LN involvement after adjustment for other confounders [OR: 15.08; 95% CI: (1.28-177.59); p=0.03] (Table 2).

Discussion

The current study examined factors influencing LN involvement in patients with EC. Our results identified the total number of

Table 1. Clinical and pathologic characteristics of patients

Variables	Values
Age, mean ± SD, years	59.3±11.2
Surgery, n (%)	
Laparoscopy	17 (13.3)
Laparotomy	111 (86.7)
Pelvic LN dissection alone	66 (51.6)
Combined pelvic and paraaortic LN dissection	62 (48.4)
Number of pelvic LNs removed, median (range)	24 (6-59)
Number of paraaortic LNs removed, median (range)	15 (1-37)
Number of total LNs removed (pelvic and/or paraaortic), median (range)	32 (9-81)
Histologic type, n (%)	
Endometrioid	96 (75.0)
Non-endometrioid	32 (25.0)
Serous	4 (3.1)
Clear cell	6 (4.7)
Mixed cell[a]	9 (7.0)
Carcinosarcoma	12 (9.4)
Undifferentiated	1 (0.8)
Grade, in patients with endometrioid histology, n (%)	
Grade 1	48 (50.0)
Grade 2	36 (37.5)
Grade 3	12 (12.5)
Tumor size, median (range), cm	3 (0.1-15)
Myometrial invasion	
<1/2	70 (54.6)
≥1/2	58 (45.3)
Lymphovascular invasion, n (%)	32 (25.0)
Cervical involvement, n (%)	21 (16.4)
Adnexal involvement, n (%)	15 (11.7)
Omental involvement, n (%)	6 (4.7)
Positive peritoneal cytology, n (%)	11 (8.6)
LN involvement (pelvic and/or paraaortic), n (%)	23 (17.9)
Pelvic LN involvement, n (%)	23 (17.9)
Paraaortic LN involvement, n (%)	20 (15.6)

[a]Endometrioid with clear cell, serous, mucinous and undifferentiated types, SD: Standard deviation, LN: Lymph node, CI: Confidential interval

Table 2. Univariate and multivariate logistic regression analysis of factors predicting lymph node metastasis

Variables		Univariate		Multivariate	
	n (%)	OR (95% CI)	p	OR (95% CI)	p
Age, years					
<60	8 (14.8)	1			
≥60	15 (25.4)	1.96 (0.76-5.08)	0.16	-	-
Histologic type					
Endometrioid	15 (17.9)	1			
Non-endometrioid	8 (27.6)	1.75 (0.65-4.70)	0.26	-	-
Grade (for endometrioid types)					
1	5 (9.3)	1			
2-3	11 (33.3)	4.90 (1.52-15.80)	0.005	1.04 (0.09-12.29)	0.92
Tumor size					
<3.0 cm	4 (10.0)	1			
≥3.0 cm	19 (29.7)	3.8 (1.19-12.17)	0.03	3.41 (1.43-9.75)	0.12
Myometrial invasion					
<1/2	2 (4.9)	1			
≥1/2	21 (33.9)	10.0 (2.19-45.45)	0.001	7.12 (0.63-195.56)	0.22
Lymphovascular invasion					
No	15 (16.7)	1			
Yes	8 (34.8)	2.67 (0.96-7.41)	0.05	-	-
Cervical involvement					
No	13 (14.0)	1			
Yes	10 (52.6)	6.84 (2.34-20.02)	0.001	3.42 (0.49-20.13)	0.15
Adnexal involvement					
No	17 (16.5)	1			
Yes	6 (66.7)	10.12 (2.30-44.46)	0.002	4.12 (0.38-32.47)	0.19
Omental involvement					
No	20 (18.4)	1			
Yes	3 (75.0)	13.35 (1.32-135.11)	0.03	6.24 (0.99-177.45)	0.17
Peritoneal cytology					
Negative	19 (18.1)	1			
Positive	4 (57.1)	6.04 (1.25-29.22)	0.03	2.64 (0.37-17.31)	0.09
Surgery					
Laparoscopy	0 (0/15)	1			
Laparotomy	23 (23.5)	N/A	0.05	-	-
Extent of LN dissection					
Pelvic alone	4 (7.8)	1			
Combined pelvic and paraaortic	19 (30.7)	5.19 (1.64-16.48)	0.004	2.25 (0.25-16.81)	0.08

Table 2. Continued

Variables		Univariate		Multivariate	
	n (%)	OR (95% CI)	p	OR (95% CI)	p
Number of pelvic LNs removed					
<25	11 (17.5)	1			
≥25	12 (24.0)	1.49 (0.60-3.74)	0.40	-	–
Number of paraaortic LNs removed					
<15	7 (23.3)	1			
≥15	14 (43.8)	2.47 (0.89-5.38)	0.09	-	–
Number of total LNs removed					
≤30	4 (7.7)	1			
>30	19 (31.2)	5.43 (1.71-17.23)	0.002	15.08 (1.28-177.59)	**0.03**

Boldface indicates statistical significance (p<0.05), OR: Odds ratio, CI: Confidential interval, LN: Lymph node, N/A: Not applied

LNs removed as the only independent predictor of LN metastasis; this finding emphasizes that as many LNs as possible should be removed irrespective of preoperative tumor characteristics in order to determine LN metastasis.

Defining the role and extent of lymphadenectomy is one of the main controversies in the management of patients with EC. Lymphadenectomy provides pathologic and prognostic data, determines the exact extent of disease, and need for adjuvant therapy. It may also have a potential therapeutic effect in patients, particularly with extrauterine disease[5-7].

Overall LN metastasis in patients with EC has been reported to range from <1% to 34%, according to tumor grade, histotype, and depth of myometrial invasion[3]. It is widely accepted that in a subset of patients (low-risk group) with low-grade endometrioid histotype, small tumor size (<2 cm) and no deep myoinvasion, lymphadenectomy may be omitted without a negative impact on prognosis[8]. This group of patients has a relatively small risk (1-3%) for lymphatic dissemination[3]. However, it is difficult to identify these low-risk patients preoperatively because of variability in tumor grade and depth of myoinvasion on final histopathology[9,10]. Therefore, the true risk may be greater than that estimated. Although two randomized controlled trials (RCTs) reported that lymphadenectomy did not improve the outcomes of patients, there are some critical issues with regard to these RCTs including adjuvant therapies, number of LNs removed, and extent of lymphadenectomies[11,12]. Radiotherapy was given to an equal number of patients in each treatment arm, which led to overtreatment of non-lymphadenectomy groups.

Sentinel LN biopsy can represent a compromise between no lymphadenectomy (leaving a small risk for LN metastasis) and full lymphadenectomy (adding a potentially morbid procedure for a significant part of the patients). It improves detection of LN metastases by allowing detection of micrometastases using ultrastaging (serial sectioning) of target LNs. In a multicenter study of 304 women with presumed low- or intermediate-risk disease, sentinel LN biopsy and ultrastaging detected metastatic LNs in three-fold greater than standard lymphadenectomy (16% vs. 5%)[13]. However, the implications and management of micrometastases or isolated tumor cells detected through ultrastaging are not yet clear. No prospective RCTs have compared outcomes of disease between patients who underwent sentinel LN biopsy and those who received systematic LND. In addition, risk of non-sentinel LN positivity (false negativity), which has been reported as approximately 5%, is a potential handicap for sentinel LN biopsy[14].

Today, systematic pelvic lymphadenectomy is still the safest way to detect LN metastasis in patients with EC who have low-risk features. It allows elimination of LN metastasis in approximately 99% of patients. Potentially missed cases are patients with isolated paraaortic LN metastasis[15]. Combined pelvic and paraaortic lymphadenectomy may be reserved for selected patients with high-risk features[16].

Study Limitations

As with all studies, the results of this study are not without limitations. Retrospective single center studies, such as the current one, are inherently susceptible to selection and referral bias. On the other hand, the main strengths of our study include the detailed analyses of various clinicopathologic factors that may have an impact on LN metastasis, and performance of uniform staging surgeries using a consistent surgical policy by subspecialized gynecologic oncologists.

Conclusion

In conclusion, the current study demonstrates that the more LNs removed during staging of EC, the greater the probability of finding LN metastasis. Following clarification of the most

appropriate adjuvant therapy regimens for sentinel LN biopsy procedures in pending trials, the role and therapeutic effect of lymphadenectomy may be assessed more effectively.

Ethics

Ethics Committee Approval: This study has been approved by the Local Ethics Committee of the Akdeniz University (Date and approval number: 2012/1205), Informed Consent: A written informed consent is not required for this type of retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.T., T.Ş., Ş.K., Concept: T.T., T.Ş., Design: T.T., T.Ş., Data Collection or Processing: T.T., Ş.K., Analysis or Interpretation: T.T., Literature Search: T.T., Writing: T.T., T.Ş.

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Clinical analyses of successful and previously failed intracytoplasmic sperm injection cycle parameters in patients with poor ovarian reserve

Düşük over rezervli olgularda başarılı ve başarısız siklusların klinik analizi

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Abstract

Objective: To determine some major characteristic differences between two consecutive successful and unsuccessful intracytoplasmic sperm injection (ICSI) cycles in poor responders.

Materials and Methods: Sixty women with poor ovarian response as determined using the Bologna criteria underwent ICSI cycles following an unsuccessful trial. Some parameters of both cycles including age, body mass index (BMI), serum follicle-stimulating hormone (FSH) and estradiol levels, antral follicle count, gonadotropin dosage, duration of stimulation, antagonist starting day, duration of antagonist administration, endometrial thickness at trigger day, number of total and fertilized oocytes, embryo transfer day, number of embryo cells, and fertilization rate were compared in the same patients to identify predictors of cycles with clinical pregnancy.

Results: The mean age, BMI, serum FSH, estradiol concentrations, and antral follicle count were 35.9 years (range, 30-42 years), 25.9 kg/m^2 (range, 18.4-33.5 kg/m^2), 10.9 IU/mL (range, 7-13 IU/mL), 52.9 pg/mL (range, 11.6-75 pg/mL), and 4.7 (range, 2-10), respectively. A comparison of cycle characteristics showed a significantly higher total number of mature and fertilized oocytes in successful cycles. The fertilization rate was also significantly higher in cycles with clinical pregnancy. Early initiation of antagonist was shown to result in favorable outcomes. A comparison of embryo characteristics showed that transfer of higher-stage embryos and embryos with higher numbers of cells had a significant impact on cycle outcomes.

Conclusion: Our comparison of parameters of failed and successful ICSI cycles in poor responders revealed significantly earlier antagonist initiation, higher total number of mature and fertilized oocytes, fertilization rate, and significantly higher stage of embryo development and cell numbers at transfer in cycles that resulted in clinical pregnancy.

Keywords: Poor responders, assisted reproduction, fertilization rate, gonadotropin-releasing hormone antagonist

Öz

Amaç: Zayıf cevaplı hastalarda birbirini takip eden başarılı ve başarısız intrasitoplazmik sperm enjeksiyonu (ICSI) sikluslarında bazı majör özellik farklarının ortaya konmasıdır.

Gereç ve Yöntemler: Bologna kriterlerine göre karar verilmiş 60 düşük yanıtlı hasta başarısız bir siklus sonrası ICSI tedavine alındı. Başarılı ve başarısız sikluslarda yaş, vücut kitle indeksi (VKİ), serum folikül stimülan hormon (FSH) ve estradiol düzeyleri, antral folikül sayısı, gonadotropin dozu, stimülasyon, antagonist başlama günü, antagonist uygulama süresi, tetikleme günü endometrial kalınlık, total ve fertilize oosit sayısı, embriyo transfer günü, embriyo hücre sayısı ve fertilizasyon oranlarını içeren değişkenler aynı hasta grubunda klinik gebeliği öngörmek üzere karşılaştırıldı.

Bulgular: Ortalama yaş, VKİ, serum FSH, estradiol düzeyleri ve antral folikül sayısı sırası ile 35,9 (30-42 yıl), 25,9 (18,4-33,5 kg/m^2), 10,9 (7-13), 52,9 (11,6-75 pg/mL), 4,7 (2-10) idi. Bazı siklus özelliklerinin karşılaştırılmasında, başarılı siklusta daha fazla total, matür ve fertilize oosit sayısı izlendi. Klinik gebeliğin olduğu siklusta fertilizasyon oranı daha yüksekti. Antagoniste erken başlamak daha iyi sonuçla ilişkili idi. Bazı embriyo özelliklerinin karşılaştırılmasında, ileri evredeki ve daha fazla sayıda hücreli embriyo transferinin sonuca anlamlı etkisi olduğu izlendi.

Sonuç: Düşük over yanıtlı hastalarda başarılı ve başarısız siklusların karşılaştırılması klinik gebelik olan siklusta erken antagonist başlanması, yüksek sayıda total, matür ve fertilize oosit sayısı, fertilizasyon oranı, daha ileri evre ve daha fazla hücreli embriyonun transferi ile sonuçlanmıştır.

Anahtar Kelimeler: Zayıf cevaplı hasta, yardımla üreme, fertilizasyon oranı, gonadotropin salgılatıcı hormon antagonisti

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Introduction

Women prefer to postpone their pregnancy plans to older ages due to career concerns[1-3]. Consequently, these women face a high risk of failure at conceiving in spontaneous cycles and seek assisted reproduction, especially in industrialized countries. This demand from health care providers leads to growing numbers of difficult infertile patients to be treated through assisted reproductive techniques. Moreover, these patients fail to respond to standard stimulation protocols due to poor ovarian reserve. The European Society of Human Reproduction and Embryology introduced the Bologna criteria in 2011 in order to standardize the definition of poor ovarian response[4]. Some stimulation protocols modified with adjuvant therapies and increased gonadotropin doses were tried to obtain favorable outcomes in poor responders[5]. In a study on the association between the number of eggs and live birth, the number of eggs in in vitro fertilization (IVF) was accepted to be an indirect indicator for clinical success. Analyses of data revealed a non-linear relationship between the number of eggs and live birth rate following IVF treatment. The maximum live birth rates were obtained when approximately 15 eggs were retrieved[6]. Harvesting of 4-6 oocytes has been defined to be poor response[7].

Several studies compared the cycle outcomes of gonadotropin-releasing hormone antagonist administration with flexible (according to follicular size) and fixed starting days. Meta-analyses on this issue revealed no statistically significant difference in pregnancy rate between flexible and fixed protocols. There was a statistically significant reduction in the amount of recombinant follicle-stimulating hormone (rFSH) with the flexible protocol[8].

An inter-cycle variability of responses to gonadotropin stimulation was shown in a recently published study. In the study, the authors categorized patients according to the number of follicles on the day of human chorionic gonadotropin (hCG) administration as low (0-<6), normal (6-<18), and high (≥18), and showed that only 73.9% of patients remained in the same category after a new cycle[9].

In this study, we tried to determine some major characteristic differences between two consecutive successful and unsuccessful cycles in patients with poor ovarian response.

Materials and Methods

After approval of the hospital ethics committee, this retrospective study was conducted from January 2014 to December 2014 in the IVF/intracytoplasmic sperm injection (ICSI) unit of Zeynep Kamil Women and Children's Health Training and Research Hospital (approval number: 2014-183). A total of 60 women with a failed and subsequent successful ICSI cycle were retrospectively screened from the hospital database and cycles with and without successful outcomes were compared in terms of cycle characteristics. In order to determine the minimum number of subjects needed to be enrolled in this study in order to have sufficient statistical power, sample size calculation was performed before the study. The probability of a type-1 error (α), a difference being found although a difference does not exist, was calculated. We used an alpha cut-off of 5% (0.05). All participants had regular menstrual cycles, normal serum prolactin levels, and had not received hormone treatment in the last 3 months. The patients' ages ranged from 30 to 42 years.

All patients underwent assisted reproductive technology treatment because of their previous poor response and/or poor ovarian reserves. At least two of the following three criteria had to be fulfilled to establish the definition of poor ovarian reserve: (1) advanced maternal age (>40 years) or any other risk factor for poor ovarian response; (2) a previous poor ovarian response (≤3 oocytes with a conventional stimulation protocol); (3) an abnormal ovarian reserve test [i.e. antral follicle count (AFC) less than 5-7 follicles or anti-Müllerian hormone below 0.5-1.1 ng/mL]. Women whose cycles did not reach the embryo transfer stage, and those with endometriosis, male factor infertility, and previous ovarian surgery were excluded from the study.

An antagonist protocol was used in all patients for both cycles. On the second day of the menstrual cycle, depending on the patient's response, rFSH 300-450 IU were administered and follicular growth was monitored using transvaginal sonography. The dosage of rFSH was adjusted starting from day 5 of stimulation according to the ovarian response. Follicle monitorization was performed using two dimensional measurements of growing follicles and a calculation of the mean value at each visit.

Antagonist (Cetrorelix, Merck-Serono, Geneva, Switzerland) 0.25 mg/day was administered when the follicular size was 12-14 mm. After the follicular size reached 18 mm, recombinant hCG 250 µg was administered, and follicular puncture was performed after 34-36 hours. Next, the application of 8% vaginal progesterone gel twice/daily was started. The serum hCG level was measured 2 weeks later; if the serum hCG level was more than or equal to the normal level, ultrasonography was performed in the days following serum hCG level measurement to detect a fetal pulse to confirm clinical pregnancy.

Age, body mass index (BMI), serum FSH, estradiol, AFC, stimulation protocol, gonadotropin type and dosage, duration of stimulation, duration of antagonist administration, menstrual day at embryo transfer, embryo cell number, endometrial thickness at trigger day, total number of oocytes and fertilized oocytes and fertilization rates were compared between failed and successful consecutive trials with a maximum interval of 2 months.

Data were analyzed using SPSS 15.0 for Windows. The paired samples t-test was used to compare continuous variables between two separate cycles within the group. A p value <0.05 was accepted as statistically significant.

Results

The mean age, BMI, FSH, estradiol concentrations, AFC were 35.9 years (range, 30-42 years), 25.9 (range, 18.4-33.5 kg/m2), 10.9 IU/mL (range, 7-13 IU/mL), 52.9 (range, 11.6-75 pg/mL), 4.7 (range, 2-10) respectively (Table 1). A comparison of cycle characteristics showed a significantly higher total oocyte number and fertilized oocytes in successful cycles. The fertilization rate was also significantly higher in cycles with clinical pregnancy. Early initiation of antagonist was shown to result in favorable outcomes. A comparison of embryo characteristics showed that transfer of higher-stage embryos and embryos a higher number of cells had a significant impact on cycle outcomes. All comparisons of variables between the two cycles are summarized in Table 2.

Discussion

In this study, we assessed cycle characteristics in poor responders with and without successful clinical pregnancy such as age, BMI, serum FSH, estradiol, AFC, stimulation protocol, gonadotropin dosage, duration of stimulation, duration of antagonist administration, antagonist starting day, menstrual day at embryo transfer, embryo cell number, endometrial thickness at trigger day, number of total and fertilized oocyte and fertilization rates. Our data revealed that early initiation of antagonist, higher number of total, mature and fertilized oocyte number with higher fertilization rates and transferring significantly higher stage of embryo development and embryo cell numbers led to favorable outcomes in ICSI cycles.

Table 1. Summary of some demographic characteristics of study population

	n	Minimum	Maximum	Mean	SD
Age (years)	60	30	42	35.9	2.7
FSH (IU/mL)	60	7	13	10.9	3.8
Estradiol (pg/mL)	60	11.6	75	52.9	19.1
AFC (right)	60	1	5	2.2	1.2
AFC (left)	60	1	5	2.5	1.2
BMI (kg/m2)	60	18.4	33.5	25.9	3.2

SD: Standard deviation, FSH: Follicle-stimulating hormone, AFC: Antral follicle count, BMI: Body mass index

Table 2. Comparison of some parameters of successful and preceding failed cycle in women with poor ovarian response

	n	Successful cycle (mean ± SD)	Failed cycle (mean ± SD)	p
Starting dose (IU)	60	422.03±45.9	411.86±67.3	0.209
Duration of stimulation (days)	60	8.98±1.6	8.74±1.8	0.458
Total dose (IU)	60	3728.02±820.4	3702.16±773.6	0.828
Ant starting day (days)	60	5.1±2.1	6.1±2.4	0.027
Duration of ant use (days)	60	3.7±2.1	3.3±2.3	0.309
Stimulation day at OPU	60	11.9±1.4	11.9±1.5	0.722
# fol >14 mm	60	3.7±2.4	3.9±2.7	0.605
# fol >17 mm	60	3.4±4.3	3.1±1.8	0.597
ET at hCG (mm)	60	9.6±1.7	9.7±1.6	0.372
Estradiol at hCG (pg/mL)	60	1423.1±895.9	1304.7±723.1	0.214
# Total oocyte	60	5.6±2.4	4.8±2.7	0.009
# Mature oocyte	60	4.5±2.3	3.7±2.6	0.009
# Fertilized oocyte	60	3.3±2.1	2.1±1.9	<0.001
Fertilization rate		0.73	0.55	0.002
The day of transferred embryo	60	2.7±0.6	2.2±0.9	0.011
Embryo cell #	60	5.9±2.1	4.1±3.1	0.001

SD: Standard deviation, OPU: Oocyte pickup, Fol: Follicle, ET: Embryo transfer, hCG: Human chorionic gonadotropin

Despite introduction of many protocols with different initial doses and types of gonadotropins, optimal management of patients who are poor responders is still a concern. In this study, we tried to identify characteristics of a successful cycle compared with a preceding failed cycle in the same patients with poor ovarian response. Most of the time, when responses to the standard dose of gonadotropins (225-300 IU) for a proper multifollicular growth fails, dose increments are attempted to obtain a better outcome. Therefore, high doses of gonadotropins were proposed for a couple of decades in poor responders. However, there are some conflicting data regarding the success of increased gonadotropin doses in the management of poor responders. Previous studies showed no enhanced ovarian response and/or better pregnancy rates when 450 U of increased doses of gonadotropins were used[10-12]. Furthermore, a recently published study indicated that an increased starting dose of FSH did not result in higher pregnancy rates, and outcomes were similar between groups with different gonadotropin starting doses (300 UI, 450 UI, and 600 UI) of gonadotropins with regard to retrieved oocytes, number of embryos obtained, and pregnancy rates[13]. In our study, the mean starting and total gonadotropin doses were similar between the two cycles. However, we found significantly earlier antagonist initiation in successful cycles. The modified early antagonist start protocol was introduced to improve cycle outcomes. It was claimed that improved mature oocyte yield could be enhanced through follicular synchronization. Additionally, significantly higher clinical pregnancy rates compared with the conventional antagonist protocol were reported[14]. Furthermore, delayed-start of antagonist protocol was proposed to result in favorable outcomes in terms of number of dominant follicles and mature oocytes retrieved, mature oocyte yield, and fertilization rates in poor responders. The authors concluded that this was the result of the promoting and synchronizing effect on follicle development without impairing oocyte developmental competence[15]. Besides a higher rate of fertilization, we also found significantly higher numbers of total, mature oocyte and earlier antagonist initiation in successful cycles. Especially in patients with poor ovarian reserve, the number of oocytes has a critical role for cycle outcome. Studies on this issue showed a significant relationship between the number of eggs and live birth in all age groups. A study proposed that the number of eggs in IVF was an indirect indicator for clinical success. The best outcome was obtained when approximately 15 eggs were retrieved[6]. However, a yield lower than 4-6 oocytes after stimulation has been considered to be poor response[7]. In our study, the mean total number of oocytes harvested during failed and successful cycles were 4.8 and 5.6, respectively. Although both results are within the range of the poor response definition, it seems that a minimal increase in total oocyte numbers with increased fertilization rates resulted in favorable outcomes.

Another factor is the fertilization rate, which was thought to be an indirect finding for oocyte quality and was shown to be a significant predictor for embryo implantation[16]. Some morphologic characteristics of oocytes, such as zona pellucida thickness, cytoplasm appearance, and polar bodies were investigated to select the best embryos to transfer and therefore further minimize the number of embryos transferred[17-20]. However, according to the accumulated data, most of these parameters had a minimal impact for this purpose[21,22]. Embryo grading systems were developed and found correlated with pregnancy outcomes. Despite their limitations, grading systems are the most commonly applied procedures in the selection of the most qualified embryo for transfer. Further embryo assessments focused on the zygote stage, evaluation of embryo behavior at early cleavage, and extended culture performed to day 5 showed improved pregnancy outcomes[23,24]. There are also some data at the molecular level for implantation prediction[25]. However, after adjustment of the aforementioned covariates, the fertilization rate was shown as a significant predictor for embryo implantation in a previous study[16]. As mentioned above, our data also showed significantly increased fertilization rates in cycles with clinical pregnancy.

The relationship between embryo quality and pregnancy rates has been shown in several studies[26-28]. Early cleaving 2-cell embryos have been shown to have higher pregnancy rates than patients without early-cleaving 2-cell embryos[29], and furthermore, transfer of 4-cell embryos resulted in significantly higher implantation and pregnancy rates compared with transfers of 2 and 3-cell embryos. Additionally, cell number was found as the strongest predictor of pregnancy in day 3 embryos in a scoring system based on cell number, fragmentation, and other morphologic criteria deemed specific to day 3 embryos[30-32]. According to a Cochrane review, cumulative clinical pregnancy rates from cleavage stage resulted in higher clinical pregnancy rates than from blastocyst cycles[33]. Data showed a decreased overall embryo quality score in embryos that were kept in culture till day 3[34]. In our assisted reproductive technology clinic, we try to avoid keeping embryos in culture media for more than 3 days, except when the top quality embryo has not been determined. In majority of cases, we prefer 2 to 3-day embryo transfers, especially in the event of a low number of embryos. Our data showed that number of cells in 2 to 3-day embryo transfers had a critical role in ICSI cycles; the number of cells was significantly higher in cycles with clinical pregnancy (4.1 vs. 5.9, $p<0.05$).

Conclusion

Early initiation of antagonist, higher number of total, mature oocyte yield, higher fertilization rates and transfer of embryos with higher number of cells were significant factors of successful outcomes in poor responders. Further research on this topic should be conducted with larger study populations to elaborate

on the implications of our study, and to obtain more data to modify cycles for better results in poor responders.

Ethics

Ethics Committee Approval: The study was approved by the Zeynep Kamil Women and Children's Health Training and Research Hospital Local Ethics Committee (Approval number: 2014-183), Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.Ö., T.K., P.K., H.A., B.D., İ.S., Y.Ş., B.S., A.K., Concept: T.K., Design: T.K., Data Collection or Processing: E.Ö., T.K., P.K., H.A., B.D., İ.S., Y.Ş., B.S., A.K., Analysis or Interpretation: E.Ö., Literature Search: E.Ö., Writing: E.Ö., T.K.

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Review / Derleme

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Intra-cesarean insertion and fixation of frameless intrauterine devices

Çerçevesiz rahim içi araçların sezaryen esnasında uygulanımı ve fiksasyonu

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Abstract

Various contraceptive methods are available to postpartum women including hormonal and nonhormonal barriers, as well as injectable forms. Of all the available birth control methods, intrauterine devices (IUD) are felt by many to be the near-ideal form of contraception, and are recommended by advocacy groups, physicians, and gynecological organizations worldwide. Immediate postpartum IUD insertion deserves greater attention because it can provide immediate contraception, prevents repeat unintended pregnancies, and may serve to reduce the incidence or need for secondary cesarean delivery; however, insertion of conventional T-shape IUDs immediately post placenta delivery is limited by their high expulsion and displacement rates. Anchoring of frameless-design IUDs that lack conventional cross-arms to the uterine fundal surfaces has been medically and commercially available throughout Europe for many years. The placement technique is simple, has minimal patient discomfort, and high long-term patient acceptance due to its high degree of uterine compatibility as a consequence of its small size and segmented design. Frameless-design IUD implantation appears to represent a major advance, suitable for general use, due to its lack of timing restraints and its simplicity of attachment, which only requires limited training.
Keywords: Intrauterine device, immediate contraception, frameless intrauterine devices

Öz

Postpartum kadınlar için hormonal ve nonhormonal bariyer yöntemlerin yanı sıra enjekte edilebilir formlar gibi pek çok kontraseptif metod bulunmaktadır. Mevcut doğum kontrol yöntemlerinden rahim içi araç (RİA), dünya çapında savunma grupları, hekimler ve jinekoloji organizasyonları tarafından önerilmekte ve çoğu kişi tarafından ideale yakın kontrasepsiyon yöntemi olarak düşünülmektedir. Acil doğum sonrası RİA uygulaması, acil kontrasepsiyon sağlaması, istenmeyen gebelikleri engellemesi ve sekonder sezaryen doğum gereksinimi ve sıklığını azaltmasından dolayı daha fazla dikkat çekmektedir, ancak geleneksel T-şekilli RİA'ların plasentanın doğumundan hemen sonraki uygulamaları, yüksek dışarı çıkma ve yer değiştirme oranları tarafından sınırlandırılmaktadır. Geleneksel çapraz-kollar barındırmayan, çerçevesiz dizayn edilmiş RİA'ların fundal bölgeye yerleştirilmesi, Avrupa'da medikal ve ticari olarak mümkündür. Yerleştirme tekniği basittir, minimal hasta rahatsızlığına neden olur ve küçük boyutu ve parçalı dizaynının sonucu olarak yüksek uterus uyumluluğundan ötürü uzun dönem hasta uyumu yüksektir. Çerçevesiz dizayn RİA implantasyon tekniği, zamanlama kısıtlılıklarının olmaması ve uygulama kolaylığından ötürü genel kullanıma uygun, önemli bir gelişme gibi görünmektedir.
Anahtar Kelimeler: Rahim içi araç, acil kontrasepsiyon, çerçevesiz rahim içi araçlar

PRECIS: Frameless design intrauterine device implantation appears to represent a major advance, suitable for general use due to its lack of timing restraints and its simplicity of attachment.

Introduction

The ideal time for postpartum contraception either as a precautionary measure or as a family planning tool is immediately post-delivery. Immediate contraception is convenient and timely because a woman is actively evaluating her current and future family planning options. A woman's return to fertility post-delivery is not always predictable because it can occur as soon as 3 weeks in non-lactating women and may not necessarily be accompanied by menses. The pregnancy environment represents the near-ideal timing for discussions with patients in need of contraception, the nature of the products available, and

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their individual benefit and risks. The patient's receptiveness and willingness to select a given form of contraception is a critical component in allowing a woman to adequately manage her contraception needs.

Various contraceptive methods are available to postpartum women including hormonal and nonhormonal barriers, as well as injectable forms. Unfortunately, as reviewed by Trussell[1], many of these methods although effective, have a high degree of failure when used imperfectly. For parous women, most physicians and the World Health Organization recommend an interdelivery interval of 18 to 24 months, because a second pregnancy too soon after the first could have detrimental effects on the woman herself, her ability to carry the baby to term, the viability of the infant, and its overall growth/development[2]. Women undergoing cesarean sections with an interdelivery interval shorter than 18 months have the added risk of possible uterine rupture[3]. Use of contraception as early as possible post-delivery would assure prevention of uterine rupture post-cesarean section, thus allowing for the wound to heal as well as for the woman to fully recover from her pregnancy. Effective contraception in these women will be valuable in reducing the risk of unintended pregnancies, and may allow for many women to have follow-on vaginal over cesarean deliveries.

Of all the available birth control methods, intrauterine devices (IUD) are felt by many to be the near-ideal form of contraception, and are recommended by advocacy groups, physicians, and gynecological organizations worldwide. IUDs have the advantage of high effectiveness as well as having an extremely low failure rate, in part because of the lack of involvement by the women. Immediate postpartum IUD insertion deserves greater attention because it can provide immediate contraception, prevents repeat unintended pregnancies, and may serve to reduce the incidence or need for secondary cesarean delivery[4]. Unfortunately, insertion of conventional T-shape IUDs immediately post placenta delivery is limited by their high expulsion and displacement rates[5,6]. A study conducted by Çelen et al.[7] in Turkey in 2011 noted an expulsion rate of 17.6% at 12 months with the TCu380A IUD inserted immediately following cesarean section delivery. The inability of these devices to be retained clearly affects their effectiveness, but as importantly, overall patient acceptance. Women, especially those undergoing cesarean delivery, could benefit from immediate post-placenta IUD insertion because it would allow a sufficient period for the uterus, as well as the woman, to recover from surgery via a highly effective and long-lasting contraceptive. In these women, a low expulsion risk is therefore paramount with women having the added benefit of the IUD being easily reversible with a rapid return to fertility.

Over the past decades, attempts have been made to solve the expulsion problem encountered with conventional T-shape IUDs by modifying existing devices, such as adding absorbable sutures (delta-T) or additional appendages. These attempts were minimally successful. Expulsion rates varying from 5% at 12 months to up to 50%, and even higher if partial expulsions are included, have been reported[8-10].

Timing of insertion post-placenta delivery is of critical importance with T-shape devices. Studies have shown that if inserted at times beyond 10 minutes post-delivery, expulsion rates were higher than those observed in normal women.

Anchoring of frameless design IUDs that lack conventional cross-arms to the uterine fundal surfaces has been medically and commercially available throughout Europe for many years in the form of GyneFix (Contrel Research, Belgium). The placement technique is simple, has minimal patient discomfort, and high long-term patient acceptance due to its high degree of uterine compatibility as a consequence of its small size and segmented design. Since its inception, the technology has passed through several phases of improvement, design modifications, and clinical testing intended to maximize patient comfort and tolerability producing 5-year continuation rates in excess of 90%. Clinical studies were also conducted to evaluate the impacts of immediate insertion of a frameless IUD during cesarean section, as well as after vaginal delivery, on the bleeding pattern, duration of lochia, and healing of uterus. Accordingly, no significant difference in postpartum hemorrhage, continuance of lochia, and healing of uterus, was observed[11]. A novel minimally invasive surgical approach was devised for suspending the frameless copper IUD for intra-cesarean insertion, which takes advantage of the full visualization and access to the uterus that is achieved during cesarean delivery. The technique consists of the precise placement of the anchoring knot immediately below the serosa of the uterine fundus, followed by fixing the knot in place with a conventional absorbable suture (Figure 1a, 1b). In several weeks, the uterus regains its normal tonicity, the suture is absorbed, and the anchor retained as seen in women undergoing conventional interval insertion. The procedure is simple and can be performed at any convenient post-delivery period, and takes less than 4 minutes with no discomfort to the patient and minimal surgical risk. The IUD tail is looped in the cervical canal or is cut at the level of the cervix. The anchoring technique has been shown to be easy, quick and safe in a pilot trial with no expulsions at 12 months. Ongoing studies conducted in Turkey confirm the efficacy of the technique and high acceptability of the frameless IUD by women. To check IUD placement, a follow-up sonography can be performed to localize the stainless steel marker attached to the anchoring knot (Figure 1c). Removal of the IUD is similar to the removal after interval insertion of the device accomplished by simply pulling on the IUD string. In the event that the tail is in the cavity, it is accessible by using thin alligator forceps (3 mm) if/when removal is requested. The copper releasing frameless IUD and inserter, which were specifically designed to facilitate use immediately post-placental delivery after cesarean deliveries, is now available in Turkey. Conventional insertion of frameless IUDs in normal women is already available in Turkey. The developers are also finalizing the development of

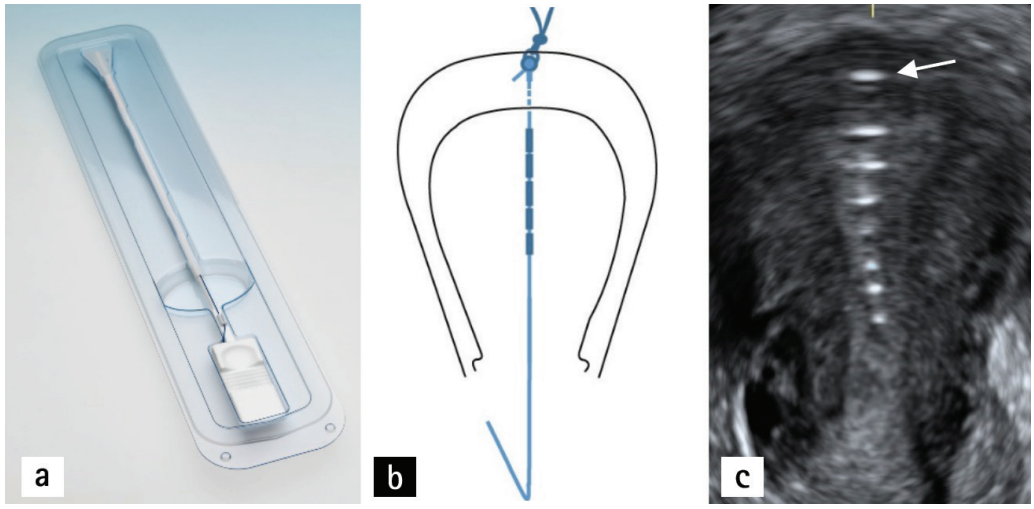

Figure 1. a) Insertion apparatus for the insertion of the frameless intrauterine devices following cesarean section delivery b) Illustration of the anchoring technique; a biodegradable suture holds the anchor in place in the uterine fundus until involution c) Coronal ultrasound of the position of the frameless intrauterine devices after involution of the uterus with an anchor marker in the fundus (arrow)

a levonorgestrel-releasing frameless system, which may have additional advantages in some women.

Frameless-design IUD implantation appears to represent a major advance, suitable for general use due to its lack of timing restraints and its simplicity of attachment, which only requires limited training. It affords the patient and her physician additional options for contraceptive control that may likely serve to reduce the number and frequency of unintended pregnancies. Frameless IUDs appear to have advantages over framed T-shaped IUDs because the latter may cause discrepancy with the uterine cavity and embedment during involution of the uterus, particularly during prolonged lactation as hyperinvolution in these women is not uncommon[12].

Disclosure

Dr. Dirk Wildemeersch has been involved in the development of novel contraceptive systems for use in the uterus. He is currently an advisor in devising new concepts in controlled release for contraception and gynecological treatment.

Ethics

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.K., A.T., Ö.Ö., D.W., Concept: A.K., D.W., Design: A.K., A.T., Data Collection or Processing: A.T., Ö.Ö., D.W., Analysis or Interpretation: A.K., A.T., D.W., Literature Search: Ö.Ö., D.W., Writing: A.K., A.T., Ö.Ö., D.W.

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Case Report / Olgu Sunumu

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Chondrosarcoma mimicking an adnexal mass: A very rare case report

Adneksiyal kitleyi taklit eden kondrosarkom: Çok nadir bir olgu sunumu

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Abstract

Chondrosarcoma is considered as a common primary bone sarcoma. These sarcomas can form large masses without any specific symptoms because there are no barriers in pelvic anatomy to prevent the enlargement of tumors, and can mimic ovarian masses. We present a pelvic chondrosarcoma in a woman aged 37 years who was misdiagnosed as having an ovarian mass due to the limited information obtained from imaging studies. Pelvic chondrosarcoma should be considered in patients who have pelvic masses with solid components. It should be kept in mind that interventions should be performed at centers where there are orthopedic surgeons with experience of this subject.

Keywords: Chondrosarcoma, diagnostic errors, ovarian mass

Öz

Kondrosarkom primer kemik sarkomların en yaygın çeşidi olarak bilinir. Bu sarkomlar önlerinde büyümesini engelleyecek bir bariyer olmadığı için, herhangi spesifik bir semptom vermeden çok büyük boyutlara ulaşabilir ve ovaryan kitleleri taklit edebilirler. Otuz yedi yaşında pelvik kondrosarkom olan kadın hastada kısıtlı görüntüleme bilgilerine dayanarak ovaryan kitle olarak yanlış teşhis edilmiş bir hastayı sunduk. Solid komponentli pelvik kitlesi olan hastalarda pelvik sarkomlar da akla getirilmelidir. Şu iyi bilinmelidir ki; bu tür hastalara yapılan müdahaleler bu işte deneyimli ortopedik cerrahları olan merkezler tarafından yapılmalıdır.

Anahtar Kelimeler: Kondrosarkom, tanısal hatalar, ovaryan kitleleri

Introduction

Chondrosarcoma is considered as a common primary bone sarcoma, which is ranked as the third primary bone malignancy. One in five cases of bone sarcomas are due to chondrosarcoma, and half of all cases affect the pelvis[1]. Moreover, this tumor arises predominantly after the second decade with a peak in the middle-aged period. Many heterogeneous groups of neoplasms are related to chondrosarcoma and cartilage matrix production is a typical feature of this tumor[2]. These sarcomas form large masses without any specific symptoms because there are no barriers in the pelvic anatomy to prevent the enlargement of tumors[3]. In this case report, we present a patient who had a tumor of undefined origin according to preoperative imaging methods, and a pelvic chondrosarcoma mimicking an adnexal mass. To the best of our knowledge, this is only the third case of pelvic chondrosarcoma in the English literature of obstetrics and gynecology.

Case Report

A 37-year-old single woman presented to our clinic with symptoms of pelvic pain, abdominal distension, and vaginal bleeding. During the pelvic examination, a mass that filled the pelvis was detected. The carcinoma antigen 125 (CA125) level was 40 U/mL. Ultrasonographic and magnetic resonance imaging (MRI) examinations revealed a solid mass 20x10 cm in diameter including calcified areas, and a mass consistent with myoma of 3.5 cm in diameter was observed in the cervico-isthmic region of the uterus. The endometrial thickness was 8 mm (Figure 1). During surgery, a mass of 18x8 cm was observed that was displacing the uterus and extending from the symphysis pubis to the pelvis with a myoma of 3.5

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cm in diameter, posterior to the uterus corpus. The ovaries were normal on inspection. Specialists from the urology and orthopedics departments were consulted intraoperatively and it was decided that the tumor originated from the pelvic bone. Partial resections with myomectomy were performed because the tumor could not be completely removed (Figure 2). The postoperative pathologic examination was reported as grade 1, well-differentiated chondrosarcoma (Figure 3). The orthopedics department requested computerized tomography (CT) imaging, which revealed masses consistent with metastasis in the liver, and a 9x8 cm diameter mass in the pubic area. The patient was referred to another healthcare unit because a skilled orthopedics team with experience of pelvic chondrosarcoma was unavailable.

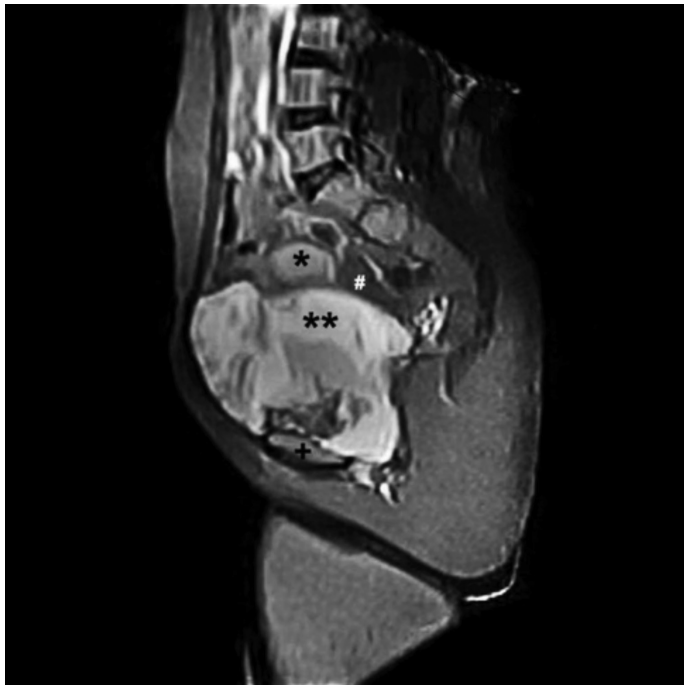

Figure 1. Magnetic resonance imaging showing a solid mass with 20x10 cm in diameter including calcified areas, and a mass consistent with myoma of 3.5 cm in diameter was observed in the cervico-isthmic region of the uterus

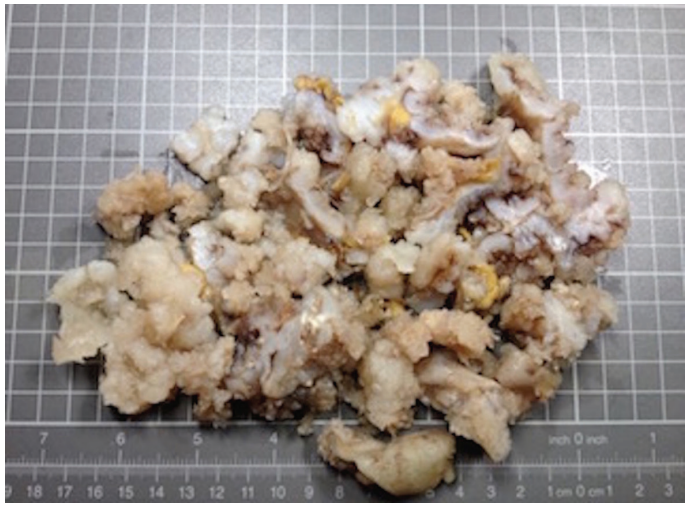

Figure 2. The macroscopic appearance of the lesion, which is seen in pieces, and has the solid-brilliant cartilaginous appearance of cross-sectional surface

Discussion

That a pelvic chondrosarcoma could masquerade as an ovarian mass was considered the peculiar part of our case. This camouflage exposes the limited role of imaging techniques and tumor markers in diagnosing pelvic tumors. Generally, chondrosarcoma has a silent course due to the special pelvic structure, which allows masses to grow feasibly without any boundaries and only become symptomatic after enlarging enough, as in our case. Thus, this tumor has a larger size in comparison with other pelvic masses when the diagnosis was established; the mean size is commonly 11 cm[4]. After reviewing all operated cases of pelvic mass in our department within the last 15 years, chondrosarcoma was the only case that was misdiagnosed as an ovarian mass, which reflects the sporadic incidence of this condition. Although all available imaging techniques, even CT and MRI, were used to assist us in mapping this tumor, we could not identify the exact margins, neither the exact organ from which this tumor derived. Moreover, the elevated CA125 was another misleading factor that increased our suspicion of ovarian mass. The surgical management of chondrosarcoma is a destructive operation for orthopedic surgeons due to the following principles: increased risk of vital organ injuries, high susceptibility to damage pelvic structural stability, challenging anatomic interactions of the pelvis, and devastating extension of the tumor. The mass could not be completely removed and the patient was considered as non-resectable and referred to another orthopedics clinic because we did not have an orthopedic surgical team skilled

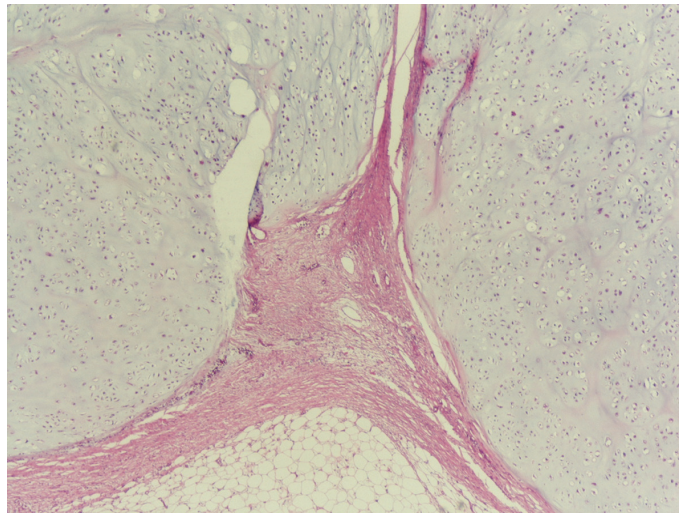

Figure 3. Microscopic appearance of the lesion, which was separated by fibrous septa, and was formed by nodular infiltrating, atypical chondrocytes, hematoxylin and eosin x40

in pelvic chondrosarcoma. Vast majority of chondrosarcoma become symptomatic after reaching a large size and this can be explained by the slow growth rate of this these tumors[5]. Grade 1 chondrosarcomas consist of profuse hyaline cartilage matrix surrounding a little cellular mass and metastasize infrequently[1]. In our case, the pathologic result was grade 1 chondrosarcoma, and there were metastatic lesions observed in the liver in abdominal tomography. Pelvic chondrosarcomas can appear in various pathologic neoplasms, other than pure chondrosarcoma arising from the pelvic bone, such as chondrogenic tumors of the ovaries or heterologous carcinosarcomas of the uterus. However, all mentioned types have very low incidence rates[6]. Moreover, mixed mesodermal tumors, commonly called carcinosarcoma, another manifestation of chondrosarcoma, are the most common heterologous sarcomas, originating from the uterus in most cases. The histologic appearance is a mixture of ectoderm and mesoderm-derived tissues. Either homologous or heterologous mesodermal tissue can be commonly found to be high grade. Heterologous tumors consist of a differentiated mesenchymal component accompanied by endometrial, stromal or undifferentiated sarcomas. Occasionally, these uterine tumors may enlarge and convert to giant pelvic masses that can destroy the uterine structure to the point where it can become unrecognizable[7]. The cornerstone of treatment in managing this tumor is wide surgical excision, that still first line treatment[8]. After performing extensive intralesional curettage, local adjuvant treatment has encouraging long-term outcomes and adequate control of local recurrence in low-grade chondrosarcomas. Local adjuvant treatment is only effective in cases with well-defined boundaries with no extension beyond the bone[9]. However, giant tumor or pelvic localization of chondrosarcoma can alter the treatment method, even in low-grade conditions, as in our case, which require wide resection as a first-line management, rather than intralesional curettage[1].

Conclusion

Pelvic chondrosarcoma should be considered in patients who have pelvic masses with solid components because preoperative evaluations (imaging studies, pelvic examination) in daily practice may be inadequate for the diagnosis of pelvic masses. As a consequence, it should be kept in mind that interventions should be performed at centers where there are orthopedic surgeons with experience of this subject.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.Ç.Ö., Ö.B., Concept: Z.B., Design: H.Ç.Ö., Data Collection or Processing: Z.B., S.S., Analysis or Interpretation: S.S., Literature Search: A.M., Writing: A.M.

Conflict of Interest: No conflict of interest was declared by the authors.

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Case Report / Olgu Sunumu

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Mayer-Rokitansky-Kuster-Hauser syndrome associated with rectovestibular fistula

Rektovestibüler fistülle ilişkili Mayer-Rokitansky-Kuster-Hauser sendromu

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Abstract

A female neonate with two openings in the introitus and an absent anal opening at the anal site presents a diagnostic challenge. Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome associated with rectovestibular fistula, though rare, should be kept in mind as a differential diagnosis of this presentation. We present such a case in a one-year-old female child with MRKH syndrome and rectovestibular fistula.

Keywords: Mayer-Rokitansky-Kuster-Hauser syndrome, atypical, rectovestibular fistula

Öz

Yenidoğan bir kız çocuğunun introitusunda iki açıklık olduğu halde anal bölgesinde hiç açıklık olmaması tanı zorluğu yarattı. Rektovestibüler fistülle ilişkili Mayer-Rokitansky-Kuster-Hauser (MRKH) sendromu seyrek olmasına rağmen bu sunumun farklı tanısı olarak görülmelidir. MRKH sendromu ve rektovestibüler fistülü olan bir yaşında bir kız çocuk olgusu sunuyoruz.

Anahtar Kelimeler: Mayer-Rokitansky-Kuster-Hauser sendromu, atipik, rektovestibüler fistül

Introduction

Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome is a rare anomaly in females that affects 1 in 5000 live births[1,2], in which there is dysgenesis of the Müllerian ducts leading to failure of development of the uterus and vagina. Ovarian function is preserved and the external genitalia are normal. The karyotype is 46, XX. There is normal development of secondary sexual characteristics at puberty. Primary amenorrhea at adolescence is the most common presenting symptom in patients with MRKH syndrome. However, when associated with anorectal malformation, this condition presents early at birth or in infancy and requires proper management[3].

MRKH syndrome has been divided into two types (Schmid-Tannwald and Hauser, 1977); type A, or the typical form, is an isolated anomaly also known as the Rokitansky sequence[4,5]. The patient has symmetrical uterine remnants and normal fallopian tubes[5]. Type B, the atypical form, is characterized by asymmetric uterine buds or abnormally developed fallopian tubes (CAMP). This atypical form is associated with anomalies that involve other systems, especially the renal, cardiac, otologic, and skeletal systems[1,4]. Anorectal malformations are uncommonly reported to be associated with MRKH syndrome, and among them, rectovestibular fistula and cloacal malformations have been commonly described[1,2,6].

We present a girl aged one year with atypical MRKH syndrome associated with rectovestibular fistula.

Case Report

A girl aged one year presented with an absent anal orifice since birth. She had been passing stools from an orifice within the introitus since birth. There was no constipation or abdominal distension. Per abdominal and systemic examinations were unremarkable.

On perineal examination, there were two openings in the introitus. There was no anal opening at the normal site (Figure 1). The anterior opening was small and the child was passing urine through this opening, which suggested a urethral opening. The posterior opening in the vestibule discharged fecal matter, thereby suggesting a fistula. No vaginal opening could be appreciated.

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Abdominal ultrasound revealed absent uterus and vagina. Both ovaries were normal and the right kidney was small. Barium enema showed a dilated rectum. Voiding cystourethrography was normal. A radio nucleotide renal study suggested a non-functioning right kidney and adequately functioning left kidney. Cystogenitoscopy showed normal urethra and bladder, absent vagina, and the presence of rectovestibular fistula confirming the diagnosis of uterovaginal agenesis (MRKH syndrome type B). A right transverse stoma was performed. Magnetic resonance imaging (MRI) confirmed uterovaginal agenesis (Figure 2).

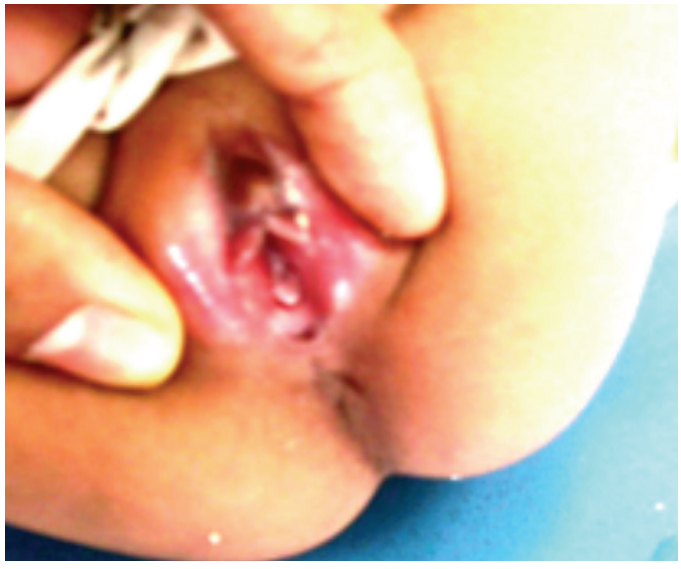

Figure 1. The perineum of the patient showing two orifices in the introitus

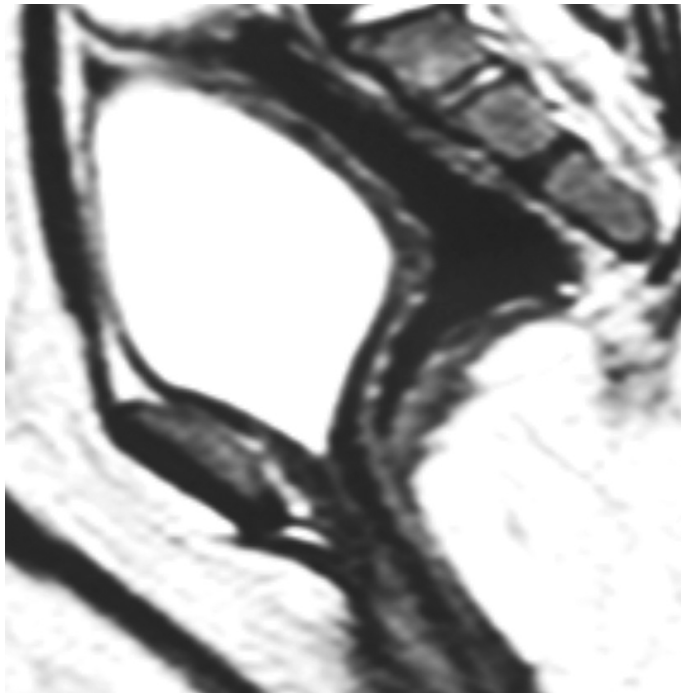

Figure 2. Magnetic resonance imaging pelvis showing uterovaginal agenesis and the dilated rectum

Posterior sagittal anorectoplasty (PSARP) with a neovagina creation using the distal end of rectum with vestibular opening was planned. Approximately 3-4 cm of the distal ano-rectum (i.e. the rectovestibular fistula itself) was retained as a neo-vagina and the proximal rectum was brought down posteriorly within the sphincter complex (Figure 3).

At follow-up after 6 weeks, a neovagina of about 6-cm length along with minimal mucus discharge was present. The colostomy was closed after 8 weeks.

Discussion

The clinical appearance of two orifices in the introitus with an absent anal opening leads to the differential diagnosis of anorectal agenesis without fistula, a rectovaginal fistula (high or low) or a rectovestibular fistula with either a urogenital sinus or MRKH syndrome. The association of rectovestibular fistula with MRKH syndrome is rare with few reports in the literature[1,2]. Levitt et al.[6], Gross[7], Ein and Stephens[8] reported 8, 2, and 2 such cases respectively[1]. Mahajan et al.[9] described MRKH syndrome associated with H-type anovestibular fistula in 2009[9]. Ein and Stephens[8] in 1971 first reported preservation of the rectum as a neovagina[1]. Gupta et al.[1] recently reported this method of neovaginal reconstruction in a girl aged one year. The etiology of MRKH syndrome is unknown; however, it is believed that there is interruption in the embryologic development during the sixth or seventh gestational week[10,11]. The spectrum of malformations associated with atypical MRKH syndrome suggests a developmental field defect involving organ systems that are closely related during

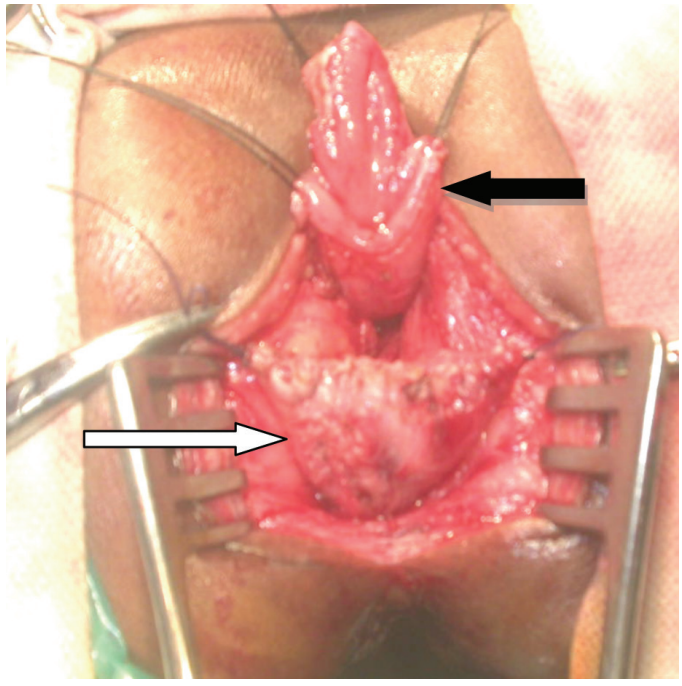

Figure 3. Intra-operative image of the patient showing the neovagina (retained distal end of rectum opening in the vestibule) (white arrow) and the pulled down bowel (black arrow)

embryogenesis[4,12,13]. MRKH syndrome has been attributed to an initial affection of the intermediate mesoderm, consequently leading to an alteration of the blastema of the cervicothoracic somites and pronephric ducts[4,12]. Mutations of the WNT4 and TCF2 genes have recently been found associated with MRKH syndrome[4,14].

The importance of the clinical examination of the perineum in a female neonate cannot be over-emphasized. This diagnosis of utero-vaginal agenesis should be made at birth itself. The clinical presentation with two openings in the introitus with fecal matter deflating through the posterior opening requires investigations to confirm diagnosis before proceeding to the definitive management. Ultrasonography, a contrast study through the opening in the vestibule, MRI, and cystogenitoscopy through both openings in the introitus help in the definitive diagnosis of absent vagina and cervix[4]. This is essential for planning the definitive management.

A possible scenario that should not be forgotten is that failure of the neonate to pass meconium through the second opening within 24 hours of birth leads to a colostomy because of the assumption of anorectal agenesis without fistula[1,6]. Due to this presumed misdiagnosis, at the time of definitive repair, the rectum would not be found because of the incorrect assumption that the rectum was the vagina[1,6]. However, a distal colostogram performed before the definitive repair would surely help in suspecting this malformation[1,6].

There are two surgical options for the definitive repair in patients with MRKH syndrome with rectovestibular fistula[1,6]. In the first method, the fistula is mobilized, traditionally by either PSARP or anterior sagittal anorectoplasty approach, and fixed within the sphincter muscle complex at the proposed anal site and a neoanus is created[1,6]. A vaginoplasty is performed at later date in these patients[1,15]. This type of repair is well suited for patients in whom MRKH syndrome was not diagnosed at infancy and presented at adolescence with symptoms of primary amenorrhea[16]. Wang et al.[17] reported three patients who presented with MRKH syndrome and rectovestibular fistula with imperforate anus and symptoms of primary amenorrhea and loose stools. A single-stage anorectovaginoplasty was performed in these patients with laparoscopic assistance in one patient[17].

The second option is to preserve the fistula at the vaginal site and leave an approximately 10-cm distal stump as a neovagina and to pull the proximal colon through the sphincter muscle complex as the neo-anorectum[1,3,6]. However, this procedure can only be performed when the correct diagnosis of MRKH syndrome with rectovestibular fistula is made pre-operatively[1]. This second option is the preferred technique because it is relatively simple to perform; there is no chance of damaging any neural innervations, and both the neovagina and neoanus are created in the same operation[1]. Neovaginas have not been reported to show tendency for stricture formation; sphincter tone is good and patients are continent[6].

Levitt et al.[6] used the PSARP approach for this procedure. The abdominoperineal approach is required when the uterus is present to allow for the anastomosis of the rectal pouch (now the neovagina) to the uterus, thereby creating continuity of the reproductive system[1].

The association of MRKH syndrome with rectovestibular fistula is rare and should be suspected as the differential diagnosis in a female neonate with two openings in the introitus. A correct pre-operative diagnosis helps to correct both malformations in the same operative procedure. Early diagnosis and simultaneous vaginal reconstruction and anorectoplasty in infancy offers added advantages; it prevents psychological trauma and avoids the need of delayed vaginoplasty through scarred perineum in these patients.

Ethics

Informed Consent: The informed consent was taken and form filled by the father of the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: C.T., H.S., K.K., M.W., Concept: C.T., H.S., K.K., M.W., Design: C.T., H.S., K.K., M.W., Data Collection or Processing: C.T., Analysis or Interpretation: C.T., H.S., Literature Search: C.T., Writing: C.T.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Letter to the Editor / Editöre Mektup

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A rare case of complete penoscrotal transposition with hypospadias in a newborn

Yenidoğanda nadir görülen bir anomali olarak komplet penoskrotal transpozisyon ve hipospadias

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Keywords: Newborn, penoscrotal transposition, hypospadias

Anahtar Kelimeler: Yenidoğan, penoskrotal transpozisyon, hipospadias

Dear Editor,

Penoscrotal transposition (PST) is an infrequent congenital external genital malformation in which the scrotum is located superior and anterior to the penis(1). PST can be defined as either complete or incomplete according to the positional exchanges between the penis and scrotum and both forms of PST are generally linked with hypospadias. Incomplete transposition is the common form of this entity and the penis lies in the middle of the scrotum, but in complete transposition, the scrotum almost entirely covers the penis, which emerges from the perineum(2). Both of these conditions are commonly reported to be linked with a wide variety of abnormalities and pathologies that affect distinct organ systems. In this case report, we present a complete PST in a patient with urinary tract abnormalities including hypospadias, polycystic renal disease, and malpositioned right kidney.

A gravida 2, para 1 woman aged 35 years was admitted to the emergency department of our institute with premature membrane rupture when she was 36 weeks' pregnant. The patient had undergone one prior cesarean delivery. The ultrasound examination revealed severe oligohydramnios. No previous histories of genetic abnormalities, illicit drug use, cigarette or alcohol consumption were reported. During her pregnancy, perinatal evaluations with ultrasound were performed at 26+6 weeks of gestation, which demonstrated a single umbilical artery, bilateral pelvic kidney, megacystitis, and penile curvature extending to the anal sphincter. Unfortunately, we were not able to obtain prenatal ultrasound pictures or a genetic analysis report because of the nature of the emergency hospital admission of the patient. A final prenatal diagnosis of PST and severe hypospadias was made based on these perinatal evaluations.

The patient underwent a cesarean section and gave birth to a male baby of 3070 grams with 8/9 Apgar score. Physical examination revealed a PST and severe hypospadias (Figure 1). Laboratory examinations were all reported to be normal. Ultrasonographic examination revealed a malpositioned right kidney (low lying) with multiple anechoic cysts of varying sizes. The newborn was transferred to the neonatal intensive care unit for further treatment.

PST is a very rare clinical situation in which the scrotum is located anterior and superior to the penis and a severe degree of PST, as in our case, with hypospadias and normal scrotum have been infrequently reported in medical literature(1,3,4). During normal human maturation, scrotal swellings move inferomedially during the 9th-11th week, and fuse in the midline caudal to the penis by the 12th week of gestation(4). The primary cause of this rare clinical disorder is a fusion defect or delay of urethral folds. Embryologically, PST is considered to result from abnormal genital tubercle development around the 6th-7th week of gestation(1).

The differential diagnosis for PST should include pseudohermaphroditism, micropenis, penile amputation in the intrauterine period, penoscrotal hypospadias, and agenesis of

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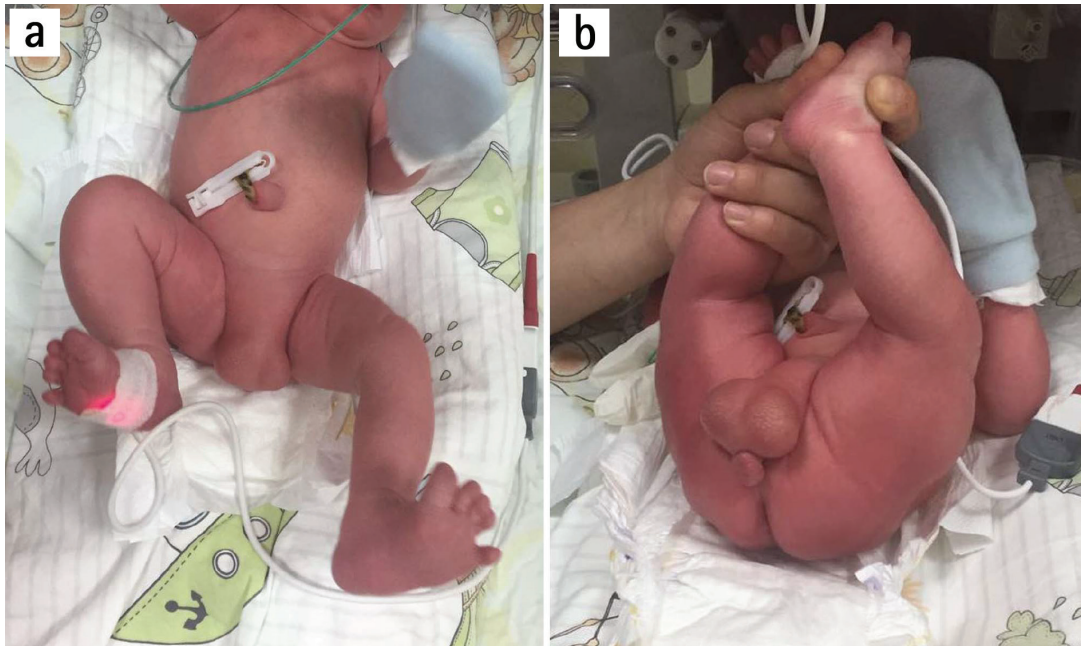

Figure 1. Complete penoscrotal transposition of a newborn a) Shows the scrotum without the penis b) Showing the penis under the scrotum

the penis accompanying a midline skin tag anterior to the anal region[5]. Moreover, a complete physical examination must be performed to detect abnormalities of the cardiovascular, central and peripheral nervous system, digestive system, urinary tract, and genital system because PST may present itself with a broad range of clinical manifestations that cause significant morbidity and mortality[6]. Surgery is the gold standard of PST management, which is usually preferred to be performed between 12-18 months. Although complete PST is rarely reported in the literature, considerable surgical skill is needed to reconstruct the penile anatomy.

Ethics

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.B., Concept: F.B., H.A., Design: F.B., Data Collection or Processing: E.P., Analysis or Interpretation: F.B., E.P., Literature Search: F.B., E.P., Writing: F.B., H.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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