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This page should only include the title of the manuscript, which should be carefully chosen to better reflect the contents of the study. No anusual abbreviations should be used in the title of the manuscript. A short title as running heading not exceeding 40 characters should be given which is desired to appear on top part of continuing pages when journal is published.

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— ***Book:*** Jones KL. Practical perinatology. New York: Springer; 1990. p. 112-9.

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Research Article

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Amniocentesis results and retrospective analysis performed in the university clinic

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Abstract

Objective: The aim of this study is to evaluate retrospectively the indications, karyotype results and complications of amniocentesis that we performed in our clinic.

Methods: Between January 2011 and January 2013 at the Department of Obstetrics and Gynecology Clinic of Kahramanmaraş Sütçü İmam University, 561 patients were analyzed retrospectively who applied amniocentesis procedure for high risk in double (1/300 and above) and triple test (1/270 and above), increased nuchal translucency (≥2.5 mm), history of child with Down syndrome, history of baby anomalies, abnormal ultrasound findings (cystic hygroma, choroid plexus cyst, diaphragmatic hernia etc.).

Results: Amniocentesis was performed in 561 patients in our clinic during 2011 and 2012. The most common indication was a high risk at triple test with 65.5%. As a result of amniocentesis, it was found that 34 patients (6.06%) had abnormal karyotypes. Abnormal karyotype was found in 18 of 368 patients (4.89%) with high risk at triple test, in one of 32 patients (3.1%) with advanced maternal age, in 4 of 63 patients (6.34%) with high risk at double test, in 9 of 80 patients (11.25%) with abnormal ultrasound findings, and 2 of 5 patients (40%) with hydrops fetalis.

Conclusion: Although it may lead to serious complications including fetal loss, amniocentesis is the most commonly and easily performed, and reliable invasive test for prenatal diagnosis of genetic disease.

Key words: Amniocentesis,indications, chromosomal abnormalities.

Üniversite kliniğinde uygulanan amniyosentez sonuçları ve retrospektif analizi

Amaç: Çalışmanın amacı kliniğimizde yapılmış olan amniyosentezlerin endikasyonlarını, komplikasyonlarını ve karyotip sonuçlarını retrospektif olarak değerlendirmektir.

Yöntem: Ocak 2011 ile Ocak 2013 tarihleri arasında Kahramanmaraş Sütçü İmam Üniversitesi Kadın Hastalıkları ve Doğum kliniğinde; ikili testte yüksek risk (1/300 ve üzerinde), üçlü testte yüksek risk (1/270 ve üzerinde), artmış ense kalınlığı, Down sendromlu bebek öyküsü, anomalili bebek öyküsü ve anormal ultrasonografi bulguları (kistik higroma, koroid pleksus kisti, diyafragma hernisi vb.) olması nedeniyle amniyosentez uygulanan 561 hasta retrospektif olarak incelendi.

Bulgular: Kliniğimizde yapılan 561 amniyosentezde en sık saptanan endikasyon %65.5 ile üçlü testte yüksek risk olan hastalardı. Amniyosentez sonuçlarında 34 (%6.06) hastada anormal karyotip saptandı. Üçlü test riski yüksek olan 368 hastanın 18'inde (%4.89), ileri anne yaşı nedeniyle amniyosentez yapılan grupta 32 hastadan 1'inde (%3.1), ikili testte yüksek riske sahip olan 63 hastadan 4 tanesinde (%6.34), anormal ultrasonografi bulguları saptanan 80 hastanın 9'unda (%11.25) ve hidrops fetalis saptanan 5 hastanın 2'sinde (%40) anormal karyotip saptandı.

Sonuç: Amniyosentez; fetal kayıp gibi ciddi komplikasyonları olmasına rağmen, prenatal tanıda ve genetik hastalıkların tanısında oldukça sık ve kolay uygulanabilen güvenilir bir invaziv yöntemdir.

Anahtar sözcükler: Amniosentez, endikasyon, kromozom anomalisi.

Introduction

Nowadays, it has become possible to diagnose many fetal chromosomal abnormalities with the help of common use of screening tests for prenatal diagnosis such as first trimester screening tests (nuchal translucency, free beta-hCG, PAPP-A) and second trimester screening tests (triple and quadruple screening tests) as a result of the rapid developments observed in biochem-

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ical and cytogenetic methods and in ultrasonography technology.[1] One of the main objectives of today's modern maternal and fetal medical science comprises the diagnosis of genetic abnormalities in prenatal period and the necessary measures taken in accordance with the types of pathologies.[2] For this purpose, amniocentesis is a common diagnosis method. Amniocentesis for genetic purposes was blindly administered through vaginal route in the past; transabdominal route started to be used in 1960s. It started to be applied under the guidance of static ultrasonography (USG) in 1980s.[3]

Classical amniocentesis is generally applied between 16-20 weeks of gestation. In this period, the transition ratio of living cells to non-living cells in amniotic fluid is higher than the ratio in late pregnancy weeks (>20th week of gestation).[4] Multicenter studies carried out so far have shown the reliability of amniocentesis for mother and fetus.[5-7]

Amniocentesis procedure has various indications such as over 35 years of maternal age, habitual abortus, history of abortus or delivery where chromosome pathologies were observed, abnormal karyotype in couples, history of infant delivery with multiple major malformation whose karyotype determination was not performed beforehand, high risk in triple test, high risk in NT test conducted in 11-14th weeks, findings which make the physicians think of the possibility of aneuploid in ultrasound analysis and anxiety.[8]

Even though amniocentesis is a reliable diagnosis method, it causes certain complications. These complications are inversely proportional to the experience of the person who applies the method.[9] Amniotic fluid leak, vaginal bleeding, uterine contractions, chorioamnionitis, sampling failure, fetal loss and possible fetal injuries are among the complications of amniocentesis. Fetal loss rate in amniocentesis is 0.5% or less.[10] In our study, we would like to share the indications and results of the amniocentesis cases which were applied to high risk pregnants during 2011 and 2012 in our clinic.

Method

We retrospectively analyzed 561 cases with some indications such as high risk in triple test (>1/270), high risk in double test (>1/300), NT thickness (≥2.5 mm), history of children with Down syndrome, history of abnormal baby, abnormality in ultrasonography (cystic hygroma, omphalocele, diaphragmatic hernia, etc.) and to which amniocentesis was applied from January 2011 to January 2013 in the Department of Obstetrics and Gynecology, Kahramanmaraş Sütçü İmam University. The families were informed about the amniocentesis procedure, the role of this method in diagnosis and also its complications before the application. Written informed consent forms were filled by the families who accepted the process.

After that, the materials which would be used in amniocentesis were prepared to be sterile and were placed on a sterile cover. Ultrasonography was administered to all patients before the amniocentesis and their placenta localizations were determined. Amniocentesis was performed by using free-hand technique together with Aloka 4000 Prosound model 3.5 MHz transabdominal probe with colored Doppler ultrasonography through amniotic pocket that is far from placenta and which does not contain the fetal parts and where the cord is not situated after the abdomen was cleaned with providone-iodine. 1-2 ml amniotic fluid which was taken in the first place was discarded in order to prevent maternal contamination. Then 15-20 ml amniotic fluid was taken from all of the patients. If the fluid was light colored and clean, it was put into an empty tube; if it was bloody or blurry, it was placed into a tube with media and the tubes were sent to the laboratory as it would be delivered within 24 hours. After the application, anti-D immune globulin was administered to the patients having Rh incompatibility. The patients took a rest in bed for 30 minutes subsequent to the application and they were asked to come to hospital for the controls for the following week and following month.

The cases were retrospectively analyzed in terms of amniocentesis indications and results.

Results

Amniocentesis was applied to 561 patients in our clinic in 2011 and 2012. The mean age of the patients was 31.5 (range: 17-48) years. The indications and rates of amniocentesis application to the patients were shown in the **Table 1.** The patients who had high risk in triple test constituted the most frequent indication with a rate of 65.5% within the patient groups.

Abnormal karyotype was detected in the results of the amniocentesis applied to total 34 (6.06%) patients. Abnormal karyotype rate was 4.89% in the patient group with high risk in triple test, 11.25% in the

Table 1. Indications and rates of amniocentesis.

Indication	n	(%)
High risk at triple test	368	65.59
High risk at double test	63	11.22
Abnormal ultrasound findings	80	14.26
History of child with Down syndrome and baby anomalies	7	1.24
Advanced maternal age	32	5.70
Hydrops fetalis	5	0.89
Severe IUGR, prenatal infection	3	0.53
Elective	3	0.53
Total	561	100

IUGR: intrauterine growth restriction

patients with abnormalities founded in ultrasonography, 6.34% in those with high risk in double test, 40% in those with hydrops fetalis and 3.1% in the patients to whom amniocentesis was administered because of age risk (**Table 2**).

Gestational week, maternal age, amniocentesis indication and karyotype results of the 34 patients who had abnormal karyotype are presented in **Table 3.** Trisomy 21 (Down syndrome) became the most commonly seen abnormal karyotype with a rate of 47% in this patient group. Trisomy 18 was 8.8% while Turner syndrome was 5.8%. Palliester-Killian syndrome was found in a patient whereas 47,XXX (triple X syndrome - trisomy X) was seen in another.

Discussion

Amniocentesis is the most commonly used and very reliable prenatal diagnosis method. Today, amniocentesis process is advised for the families with high risks detected in the fetal screening tests conducted in first and second trimesters in order to alleviate their anxiety. As it is known, the conditions such as advanced maternal age, parental balanced translocation, history of children with chromosomal abnormality, detection of fetal abnormality in USG, high risk in double-triple tests are the indications of amniocentesis.[11] Sjogren et al. specified that advanced maternal age was the most common reason for application with a case rate of 57% in the amniocentesis they applied.[12] Also, the advanced maternal age is known to be most common reason of intervention in various amniocentesis series published in our country.[13] On the other hand, Tongsong et al. stated that the percentage of indication in the amniocentesis they carried out was 86.3% for advanced maternal age, 5% chromosomal abnormality in the former child, 3.1% for chromosomal abnormality in spouse and family and 0.6% for ultrasonographic pathology.[14] In this study, we found that high risk in triple test (65.5%) was the most common amniocentesis indication. Of the patients taken part in our study, the maternal age of 228 (40.6%) was over 35 years. When the interventional treatment is applied for the purpose of prenatal diagnosis to the pregnant who is over 35 years, 25-40% of the cases with Down syndrome can be diagnosed.[15] Singh et al. determined the percentage of sensitivity of triple screening test, carried out in the second trimester, for Down syndrome in the cases of advanced maternal age as 92.3% with 0.8% margin of error.[16] Yuce et al. stated that chromosomal abnormality rate was 3.7% in the amniocentesis which they applied because of high risk in triple test in their own series while Wenstrom et al. gave this rate as 2.9% in the series of 516 cases. Bal et al. specified this rate as 3.9%.[12,17-20]

The probability of chromosomal abnormality in amniocentesis highly increases in the existence of fetal abnormality. Chromosomal abnormality rate in the amniocentesis applied after the determination of fetal

Table 2. Results of amniocentesis and indications for patients with abnormal karyotypes.

Indication	Abnormal karyotype	n	(%)
Advanced maternal age	1	32	3.1
High risk at triple test	18	368	4.89
High risk at double test	4	63	6.34
Abnormal ultrasound findings	9	80	11.25
Hydrops fetalis	2	5	40
Total	34	561	6.06

Table 3. Gestational week, maternal age, amniocentesis indication and karyotyping results of patients who were found to have abnormal karyotypes.

No	Gestational week (week+day)	Maternal age	Indication	Abnormal karyotype
1	17+6	18	High risk at triple test	46, inv (9)(p11q13)
2	18+4	31	High risk at triple test	46, t (5:9)(q13:q24)
3	17+6	32	High risk at triple test	Trisomy 21
4	20+3	40	High risk at triple test	Trisomy 21
5	17+0	35	Cystic hygroma	Trisomy 21
6	18+6	26	Hydrops, cystic hygroma	46, inv(9)(p11q13)
7	16+5	38	Cystic hygroma	Trisomy 21
8	17+0	39	High risk at triple test	Trisomy 21
9	20+0	23	High risk at triple test	Trisomy 21
10	18+6	28	High risk at triple test, pleural effusion	Trisomy 21
11	17+3	21	High risk at triple test	Trisomy 21
12	16+4	29	High risk at double test	Trisomy 18
13	17+2	43	High risk at double test	47,XXX
14	18+0	35	Bilateral pes equinavarus	Trisomy 18
15	17+4	38	High risk at triple test	Trisomy 21
16	15+0	43	Non-immune hydrops fetalis	Trisomy 21
17	18+5	44	High risk at triple test	Trisomy 21
18	16+6	38	High risk at triple test	Trisomy 21
19	19+6	31	Ventricular septal defect, choroid plexus cyst	Trisomy 18
20	16+6	28	High risk at triple test	46,+15
21	16+2	17	Cystic hygroma	45, X, Turner
22	16+4	21	High risk at triple test	46,13pss
23	17+3	42	High risk at double test	Trisomy 21
24	18+3	27	High risk at triple test	47,+mar
25	19+5	33	High risk at triple test	Trisomy 21
26	21+6	39	High risk at triple test	47,+mar
27	18+4	37	Advanced maternal age	46,21cenh+
28	22+4	36	Diaphragmatic hernia, ventriculomegaly	47,+i(12)(P10)
29	17+4	36	High risk at triple test	46,inv(9)(p11q13)
30	22+0	38	Complete atrioventricular defect	Trisomy 21
31	18+0	25	High risk at triple test	46,inv(9)(p11q13)
32	18+4	35	High risk at double test	46,inv(12)(p11 2q15)
33	15+4	34	Hydrops fetalis	45, X, Turner
34	20+3	41	High risk at triple test	Trisomy 21

abnormality in ultrasonography ranges between 4% and 27%.[21-23] Rizzo et al. found out the rate of chromosomal abnormality as 16.8% in the fetuses having abnormality observed in USG[19] whereas this rate was 27.1% in the study of Dallaire et al.[20] In our study, amniocentesis was applied to 80 mothers (14.3%) in consequence of abnormality findings specified in USG analysis. It was found that 9 (11.25%) of those patients had chromosomal abnormality.

It has been stated in certain studies that frequency of complication related to the operation increases when transplacental amniocentesis is applied.[24] Some

reports indicate that the rate of complication, which may occur subsequent to amniocentesis, increases because of making needle insertion more than once.[25] The rate of fetal loss related to amniocentesis ranges between 0.05% and 1% in the hands of experienced physicians. According to Eddleman et al., the fetal loss rate was 0.15% in the series of 1605 cases.[23] Armstrong et al. gave this rate as 0.2% in the series of 28,163 cases.[26] In the series carried out in our country, fetal loss rate in amniocentesis ranges between 0.6% and 3.3%.[27,28] In a study conducted in our country, Sener et al. expressed that amnionitis leak may be observed in a rate of 0.1% while this leakage rate may be 1-2% for amniotic fluid subsequent to amniocentesis.[29] Possible complications on mothers may be seen less often in amniocentesis. These complications are perforation in visceral organs, amniotic fluid embolization and Rh sensitization.[30] Rh isoimmunisation risk rate has been determined as 1.4-3.4% subsequent to amniocentesis in certain studies.[31] In normal pregnancies, immunization rate is 1.1-2.2%; such increase of risk was not observed in some studies.[32] Non-reproduction rate in the culture is found as 0.6-1% subsequent to amniocentesis carried out between 15-20th weeks in the literature.[33] We found this rate as 2.1% in our study.

Conclusion

As a result, although it might lead to serious complications including fetal loss, amniocentesis is the most commonly and easily performed, and reliable invasive test for prenatal diagnosis of genetic disease. Genetic amniocentesis has a high success rate when performed by experienced physician in 15-20 weeks of gestation. It should be offered to patients when the patient has a correct indication.

Conflicts of Interest: No conflicts declared.

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Newborn autopsies: experience of referral level III neonatal intensive care unit in Turkey

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Abstract

Objective: Neonatal autopsies are a guide to explore the causes of the perinatal mortalities which is important marker for evaluation of the health policies. Multidisciplinary approach which includes obstetrician, pediatrician, pathologist and geneticist is required for the neonatal autopsies. In our study, we have examined the significance of neonatal autopsy in neonatal deaths occurred in our clinic within 2 years, and analyzed whether neonatal autopsy has any impact on confirming and/or modifying reason of death.

Methods: Thirty-eight neonatal autopsies between January 2009 and December 2010 were evaluated in respect to demographic characteristics, clinical and pathological diagnosis retrospectively.

Results: Totally 7055 neonates were hospitalized in our neonatal intensive care unit between January 2009 and December 2010. Among them, 404 of the neonates passed away (5.7%). Only 38 (9.4%) of the neonates' parents gave permission for autopsy. Fifteen of these neonates were female (39%) and 23 of them were male (61%). Sixty percent of these neonates were premature. Prematurity was higher in male neonates (p=0.001). Median week of gestation was 32 (22-41). Median overall survival of the neonates were 4 (0-80) days. When compared according to gender, there was statistically no significant difference between survival periods. Prematurity rate was quite high among male neonates (p=0.001). Eighty-three percent of the clinical diagnoses were correlated with the pathological diagnosis. Sixty percent of the clinical and pathological diagnoses were cardiovascular anomalies, diaphragmatic hernia, perinatal asphyxia and prematurity. Two neonates had pneumonia diagnosis by the autopsy. Only one of these cases had chorioamnionitis in the placenta.

Conclusion: Neonatal autopsy rates should be increased to decrease the neonatal mortality rate in our country. Neonatal autopsies should be done with multidisciplinary approach and become prevalent and get more progress in our country.

Key words: Newborn autopsies, mortality, intensive care.

Yenidoğan otopsileri: Tek merkez deneyimi

Amaç: Yenidoğan otopsileri, sağlık politikalarının değerlendirilmesinde önemli olan perinatal mortalitenin sebeplerinin belirlenmesinde yol göstericidir. Yenidoğan otopsisi, kadın doğum ve klinik genetik uzmanı, pediatrist ve patologdan oluşan bir ekip işidir. Çalışmamızda, ünitemizde 2 yıllık süreçte meydana gelen neonatal ölümlerde yenidoğan otopsisinin yeri, otopsinin, ölüm nedenini kesinleştirme ve/veya değiştirmede etkili olup olmadığı incelenmiştir.

Yöntem: Ünitemizde Ocak 2009 - Aralık 2010 tarihleri arasında otopsi izni alınan 38 hastanın demografik özellikleri, klinik ve patolojik tanıları retrospektif olarak incelendi.

Bulgular: Belirtilen tarihler arasında 7055 hasta yenidoğan yoğun bakım ünitesine yatırılmış, 404 hasta kaybedilmiş (%5.7) ve bunların 38'inden (%9.4) otopsi izni alınmıştır. Bu hastaların 15'i (%39) kız, 23'ü (%61) erkekti. Otopsi yapılan yenidoğanların %60'ı prematüre idi. Hastaların ortanca gebelik haftası 32 (22-41) hafta bulundu. Hastaların ortanca ölüm süresi 4 (0-80) gün idi. Cinsiyete göre gruplandırıldığında ölüm süresi arasında istatistiksel anlamlı bir fark saptanmadı. Erkek bebeklerde prematürite oranı belirgin olarak yüksekti (p=0.001). Klinik tanı patolojik tanı ile %83 oranında uyumlu idi. Klinik ve patolojik tanıların %60'ını kardiyovasküler anomali, diyafram hernisi, perinatal asfiksi ve prematürite oluşturmakta idi. Otopsi ile 2 olguda pnömoni tanısı konuldu. Bu olguların sadece birinin plasentasında koryoamniyonit tespit edildi.

Sonuç: Ülkemizde neonatal mortalitenin düşürülmesi için neonatal otopsi oranları arttırılmalı, neonatal otopsinin ülke genelinde yaygınlaşması için ekip çalışması yönündeki eğilimlerin yaygınlaştırılması ve geliştirilmesi gereklidir.

Anahtar sözcükler: Yenidoğan otopsileri, mortailite, yoğun bakım.

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Introduction

The word autopsy is formed of 'autos' which means 'self' and 'opsis' which means 'view'. It briefly means the act of seeing with one's own eyes. Autopsy contributes to detect reason of death and to confirm diagnoses unknown previously, to understand new diseases, and to establish efficiency and reliability of new diagnostic and therapeutic approaches of clinical diagnosis. Its contribution to public health statistics and training is indisputable. Newborn autopsy provides very valuable information for offering consultancy to parents who lose their babies. Also, showing actual reason of death by autopsy may relieve the guilt feelings of parents due to maternal diseases or medication. Perinatal autopsy is obligatory for learning actual reason of death and follow-up next pregnancies of individual. Basic reason of such examinations is to determine the recurrence risk of event and to guide prenatal diagnosis and follow-up for next pregnancies addition to find actual reason of death.

By the studies performed, it has been shown that the data obtained by perinatal autopsy is able to change 22-76% of clinical diagnoses, 40% of estimated recurrence risk, 9% of preconceptional care recommendations, 21% of prenatal diagnostic procedures, 7% of prenatal management, and 3% of neonatal management.[1] Despite the advanced modern clinical researches, autopsy has been modifying 30% of antemortem misdiagnoses.[2] It has been shown in the study performed by Kumar et al. that neonatal autopsy gives a chance for new diagnosis at a rate of 44%.[3] Some particular pathologic diagnosis in perinatal autopsy has a role to give clue for diagnosing specific diseases. For example, when intraluminal calcifying meconium may indicate trisomy 21, intestinal atresia or cystic fibrosis, cardiac rhabdomyoma may indicate tuberous sclerosis, myocardial infarct, and secondary calcifying focus may indicate trisomy 21 or 13.

In our study, we have examined the significance of neonatal autopsy in neonatal deaths occurred in our clinic within 2 years, and analyzed whether neonatal autopsy has any impact on confirming and/or modifying reason of death.

Method

Demographic data, and clinical and pathologic diagnoses of 38 neonates with autopsy permission were examined retrospectively between January 2009 and December 2010.

Results

Totally 7055 neonates were hospitalized in our neonatal intensive care unit between January 2009 and December 2010, 404 of them passed away (5.7% mortality) and autopsy permission was obtained for 38 of them (9.4%). While 15 of them were female (39.4%), 23 of them were male (60.6%). Sixty percent of these neonates were premature. Median week of gestation was found to be 32 (22-41). Median overall survival of the neonates were 4 (0-80) days. When compared according to gender, there was statistically no significant difference between survival periods. Prematurity rate was quite high among male neonates (94% vs. 33%; p=0.001).

The correlation of clinical diagnosis with pathologic diagnosis was 83.3%. Sixty percent of the clinical and pathological diagnoses were cardiovascular anomalies (CVS), diaphragmatic hernia, perinatal asphyxia and prematurity. The most frequent diagnoses were CVS anomaly in 4 cases, diaphragmatic hernia in 2 cases, and perinatal asphyxia in 2 cases. The most frequent secondary diagnosis accompanying the reason of death was prematurity, while the most frequent pathologic new diagnosis was pneumonia in 2 cases. Autopsy results and characteristics are listed in **Table 1.**

Discussion

Death at neonatal period may depend on many reasons. Metabolic diseases such as disorders of long chain fatty acid metabolism may cause sudden infant deaths in the very first days of life. This disease can be defined by checking carnitine/acylcarnitine profile in Guthrie sample or showing increased chylomicron in liver or heart tissue to be taken in no time, and DNA may be extracted from these samples. Therefore, sample should be taken to Guthrie card in newborn deaths. Routine autopsy diagnosis of metabolic diseases is nonspecific. No diagnosis is established during autopsy except the diagnoses coherent with sepsis in many cases. There is no way to establish diagnosis other than taking samples just before or after death. In fact, it is recommended to inform family about deterioration, and to ask permission for biopsy and even autopsy before baby is lost. Even though such permission cannot be obtained, it is significant to get required samples for diagnosis: blood sample to be taken onto Guthrie card, blood sample, plasma or serum sample to be taken into tube with EDTA, and sterile urine sample.

Table 1. Characteristics of autopsy cases.

Autopsy number	38
Delivery week	32 (22-41)
Birth weight	1685 (436-3330)
Gender (F/M)	15 (%39.4) / 23 (%60.6)
Median death day	4 (0-80)
Maternal age	27 (20-36)
Coherence rate of clinical diagnosis - autopsy diagnosis	32/38
Prematurity in diagnosis	
Available	23/38 (%60)
N/A	15/38 (%40)
Anomaly in diagnosis	
Available	17/38 (%44.7)
N/A	21/38 (%55.3)
CNS anomaly in diagnosis	
Available	2/38 (%5.2)
N/A	36/38 (%84.8)
CVS anomaly in diagnosis	
Available	4/38 (%10.4)
N/A	34/38 (%89.6)

CNS: Central nervous system, **CVS:** Cardiovascular system.

Skin biopsy, and if possible, muscle and liver, brain and heart muscle tissue samples to culture are very helpful for diagnosis.

The medical history which is very significant in pediatric approach also has a serious impact on neonatal autopsy results. Ethnical origin, consanguinity background, maternal diseases, and previous pregnancy history enlighten diseases to be researched. For instance, the deficiency of long chain 3-OH acyl coenzyme A in fetus causes HELLP syndrome, acute hepatic lipidosis, and persistent emesis in pregnant woman. As another example, steroid sulfatase deficiency causes prolonged labor since it is the reason of decreased placental estrogen production. Oligohydramnios and polyhydramniosis histories are also helpful to detect pathology in fetus.

Photographing postmortem patient also helps to diagnose. Not only abnormal findings but also normal findings can be helpful. For example, pictures showing the presence of normal nails and normal fingers may help to rule out many syndromes.

Although direct postmortem radiological imaging may provide very detailed data, it is frequently overlooked in Turkey. However, by the imaging, gestational age can be guessed by checking ossifications, it becomes possible to determine fractures (if any) and their timings, and significant data can be obtained by determining abnormal gas flatulency and calcifications in extra-osseous organs (i.e. meconium peritonitis, hepatic, adrenal calcification). The radiography to be performed should include entire anteroposterior-lateral body, head should be positioned straight, nose should be aligned with umbilicus and upper and lower limbs should be in anatomical position. Kalifa et al. showed in their study that postmortem direct imaging provided significant data at the rate of 13.5%, and additional data at the rate of 34.5%.[4] Gronvall and Graem stated that abnormalities were detected at a rate of %59 by direct graphies.[5] It is recommended to do radiological imaging, if possible, in cases where autopsy is especially refused.[6]

Also, many new methods have been discussed for cases where autopsy is impossible. There are on-going studies on needle autopsy, endoscopic autopsy, ultrasonographic autopsy (echopsy), verbal autopsy and magnetic resonance (MRI) autopsy.[7] Although MRI autopsy performed by postmortem MR imaging seems to be non-invasive and more advantageous than conventional autopsy for showing cranial pathologies, the golden standard is still the conventional autopsy,[8] because MRI autopsy is still insufficient for cardiac pathologies, and it has a high rate of false positivity since it detects intraventricular bleeding and hematomas which cannot be detected in conventional autopsy. Also, it does not allow performing histopathological examination.

One of the most significant reasons for low rates of autopsy is the difficulty to get autopsy permission. There are some reasons preventing to get autopsy permission. It was reported in a study performed that hospitalization is a significant factor, and that autopsy permission was obtained for 82% of those who survived 1 day or less, for 75% of those who survived longer than 3 months and for 52% of those who survived 2-92 days.[9] In another study, it was shown that number of autopsy permission obtained increases as postnatal age and hospitalization in intensive care unit increase.[10] It was also indicated that premortem diagnosis is significant. The rate of obtaining autopsy permission for babies with asphyxia diagnosis was two times higher

than those with cardiac pathology.[9] Another significant factor is doctor who attempts to obtain permission. It was reported that a doctor who is in a consultant position or performs follow-up of baby continuously has a higher rate to get the permission.[9] Also, doctors sometimes have hesitations for asking autopsy permission. There are three reasons: not being a perinatal pathologist, not to upset family anymore, or the necessity to ask signing another informed consent form. Another reason for the hesitation is the concern that autopsy result may cause to question clinical judgments.[11]

Religious beliefs also have a significant impact on autopsy permissions. In Turkey, 88.7% of the population defines themselves as Muslim. In Islam, a voluntary autopsy cannot be allowed since it is believed that autopsy ruins the body and makes it ugly. Also Islam advises to bury dead bodies before sunset, and it is thought that autopsy may delay the burial.[12] According to Islam, death is the will of Allah and is a natural part of life, so autopsy can be seen as necessary.[13] Besides, it is stated that hurting dead one is equivalent to hurt living one.[14] Special procedures are required to prepare body for the life after death, and it is thought that autopsy may ruin such preparations.[13] Since Islam advises to bury dead bodies in a short time, a Muslim family should be assured when asking for autopsy permission that autopsy will be done timely.[15] Also, informing family that the body will be buried intact, and that internal organs can be replaced after examination may help to obtain autopsy permission easily.[12] Family should be communicated well; communication with spouse who is head of family or the oldest individual in family may help to communicate for autopsy permission.[12,14] Additionally, during decision making, family can discuss with an Islamic scholar or imam.[14] Islam does not allow tormenting dead ones; so, family should be informed that such torment will not occur, and advantages of autopsy should be communicated.

Autopsy form of all patients with obtained autopsy permission should be filled completely, death certificates should be completed properly in all infant deaths, and information form for perinatal and neonatal deaths should be filled as reason of death includes a single diagnosis.

Ideally, newborn autopsy is performed by a perinatal pathologist. However, even though pathologist is very experienced and well-educated, briefing by clinician changes the result and quality of autopsy distinctly. Sharing medical history of patient and mother, laboratory and imaging results, rare findings in patient, and negative and positive findings about diagnoses considered by clinician may guide autopsy. If required, slide, photograph, radiological findings, and consultation results should be reported to pathologist.

The method to be followed during autopsy may vary according to birth weight, being term or preterm, and presence of anomaly or hydrops in case (**Fig. 1**). No matter what method is followed by pathologist, it is important to remember that placenta is also a fetal organ and should be examined in detail. It provides significant information about prenatal period, and also postnatal prognosis and late phase diseases.[16-18] For example, presence of non-occlusive mural thrombus is associated with increased fetal thromboembolic complication risk in term baby.[19] Chorionic villus edema detected before any particular chorionic vasculitis is associated with increased cerebral palsy and decreased neurological function risk in babies with extremely low birth weight. Naeye et al. associated chorionic villus edema with increased mortality and morbidity in preterm babies, and reported that it can be the indicator of decreased fetal cardiac functions.[20] In another study, acute chorioamnionitis was associated with low scores of childhood cognitive tests.[21] Also, very important placental findings showing whether fetal ischemia is chronic or acute are especially helpful for forensic cases.[22] Moreover, when autolysis occurs in stillbirth cases, the most appropriate location for karyotype analysis is placenta. In placenta examination, cord length and blood vessel number is important. For example, a short cord indicates a neuromuscular disease while long cord indicates heart failure, and changes in blood vessel number indicates concomitant anomalies. A swab culture to be taken from placenta by stripping corio is a suitable medium for generating microorganisms which are the reason of death. It has been shown that the cells on fetal part of placenta may survive a few weeks even after death of fetus. When required, karyotyping can be carried out by taking biopsy under sterile conditions from fetal membrane or chorion. Consequently, placenta is a fetal organ and an essential part of autopsy. In addition to placenta, cord examination in stillbirths is recommended particularly.[23]

Congenital anomalies are the reason of a significant part of deaths during perinatal period. Most of the congenital anomalies are caused by chromosomal abnor-

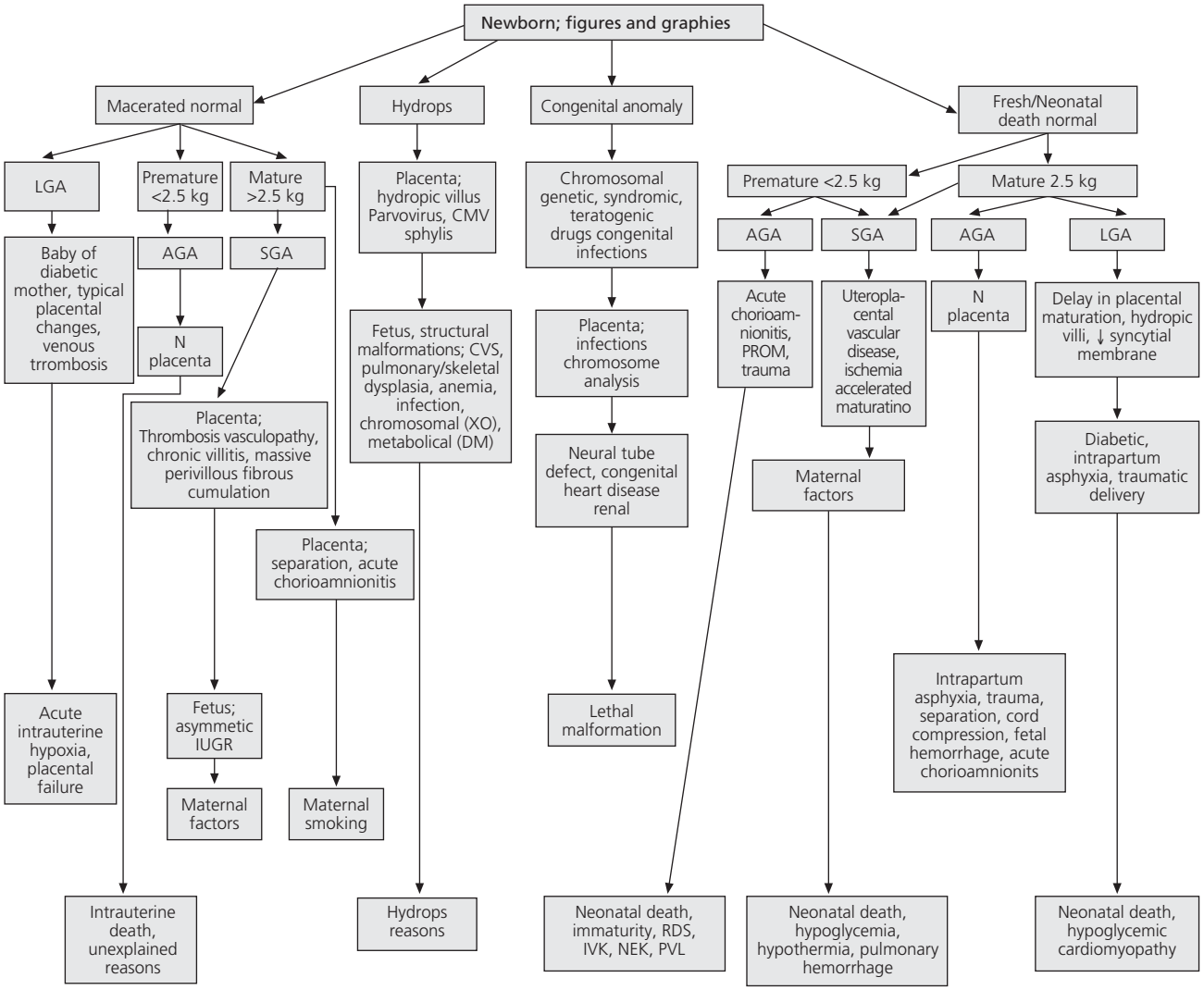

Fig. 1. The method to be followed in newborn autopsy.

AGA: appropriate for gestational age, **CMV:** cytomegalovirus, **CVS:** cardiovasculsr system, **DM:** diabetes mellitus, **IUGR:** intrauterine growth restriction, **IVG:** intraventricular bleeding, **LGA:** large for gestational age, **N:** normal, **NEC:** necrotizing enterocolitis, **PROM:** premature rupture of membranes, **PVL:** periventricular leukomalacia, **RDS:** respiratory distress syndrome, **SGA:** small for gestational age.

malities or are a part of a syndrome. Especially in these cases, information to be obtained by autopsy or chromosome study is quite essential and required to determine the recurrence risk and to follow up next pregnancies. When a genetic disease is considered, patient should be examined by genetic expert when alive and tissue sample should be reserved. If this is not possible, genetic expert should be consulted during autopsy. If patient has skeletal dysplasia or craniosynostosis, tissue should be retained for karyotyping and DNA study, and long bone should be frozen if possible. If arthrogryposis is present, karyotyping, muscle and spinal cord biopsy should be planned, and skin and muscle tissue should be retained. If patient has renal anomaly, urine analysis and karyotyping should be performed, and skin or renal tissue should be frozen. If congenital metabolic disease is suspected, gall sample, skin, brain, muscle and liver tissues should be retained. If a baby with hydrops fetalis dies before examinations are performed, appropriate samples should be taken immediately for hemogram, peripheral smear, blood type, viral culture and karyotyping.

Cytogenetic study should be conducted if patient has clinical suspicion, mother has 3rd loss, and there are non-immune hydrops fetalis, serious growth failure, there are more than two anomalies, a particular specific anomaly exists (i.e. complete atrioventricular canal defect), mother or father has known translocation, and if abnormal amniocentesis karyotype is detected.

Although progress has been made in pathological procedures such as immunohistochemistry, electron microscope, there has been a serious decline in newborn autopsy rates during the last decade. In a study performed, this rate has decreased from 71.2% (1984-1988) to 47.7% (1989-1993) in the USA.[3] This can be associated with various reasons. Increase in trust to imaging methods, actions for compensation, and lack of communication between pathologist and clinician may cause these reasons.[24,26]

In the study performed by Feria-Kaiser et al., two thirds of neonatal autopsies are congenital cardiopathy, prematurity, congenital syndromes and respiratory distress syndrome diagnoses .[27] In the study carried out on neonatal autopsies by Özkınay et al., it was observed that lethal anomalies (21%) in fetal autopsies are the second most frequent fetal death reason after asphyxia, while lethal anomalies in neonatal autopsies are the second most frequent fetal death reason after issued associated with prematurity and immaturity.[28] In our study, 60% of newborns autopsied were premature and anomalies were present in 44.7% of them. We consider the reason as our center is perinatology reference center.

Özdemir et al.[29] reported by their study that there was no change in diagnosis of 25 cases (73.5%) after autopsy, there were additional findings in 4 cases (11.7%), that diagnosis was changed in 4 cases (11.7%), and diagnosis was completely discordant in one case (2.9%). In our study, 83.3% of the clinical diagnoses were correlated with the pathological diagnosis; in 2 (5.2%) cases, diagnosis was changed completely.

Conclusion

Perinatal mortality rate is an inseperable part of common health policy of the country, and it is an essential criterion to evaluate the efficiency of primary pediatric health services in the society, and to compare with other countries. In perinatal deaths, autopsy should be carried out in order to examine the actual reason of deaths, to scrutinize the accuracy of clinical interpretation considered as death reason and to determine congenital anomalies. Multidisciplinary approach which includes obstetrician, pediatrician, pathologist and geneticist is required for the perinatal autopsies. Within a team work, obstetrician should provide detailed information about the follow-up and delivery, and pediatrician should provide detailed information about neonatal history. When required during autopsy, clinical geneticist should examine infant before autopsy and work with pathologist for syndrome considered. Normal and abnormal conditions should be documented, and anomalies which are hard to express verbally should be photographed. Full body radiography (lateral and anteroposterior) should be a routine part of the autopsy. Karyotype examination may be helpful in those with malformation, intrauterine growth retardation, maternal anamnesis, and fetal loss anamnesis in previous pregnancies. In fetal deaths, and in neonatal deaths if possible, placenta and cord should certainly be examined histologically. Autopsy is still of great value for final diagnosis and confirming diagnosis.

Conflicts of Interest: No conflicts declared.

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Placental abruption and analysis of risk factors

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Abstract

Objective: It was aimed to evaluate pregnancies with suspected placental abruption and investigate the related risk factors.

Methods: Ninety-four pregnancies who delivered by cesarean section for suspected placental abruption in Zeynep Kamil Hospital between 01.03.2012 and 31.01.2013 were included in this study. During the operation, the placenta was examined macroscopically. The presence of retroplacental bleeding or clots in the placenta confirmed the diagnosis of placental abruption. Age, parity, height, weight, blood group, placental localization, previous delivery type, presenting symptoms, pregnancy complications were recorded.

Results: The diagnosis of placental abruption was confirmed in 43 (46%) patients while 51 of them (54%) were not confirmed. There was no significant difference between the groups in terms of maternal age, gestational age and body mass index. Mean arterial pressure (MAP) was 95.1±17.8 at the group with placental abruption confirmed and 85.4±8.7 (p=0.006) at the group with placental abruption not confirmed. Placental abruption is more frequent in patients with preeclampsia (OR=8.5; p=0.022). When the groups were compared according to their blood groups; 87.5% of pregnant women with 0 Rh (+) blood group was confirmed for diagnosis of placental abruption (OR=8.7; P=0.005).

Conclusion: Identification of risk factors for placental abruption is the basic criterion for the management and reduction of potential complications.

Key words: Abruptio placentae, mean arterial blood pressure, preeclampsia, 0 Rh (+) blood group.

Dekolman plasenta ve risk faktörleri

Amaç: Dekolman plasenta şüphesi olan gebeliklerin değerlendirilmesi ve risk faktörlerinin tanımlanması amaçlanmıştır.

Yöntem: Bu çalışmaya 01.03.2012-31.01.2013 tarihleri arasında Zeynep Kamil Kadın ve Çocuk Hastalıkları Hastanesi'nde dekolman plasenta şüphesi ile sezaryenle doğum yapan 94 hasta dâhil edildi. Operasyon esnasında plasenta makroskopik olarak incelendi. Plasenta da retroplasental kanama veya pıhtı görülmesi ile dekolman plasenta tanısı doğrulandı. Gebelerin yaş, parite, boy, kilo, kan grubu, plasenta lokalizasyonu, gebelik sürecindeki hastalıkları, önceki doğum şekli, başvuru şikâyeti, gebelik komplikasyonları kayıt edildi.

Bulgular: Olguların 43'ünde (%46) dekolman plasenta tanısı doğrulanırken, 51'inde (%54) doğrulanmadı. Gruplar arasında maternal yaş, gebelik haftası ve vücut kitle indeksi açısından fark saptanmadı. Ortalama arteriyel basınç dekolman plasenta saptanan grupta 95.1±17.8 iken dekolman plasenta saptanmayan grupta 85.4±8.7 (p= 0.006) olarak tespit edildi. Preeklampsi gelişen olgularda dekolman plasenta daha fazla saptandı (OR=8.5; p=0.022). Kan gruplarına göre gruplar karşılaştırıldığında; 0 Rh (+) kan grubuna sahip gebelerin %87.5'inde dekolman plasenta tanısı doğrulandı (OR=8.7; p=0.005).

Sonuç: Dekolman plasenta risk faktörlerinin tanımlanması; olguların yönetimi ve olası komplikasyonların azaltılmasında temel kriterdir.

Anahtar sözcükler: Dekolman plasenta, ortalama arteriyel kan basıncı, preeklampsi, 0 Rh(+) kan grubu.

Introduction

Placental abruption is defined as the case where placenta is separated from the uterus completely or partially. Approximately between 0.4% and 1% of pregnancies are complicated by placental abruption. Placental abruption is one of the most significant reasons of maternal and fetal morbidity and mortality.[1] Its clinical findings are vaginal bleeding, uterine tension and painful tetanic contractions. Its most significant risk factor is the placental abruption during pregnancy

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and advanced maternal age, intrauterine infections, oligohydramnios, polyhydramniosis, intrauterine growth retardation, extended rupture of membrane, preeclampsia, hypertension, multiple pregnancies, uterine anomalies, trauma, smoking and cocaine use are the other risk factors.[1-6]

The ultrasound diagnostic criteria for placental abruption are considered as the presence of intraamniotic, subchorionic or marginal hematoma, increase of placental thickness (>5 cm) and heterogeneity, preplacental and retroplacental collections, and ' jelly-like' movements on chorionic surface when fetus moves. More than 50% of the cases with placental abruption are not detected during ultrasound imaging and placental abruption diagnosis cannot be excluded if normal ultrasound findings are detected.[2,7]

In this study, we aimed to analyze gestational outcomes together with the demographical and clinical data of cases who delivered by cesarean section for suspected placental abruption.

Method

Ninety-four pregnancies, who delivered by cesarean section for suspected placental abruption in Zeynep Kamil Hospital between 01.03.2012 and 31.01.2013, were included in the study. Multiple pregnancies and those with chromosomal and structural abnormalities were excluded.

Pre-diagnosis of placental abruption was confirmed by clinical findings (vaginal bleeding, uterine sensitivity, and pain) and ultrasound findings (subchorionic or retroplacental hematoma, heterogeneity and thickness increase in placenta). Patients were planned to have cesarean section. During operations, placenta was examined macroscopically. Placental abruption was confirmed by the presence of retroplacental bleeding or clots in the placenta. When retroplacental bleeding or clot was not detected in the placenta, then the diagnosis of placental abruption was ruled out.

Patients who participated in the study were separated into two groups as those with confirmed placental abruption diagnosis and those without confirmed placental abruption diagnosis. Data of patients such as age, week of gestation, parity, blood type, complaint and mean arterial pressure (MAP=[systolic blood pressure + 2 x diastolic blood pressure]/3), body mass index (BMI; kg/m^2), gestational outcomes and complications, fetus gender, birth weight, Apgar score and whether newborn needs intensive care or not were recorded.

Statistical methods

Patient data were analyzed in SPSS 20 package program (SPSS Inc., Chicago, IL, USA). Definitive statistical analyses were carried out. Normal range coherences of variables were evaluated by Kolmogorov-Smirnov test. Independent samples T test was used in the comparison of the parameters with normal ranges while Mann-Whitney U test was used in the comparison of the parameters with abnormal ranges. Chi-square test and Fisher's exact test were used for the comparison of non-qualitative parametric data. The value $p<0.05$ was accepted as statistically significant.

Results

Ninety-four cases with placental abruption pre-diagnosis were included in our study. While the diagnosis of placental abruption in 43 (46%) of the cases, it was not confirmed in 51 (54%) of them. Encephalocele was detected in one of the cases with confirmed placental abruption diagnosis; data of the twelve cases could not be recorded. Thirteen cases were excluded from the study. In the group with confirmed placental abruption diagnosis, mean age was 28.6±6.8, mean parity was 1.0±1.1, mean week of gestation was 32±1, and mean BMI was 29.3± 4.8 kg/m^2; while these values were 28.7±5.7, 0.8±1.1, 33±16 and 28.5±4.4 kg/m^2 in the group with confirmed placental abruption diagnosis, respectively. There was no significant difference between two groups ($p\geq0.05$) (**Table 1**). No significant difference was observed when groups were compared in terms of their complaints (pain, vaginal bleeding, water break [amniotic fluid], decrease in fetal movements etc.) ($p=0.55$) (**Table 2**). There was also no significant difference between the groups in terms of placental localizations ($p=0.22$) (**Table 3**). However, placentation could not be detected during ultrasound imaging in one of the cases with confirmed placental abruption diagnosis, and emergency cesarean section was performed due to fetal bradycardia.

Mean arterial pressure (MAP) was 95.1±17.8 mmHg in the group with confirmed placental abruption diagnosis while it was 85.4±8.7 mmHg in the group without confirmed placental abruption diagnosis. As mean arterial pressure was higher than 95 mmHg, OR was found

Table 1. Definitive characteristics of groups with/without confirmed placental abruption diagnosis.

	Group without confirmed placental abruption diagnosis (n=38)	Group with confirmed placental abruption diagnosis (n=43)	p
Age	28.7±5.7	28.6±6.8	0.89
Parity	0.8±1.1	1.0±11	0.52
Week of gestation	33±6	32±1	0.72
BMI	28.5±4.4	29.3±4.8	0.47
MAP	85.4±8.7	95.1±17.8	0.006
1st min. Apgar score	6.7±2	4.5± 2.6	<0.001
5th min. Apgar score	8.2±2.1	6.2±3	0.003
Birth weight	2246±798	1667±718	0.001

BMI: Body mass index, **MAP:** Mean arterial pressure.

5.2 (95% Cl: 1.7-16) for the placental abruption (p=0.006). When groups were compared according to their blood types, placental abruption was detected in 87.5% of cases with 0 Rh (+) blood type (n=16) (OR=8.7; 95% CI: 1.8-41.4) (p=0.005). There was no significant difference between groups in terms of other blood types (p>0.05) (**Table 4**). Although there was no significant difference between groups in terms of smoking habit, cases who were smoking had a high rate of placental abruption (OR=4.8; 95% CI: 0.96-23.7) (p=0.84). Placental abruption diagnosis was confirmed in 88.9% of cases diagnosed with preeclampsia (OR=8.5; 95% CI: 1.1-71) (p=0.022). Placental abruption diagnosis was also confirmed in 71% of cases with intrauterine growth retardation; however, there was no significant difference between groups in terms of intrauterine growth retardation (OR=2.6; 95% CI: 0.74-9) (p=0.22). In 87.5% of the cases with intrauterine fetal death, the diagnosis of placental abruption was confirmed (OR=7.2; 95% CI: 0.84-61.5) (p=0.93). Three of the cases with confirmed placental abruption diagnosis had oligohydramnios, one of them had polyhydramniosis, two of them had uterine septum, one had IVF pregnancy, four of them had asthma in their medical histories, two of them had hypothyroidism in their medical histories and one of them had hyperthyroidism in the medical history, but there was no difference between groups (**Table 5**). Nineteen percent of the cases placental abruption previously had cesarean section (p=0.281). Babies of 61% of the cases with placental abruption were male but there was no significant difference (OR=2.4; 95% CI: 0.96-5.7) (p=0.096).

In the group with placental abruption, hysterectomy was performed in one case since the active bleeding could not be stopped due to atonia. Couvelaire uterus (with 100% and 60% placental abruption) was detected in two cases. In the control group, postoperative percu-

Table 2. Distribution of the complaints of the cases.

Complaint	Group without confirmed placental abruption diagnosis (n=38)	Group with confirmed placental abruption diagnosis (n=43)
Premature rupture of membrane	100.0% (1)	0.0%
Decrease in baby movements	42.9% (3)	57.1% (4)
Vaginal bleeding	43.3% (13)	56.7% (17)
Bloody water break	33.3% (1)	66.7% (2)
Decrease in baby movements + vaginal bleeding	0.0%	100.0% (1)
Pain + vaginal bleeding	25.0% (1)	75.0% (3)
Labor follow-up	54.2% (19)	45.8% (16)

Table 3. Distribution of placental localizations.

Placentation	Group without confirmed placental abruption diagnosis (n=38)	Group with confirmed placental abruption diagnosis (n=43)
Anterior	39.5% (17)	60.5% (26)
Posterior	53.3% (8)	46.7% (7)
Fundus	55.6% (5)	44.4% (4)
Right lateral	100.0% (3)	0.0% (0)
Left lateral	33.3% (1)	66.7% (2)
Right anterior	100.0% (1)	0.0% (0)
Right posterior	100.0% (1)	0.0% (0)
Sol anterior	40.0% (2)	60.0% (3)
Unknown	0. 0% (0)	100.0% (1)

Table 4. The blood types of the cases.

Blood types	Group without confirmed placental abruption diagnosis (n=38)	Group with confirmed placental abruption diagnosis (n=43)
0 Rh (+)	12.5% (2)	87.5% (14)
0 Rh (-)	33.3% (1)	66.7% (2)
A Rh (+)	50.0% (16)	50.0% (16)
A Rh (-)	57. 1% (4)	42.9% (3)
B Rh (+)	58. 8% (10)	41.2% (7)
AB Rh (+)	80.0% (4)	20.0% (1)
AB Rh (-)	100.0% (1)	0.0%

taneous hematoma was observed in one case in the control group. There was no significant difference between groups in terms of newborn intensive care need.

Discussion

The frequency of placental abruption which is one of the most significant reasons of perinatal mortality and morbidity was reported between 0.9% and 1.38% in Turkey.[8,9] Placental abruption is a clinical diagnosis and it is confirmed by pathological examination of the placenta. The most frequent complaint of the cases is vaginal bleeding. Vaginal bleeding may begin suddenly at second or third trimester and may be accompanied by contractions and pain. Although vaginal bleeding is the characteristic finding of placental abruption, it is observed only in 70-80% of the cases.[1,2,7]

Placental abruption was confirmed in 46% of 94 cases that were included into our study, diagnosed with placental abruption and had cesarean section. Vaginal bleeding was observed as the most frequent finding in cases with confirmed placental abruption diagnosis. Tikkanen et al. reported that vaginal bleeding was the most frequent clinical finding in 70% of the cases while it was abdominal pain in 51% of them, hemorrhagic amniotic fluid in 50% of them, fetal heart rate anomaly in 69% of them, and that 19% of the cases did not have any bleeding and pain. Also, retroplacental bleeding area or clot was detected only in 15% of the cases by ultrasound imaging.[10]

Ananth et al. found in their studies that preeclampsia (OR=1.73; 95% CI: 1.47-2.04), chronic hypertension (OR=3.13; 95% CI: 2.04-4.80), and premature rupture of membrane (OR=3.05; 95% CI: 2.16-4.32)

Table 5. Distribution of clinical findings in groups with and without confirmed placental abruption diagnosis.

Clinical findings	Group without confirmed placental abruption diagnosis (n=38)	Group with confirmed placental abruption diagnosis (n=43)
MAP>95 mmHg	13.2% (5)	44.2% (19)
Preeclampsia	2.6% (1)	18.6% (8)
Intrauterine growth retardation	10.5% (4)	23.3% (10)
Oligohydramnios	2.6% (1)	7% (3)
Polyhydramniosis	2.6% (1)	2.3% (1)
Intrauterine fetal death	2.6% (1)	16.3% (7)
IVF pregnancy	2.6% (1)	2.3% (1)
Asthma	5.3% (2)	9.3% (4)
Diabetes mellitus	2.6% (1)	2. 3% (1)
Hypothyroidism	0.0%	4. 7% (2)
Hyperthyroidism	0.0%	2.3% (1)
Uterine septum	2.6% (1)	4.7% (2)
Smoking	5.3% (2)	20.9% (9)
Male fetus	39.5% (15)	60.5% (26)

were associated with the increased risk of placental abruption.[11] Tikkanen et al. showed that preeclampsia (adjusted odds ratio [aOR]=2.7; 95% CI: 1.3-5.6), chorioamnionitis (aOR=3.3; 95% CI: 1.0-10.0) and placenta previa (aOR=5.7; 95% CI: 1.4-23.1) are independent risk factors for placental abruption.[10] In Turkey, Kale and Ecer reported in their studies that maternal age higher than 30, multiparity and and hypertensive diseases are risk factors.[8] In our study, mean age for the cases with confirmed placental abruption diagnosis was 28.6±6.8 and mean week of gestation was 32±1. Placental abruption diagnosis was confirmed in 88.9% of the cases diagnosed with preeclampsia and when OR=8.5 (95% CI: 1.1-71) and MAP was higher than 95 mmHg, it was found that its OR was 5.2 (95% CI: 1.7-16). Also in 71% of the cases with intrauterine growth retardation (OR=2.6; 95% CI: 0.74-9) and in 87.5% of cases found to have intrauterine fetal death (OR=7.2; %95 CI: 0.84-61.5), placental abruption was confirmed but no significant difference was found. Moreover, in three of the cases with placental abruption had oligohydramnios, one of them had polyhydramniosis, two of them had uterine septum, one had IVF pregnancy, four of them had asthma in their medical histories, two of them had hypothyroidism in their medical histories and one of them had hyperthyroidism in the medical history.

Matsuda et al. indicated in their studies defining risk factors of placental abruption that age higher than 35 (adjusted relative risk; RRs=1.2), IVF pregnancy (RRs=1.38), preterm labor (RRs=1.63), hypertension (RRs=2.48) and hypertension induced by pregnancy (RRs=4.45) are the risk factors.[12] Hasegawa et al. found a different result showing that anemia presence before 20 weeks of gestation (aOR=4.05), presence of SGA (small for gestational age) (aOR=5.20), and the presence of SGA fetus (aOR=5.39), preterm uterine contractions (aOR=5.96) and preeclampsia (aOR=3.37) were the risk factors for placental abruption.[13] Arnold et al. reported that iron deficiency anemia at early gestational period (Hb <10 mg/dl) increased risk of placental abruption for 3.6 times.[14]

Hung et al. analyzed risk factors of placental abruption in Asian population and reported the coefficients of gestational hypertension (aOR=4.9; 95% CI: 3.3-7.3), oligohydramnios (aOR=4.2; 95% CI: 2.7-6.7), polyhydramniosis (aOR=3.3; 95% CI: 1.4-7.7), preterm premature rupture of membrane (aOR=1.9; 95% CI: 1.1-3.1), maternal age higher than 35 (aOR=1.5; 95% CI: 1.1-2) and low BMI value (aOR=1.3; 95% CI: 1.0-1.6) for placental abruption.[15] Deutsch et al. showed in their study conducted in 2010 that placental abruption risk was increasing in slim women (OR=1.4; 95% CI: 1.3-1.5).[16] Salihu et al. indi-

cated that placental abruption risk was increasing if weekly weight gaining of pregnant women with normal weight is ≤0.22 kg/week (aOR=1.8; 95% CI: 1.5-2.2), and the risk was decreasing in obese women.[17] In our study, mean BMI was found as 29.3±4.8 in the group with confirmed placental abruption diagnosis, but there was no significant difference when groups were compared.

Tikkanen et al.[10] reported the aOR of smoking habit for placental abruption as 1.8 (95% CI: 1.1-2.9) while Hung et al.[12] reported the aOR as 8.4 (95% CI: 3.0-23.9).[14] In our study, although there was no significant difference between groups in terms of smoking (p=0.84), placental abruption was found to be higher in smoking women. Also, no association was observed in our study in terms of fetal gender (p=0.096), and Aliyu et al. reported that the placental abruption risk was decreasing in female fetuses (OR=0.89; 95% CI: 0.86-0.93).[18]

In our study, unlike other studies, the placental abruption diagnosis was confirmed in 87.5% of the cases with 0 Rh(+) blood type, and OR was found to be 8.7 (95% CI: 1.8-41) for placental abruption. No study was seen in the literature showing association between blood types and placental abruption.

Conclusion

In conclusion, analyzing risk factors of placental abruption is significant in order to decrease maternal and fetal morbidity and mortality, and to avoid unnecessary surgical interventions and their potential complications.

Conflicts of Interest: No conflicts declared.

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PERINATAL JOURNAL

Research Article

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The efficacy of the measurement of cervical length at 18-22 weeks of gestation for the prediction of preterm delivery in low risk asymptomatic pregnancies

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Abstract

Objective: The aim of this study was to determine the relationship between cervical length and gestational weeks and to evaluate the efficacy of the measurement of the cervical length in predicting preterm delivery.

Methods: In this prospective study, we performed cervical length measurement by vaginal ultrasonography at 18 and 22 weeks of gestation in 337 women with asymptomatic singleton pregnancies. The distribution of cervical length was established according to gestational weeks. We then assessed the relation between the length of the cervix and the risk of preterm delivery. Delivery occurring at less than 37th week was referred as preterm delivery.

Results: Preterm delivery (before 37 weeks) occurred in 25 pregnancies (7.4%). The mean cervical length in the preterm group was 33.2±5.7 mm while it was 37.8±4.8 mm in the term group, and the difference was statistically significant (p<0.001). It was found that cervical length did not change significantly between 18th and 22nd weeks of gestation in cases resulted with term delivery, and the 5th, 50th and 95th percentile values of cervical length were 30, 38 and 46 mm respectively. The area under the receiver-operating characteristics curve (ROC) was 0.74 (95% CI: 0.62-0.85) for the prediction of preterm delivery (p<0.001). The values of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and OR for the prediction of preterm delivery at 18-22 gestational weeks cervical length ≤30 mm were (5th percentile) 36.6%, 92.6%, 28.1%, 94.8 and 7.1 (95% CI: 2.8-17.8), respectively.

Conclusion: Cervical length measurement is considered to be a useful method for preterm delivery prediction in asymptomatic patients.

Key words: Cervical length, preterm delivery, cut off.

Düşük riskli asemptomatik gebeliklerde 18-22. gebelik haftaları arasında servikal uzunluk ölçümünün preterm doğum öngörüsündeki değeri

Amaç: Çalışmamızda, servikal uzunluğun gebelik haftası ile olan ilişkisini ve preterm doğumu öngörmedeki değerini belirlemeyi amaçladık.

Yöntem: Bu prospektif çalışmada; 18-22. gebelik haftaları arasında, 337 asemptomatik tekil gebeliğin transvajinal ultrasonografi ile servikal uzunluk ölçümü yapıldı. Servikal uzunluğun gebelik haftasına göre dağılımı çıkarıldı. Servikal uzunluk ile preterm doğum arasındaki ilişki değerlendirildi. Preterm doğum sınırı olarak 37 hafta alındı.

Bulgular: Yirmi beş gebelik preterm doğumla (<37 hafta) sonuçlandı (%7.4). Preterm doğum yapan gebelerde ortalama servikal uzunluk 33.2±5.7 mm, term doğum yapanlarda da 37.8±4.8 mm bulundu ve aradaki fark istatistiksel olararak anlamlıydı (p<0.001). Term doğum ile sonuçlanan olgularda 18-22 gebelik haftaları arasında servikal uzunluğun değişmediği saptandı ve servikal uzunluğun 5, 50 ve 95. persentil değerleri sırasıyla 30, 38 ve 46 mm bulundu. 18-22 gebelik haftaları arasında servikal uzunluğun, preterm doğumu öngörmedeki değerini araştırdığımızda; ROC (alıcı çalışma karakteristiği) eğrisi altındaki alan 0.74 (%95 CI: 0.62-0.85; p<0.001) ve ≤30 mm (5. persentil) servikal uzunluk için %36.6 duyarlılık ve %92.6 özgüllük, %28.1 pozitif prediktif değer (PPD), %94.8 negatif prediktif değer (NPD) ve göreceli olasılık oranı (OR) 7.1 (%95 CI: 2.8-17.8) tespit edildi.

Sonuç: Asemptomatik gebelerde preterm doğumu öngörmede servikal uzunluk ölçümünün faydalı olacağı düşünülmektedir.

Anahtar sözcükler: Servikal uzunluk, preterm doğum, eşik değer.

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Introduction

Preterm delivery (PTD) is defined as the delivery occurred before 37th week of gestation. Although its prevalence varies according to societies, it is between 5 and 13%. Preterm delivery is the most significant reason of perinatal mortality and morbidity today. It would be an appropriate approach to determine risk factors for decreasing preterm delivery rates, and to predict the preterm delivery diagnosis.[1-3] It has been reported that risk scoring systems, digital examination of cervix, analysis of cervix by ultrasonography and various biochemical reagents can be used to predict preterm delivery beforehand.

Evaluation of cervical length (CL) can be done transabdominally, transperineally and transvaginally. However, the most preferred and suggested method is to measure cervical length by ultrasonography. Cervical length is 25-70 mm, and width of endocervical canal is 2-4 mm during pregnancy.[2] The period between 18th and 24th week of gestation is recommended for the measurement of cervical length. Many studies reported that the shortest cervical length measured between these weeks is associated with PTD. It is difficult to distinguish cervix and sub-segment before 14-16t weeks of gestation, and measurement of cervical length should be done after this period since it causes faulty measurement. Also, it has been reported that there was no significant difference between cervical lengths measured before 14th week of gestation, and significant cervical changes occurred after this period in pregnant women who had preterm and term delivery.[4,5] On the other hand, Greco et al. reported in their study that cervical length could be measured between 11 and 14 weeks of gestation, and short cervix was associated with early PTD.[6]

In our study, we aimed to determine the relationship between cervical length and gestational week and to predict preterm delivery in this way by measuring cervical length via transvaginal ultrasonography between 18 and 22 weeks of gestation.

Method

In this study, we aimed to investigate the relationship between gestational week & PTD with cervical length measured in asymptomatic pregnant women who admitted to our clinic between 01.08.2009 and 01.02.2011 and were at low risk in terms of preterm delivery. Study protocol was established for this research and required approval was obtained from Ethics Committee of Clinical Researches. All patients were informed and their written consents were received.

Our study group was consisting 337 women with singleton pregnancy at 18-22 weeks of gestation. Gestational week was based on last menstrual period (LMP), or for those who did not know their LMP, crown-rump length at first trimester or biparietal diameter at second trimester. Women with preterm delivery history, previous cervical failure, undergone cervical circlage, or pregnant women with preterm contractions, those with placenta praevia, or structural or karyotype anomalies at fetus, having preeclampsia or eclampsia, those below 18 years old, and those with systemic disease, uterine mullerian anomaly or uterus myomas were all excluded from the study. Preterm delivery limit was considered as 37 weeks.

Ultrasonographic measurements were done by a single specialist with transvaginal approach (7 MHz) by Toshiba Xario ultrasound device. Also, by transabdominal approach, biometric evaluations of fetus together with detailed fetal structures were analyzed. The probe was proceeded within vagina by transvaginal ultrasonography, and sagittal image of cervix was obtained by taking care not to pressure on cervix. Cervical measurements were done at a view as covering 3/4 of the screen and where internal os, external os, cervical canal and endocervical mucosa can be viewed at the same time. When the length between internal os and external os cannot be measured on a straight line due to the curved cervix, measurements taken as linear sections were summed up and cervical length was calculated. Measurements were performed three times on each pregnant woman and the shortest one with the best image quality was recorded.

Statistical methods

Patient data was analyzed by SPSS 20 package program (SPSS Inc., Chicago, IL, USA). Descriptive analyses (mean, standard deviation, standard error and percentile distribution) were done. Parameters were tested by Kolmogorov-Smirnov test to check whether they were within normal range. Statistical analyses were carried out by using *independent samples* T test to compare parameters within normal range, and Mann-Whitney U test to compare parameters not within nor-

mal ranges. One-way Anova test was used to compare cervical lengths according to gestational weeks. Homogeneity of variants was evaluated by Levene test. Also, the impact of cervical length measurements for predicting preterm delivery was evaluated by ROC curve analysis. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and relative odds ratio (OR) of threshold values were calculated. P<0.05 was considered statistically significant.

Results

Our study included 337 pregnant women complying with research criteria. Totally 312 pregnancies resulted at or above 37 weeks, and 25 pregnancies resulted below 37 weeks. Preterm delivery rate was found to be 7.4%. Also, ten of preterm deliveries were at or below 34 weeks. Early preterm delivery rate was found to be 3%. There was no difference between pregnancies resulting in term delivery and pregnancies resulting in preterm delivery in terms of maternal age, gravid, parity, abortus and gestational week in which evaluation was performed. While mean cervix length was 37.8±4.8 mm of term delivery group, it was 33.2±5.7 mm in preterm delivery group (p<0.001). Other definitive characteristics of the groups are given in **Table 1.**

In cases resulted in term delivery, mean cervix lengths for each week between 18 and 22 weeks of gestation were 37.9±4.9, 37.8±5.2, 38±5.1, 37.4±4, 37.6±4.4 and 37.8±4.8 mm, respectively; and it was found that CL measurements did not change significantly according to gestational weeks (p=0.98). **Table 2** shows CL distributions according to gestational weeks. Also, percentile distribution of CL between 18 and 22 weeks of gestation is shown at **Table 3.** Cervical length was found to be 30 mm, 38 mm and 46 mm for 5th percentile, 50th percentile and 95th percentile, respectively. In terms of the relationship between cervical length and parity, mean CL was 36.5±4.2 mm in nullipara pregnancies, 37.5±4.3 mm in primipara pregnancies, and 39.2±5.8 mm in multipara pregnancies; and it was found that there was a significant difference among them.

Considering the significance of cervical length between 18 and 22 weeks of gestation for predicting PTD, the field below ROC curve was found to be 0.74 (95% CI: 0.62-0.85, p<0.001). So, measuring cervical length between 18th and 22nd weeks of gestation was

Table 1. Definitive characteristics of term and preterm delivery cases.

	Term delivery cases (n=312)	Preterm delivery (n=25)	p
Maternal age	30.7±6	29.3±5.9	0.27
Gestational week	19.6±1.4	19.4±1.4	0.1
Gravida	2.5±1.5	2.0±1.1	0.067
Parity	1.1±1.5	0.8±0.9	0.141
Abortus	0.3±0.5	0.2±0.5	0.257
Cervical length (mm)	37.8±4.8	33.2±5.7	0.000
Delivery week	38.9±1.1	34±2.3	0.000
Newborn weight (g)	3319.0±465.9	2468.8±688.4	0.000

Table 2. Cervical length (mm) measurements in term delivery cases according to gestational week at 95% CI.

Gestational week	Case Number	Mean	Shortest	Longest
18	97	37.9±4.9	25	52
19	77	37.8±5.2	26	57
20	52	38±5.1	26	56
21	39	37.4±4.0	29	46
22	47	37.6±4.4	28	51
Total	312	37.8±4.8	25	57

Table 3. Percentile distribution of cervical length between 18th and 22nd weeks of gestation.

Percentile	3rd	5th	10th	25th	50th	75th	95th
Cervical length (mm)	29	30	32	35	38	40	46

found to be a useful scanning method for predicting PTD. The sensitivity was 32% and the specificity was 96.2% for ≤29 mm CL (3rd percentile); the sensitivity

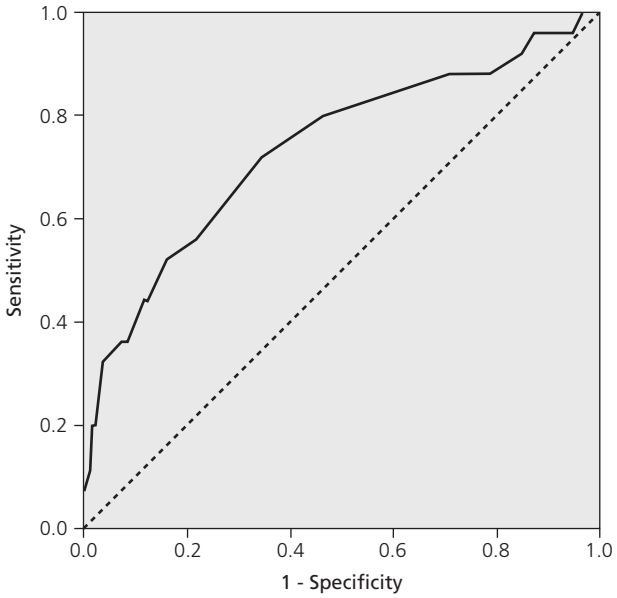

Fig. 1. The ROC curve of the prediction of cervical length for preterm delivery.

was 36.6% and the specificity was 92.6% for ≤30 mm CL (5th percentile); and the sensitivity was 44% and the specificity was 88.1% for ≤32 mm CL (10th percentile). Predictivity of ROC curve and CL to predict PTD has been given in **Fig. 1** and **Table 4.**

Discussion

Preterm delivery is the most significant reason for neonatal mortality and morbidity. Predicting and preventing preterm delivery and its complications are one of the most critical missions of obstetrics. Today, many studies have reported that evaluating cervix by transvaginal ultrasonography may be helpful for predicting PTD.

PTD was found in 7.4% of pregnancies in our study, and mean CL was found to be 37.8±4.8 mm in pregnancies resulted in term delivery and it was 33.2±5.7 mm in pregnancies resulted in preterm delivery. In cases resulted in term delivery, mean CL between 18 and 22 weeks of gestation was found to be 37.9±4.9, 37.8±5.2, 38±5.1, 37.4±4, 37.6±4.4 and 37.8±4.8 mm, respectively, and it was found that cervical length did not change significantly according to gestational weeks. Also, percentile distribution of cervical length between 18th and 22nd weeks of gestation was found to be 30 mm at 5th percentile, 38 mm at 50th percentile and 46 mm at 95th percentile. Gramellini et al. reported in their study where they measured CL by TV USG on 321 pregnants (185 nullipara and 136 multipara cases) that cervical length decreased by gestational week (r2=085, p<0.01).[7] Qu et al. conducted a study on 5277 pregnants and reported that mean CL significantly decreased with gestational week and it was 38.8±4.0 mm between 22 and 24 weeks of gestation, and 34.6±4.8 mm between 28 and 32 weeks of gestation.[8] Also Liabsuetrakul et al. reported that CL was decreased with gestational week between 24 and 34 weeks of gestation.[9] In our study,

Table 4. The impact of cervical length measured between 18th and 22nd weeks of gestation for predicting preterm delivery.

Threshold cervical length (mm)	Sensitivity	Specificity	PPV	NPV	OR (95% CI)
≤29 (3rd percentile)	32	96.2	40	94.6	11.8 (4.3-32.6)
≤30 (5th percentile)	36	92.6	28.1	94.8	7.1 (2.8-17.8)
≤32 (10th percentile)	44	88.1	22.9	95.2	5.8 (2.5-13.8)

NPV: negative predictive value, **OR:** odds ratio, **PPV:** positive predictive value.

CL did not change significantly with gestational week and we consider the reason that gestational week range is very narrow compared to other studies.

In terms of the relationship between cervical length and parity, mean CL was found to be 36.5±4.2 mm in nullipara pregnancies, 37.5±4.3 mm in primipara pregnancies and 39.2±5.8 mm in multipara pregnancies ($p<0.05$). While Gramellini et al.[7] reported that there was no relationship between CL and parity, Liabsuetrakul et al.[9] reported that CL was significantly longer in multipara cases. Iams et al. found that mean CL at 24th week of gestation was 34.0±7.8 mm nullipara cases, 36.1±8.4 mm in multipara cases while mean CL at 28th week of gestation was 32.6±8.1 mm in nullipara cases and 34.5±8.7 mm in multipara cases. They reported that this difference was statistically significant; however, it did not have any clinical significance.[10]

Considering the significance of cervical length between 18 and 22 weeks of gestation for predicting PTD, field under ROC curve was found to be 0.74 (95% CI: 0.62-0.85, $p<0.001$). The sensitivity was 32% and the specificity was 96.2% for ≤29 mm CL (3rd percentile); the sensitivity was 36.6% and the specificity was 92.6% for ≤30 mm CL (5th percentile); and the sensitivity was 44% and the specificity was 88.1% for ≤32 mm CL (10th percentile). Çelik et al. researched the relationship between CL and PTD on 58,807 singleton pregnancies at 20+0-24+6 weeks of gestation, and found the field under ROC curve for predicting delivery as 0.90, 0.82, 0.78 and 0.62, respectively before 28th week, at 28-30, 31-33, and 34-36 weeks of gestation. They showed that CL measurement is a useful scanning method for predicting especially early PTD cases. They also reported that 5% false-positivity value of CL had 66% sensitivity for predicting delivery before 28th week of gestation, 40.1% sensitivity for predicting delivery at 28-30 weeks of gestation, 32.6% sensitivity for predicting delivery at 31-33 weeks of gestation, and 12.7% sensitivity for predicting delivery at 34-36 weeks of gestation.[3]

Iams et al. found threshold values by CL measurements at 24th and 28th weeks in 2915 singleton pregnants with low risk. When threshold value was accepted as 30 mm at 24th week of gestation, sensitivity was 54%, specificity was 76.3%, PPV was 9.3% and NPV was 97.4% for predicting deliveries before 35th gestational week, and when threshold value was accepted as 30 mm at 28th week of gestation, sensitivity was 69.9%, specificity was 68.5%, PPV was 7% and NPV was 98.5%.[10] Barber et al. performed a study where they measured CL on 2351 pregnant women between 18 and 22 weeks of gestation, and similar to our study, they reported that threshold CL had low sensitivity and high specificity for predicting preterm delivery (<37 weeks). They reported sensitivity as 26% and specificity as 98% for 3rd percentile, sensitivity as 34% and specificity as 97% for 5th percentile, and sensitivity as 39% and specificity as 92% for 10th percentile (**Table 5**). They also reported that CL measurement would be helpful for PTD risk in asymptomatic pregnants during routine fetal examination between 18th and 22nd weeks of gestation.[11]

Table 5. Comparison of studies researching the impact of transvaginal CL in asymptomatic pregnancies with low risk for predicting preterm delivery.

Studies	Case number	USG (GW)	Result (GW)	Threshold value (mm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Current study	**337**	**18-22**	**<37**	**≤30**	**36**	**92.6**	**28.1**	**94.8**
Tongsong et al.[12]	730	28-30	<37	<35	65.9	62.4	19.4	92.8
Iams et al.[10]	2915	24	<35	≤30	54	76.3	9.3	97.4
		24	<35	≤25	37.3	92.2	17.8	97
	2531	28	<35	≤30	69.9	68.5	7	98.5
	28	<35	≤25	49.4	86.8	11.3	98	
Fukami et al.[13]	3030	16-19	22-31	≤30	50	98.5	8.3	99.9
			32-36	≤30	18.2	98.9	33.3	97.6
Pires et al.[14]	338	21-24	<37	<20	18	98.1	40	94.8
			<35	<20	27.3	97.9	30	97.6
Barber et al.[10]	2351	18-22	<37	<30	39	92	31	94
Qu et al.[8]	5277	22-24	<37	<30	3	99	19	96

GW: gestational week, **NPV:** negative predictive value, **PPV:** positive predictive value, **USG:** ultrasonography.

In the study performed by Qu et al., it was shown that CL threshold value below 30 mm had 3% sensitivity and 99% specificity for predicting PTD between 22nd and 24th weeks of gestation. Also, it was found that OR was 5.2 if CL was lower than 30 mm for PTD, 11.1 mm if CL was lower than 25 mm, and 13.8 mm if CL was lower than 15 mm.[8)] In Turkey, Özdemir et al. conducted a study on 79 singleton pregnant women between 20 and 24 weeks of gestation, and when 27 mm was threshold value, they found sensitivity as 77.8%, specificity as 100%, PPV as 100%, NPV as 97% and OR as 33.5 for PTD prediction.[15] The sensitivity and specificity values of the study seem quite high, which may be caused by insufficient number of cases. Hibbard et al. measured cervical lengths of 760 pregnant women between 16 and 22 weeks of gestation and found CL as 30 mm at 10th percentile, 27 mm at 5th percentile, and 22 mm at 2.5 percentile. They reported relative risks of cervical length for deliveries before 37th week of gestation as 3.8 for 10th percentile, 5.4 for 5th percentile, and 6.3 for 2.5 percentile.[16] Barber et al. presented ORs of 3rd, 5th and 10th percentile values of cervical length for PTD as 25.47 (95% CI: 15.5-41.73); 16.98 (95% CI: 11.51-25.05) and 7.55 (95% CI: 5.44-10.5), respectively. In our study, OR values were found to be lower for PTD, as 11.8 (95% CI: 4.3-32.6) for 3rd percentile, 7.1 (95% CI: 2.8-17.8) for 5th percentile, and 5.8 (95% CI: 2.5-13.8) for 10th percentile.[11]

Conclusion

Consequently, transvaginal cervical length measurement is a useful method for PTD scanning in asymptomatic pregnancies with low risk. It has been reported that cervical length has a high specificity for predicting preterm delivery and the value of ≤30 mm can be used as threshold.

Conflicts of Interest: No conflicts declared.

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PERINATAL JOURNAL

Research Article

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The importance of micronutrient deficiency in the etiology of anemia in the first trimester pregnancy

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Abstract

Objective: To determine the frequency of anemia in pregnant women admitted to our hospital for the purpose of examination in the first trimester, to determine the location of micronutrient deficiencies in the etiology of anemia and to make analysis of demographic factors associated with anemia.

Methods: This study included 366 pregnant women below 12 weeks of gestation between November 2011 and February 2013. Pregnant women together with demographic data were examined in terms of hemoglobin, hematocrit, serum iron, total iron binding capacity, ferritin, folate, vitamin B12 levels. Tests were statistically evaluated with demographic analysis.

Results: The mean maternal hemoglobin, hematocrit, serum iron, total iron binding capacity, ferritin, folate, and vitamin B12 levels were respectively 12.6±1.02 g/dl, 36%±4.12, 76.63±44.76 µg/dl, 302.28±93.14 ng/dl, 19.35±20.43 ng/ml, 11.2±8.31 ng/ml and 187.2±101.14 pg/ml. The study evaluated 344 pregnant women and anemia was detected in 79 of them. In our study, the frequency of anemia was calculated to be 22.96%. Analyzing the etiology of anemic pregnant women, iron deficiency anemia was diagnosed in 35 patients (44.3%), vitamin B12 deficiency in 44 patients (55.7%), combination of vitamin B12 and iron deficiency was found in 9 patients. None of the patients were found to have folic acid deficiency.

Conclusion: The frequency of anemia in pregnant women was found as 22.96%, which shows that the vitamin B12 deficiency is important in the etiology of anemia as frequent as iron deficiency.

Key words: Pregnancy, anemia, micronutrient deficiency.

Gebeliğin ilk trimesterindeki anemi etyolojisinde mikrobesin eksikliğinin önemi

Amaç: İlk trimester muayenesi amacıyla hastanemize başvuran gebelerde anemi sıklığını belirlemek, mikrobesin eksikliklerinin anemi etiyolojisindeki yerini saptanmak ve anemiyle ilişkili demografik faktörlerin analizlerini yapmak.

Yöntem: Kasım 2011 - Şubat 2013 tarihleri arasında polikliniğimize başvuran 12 ve altı gebelik haftasındaki 366 gebe çalışmaya dahil edildi. Gebelere ait demografik verilerle beraber, hemoglobin, hematokrit, serum demir, total demir bağlama kapasitesi, ferritin, folat, B12 vitamini seviyeleri incelendi. Tetkikler demografik analizlerle beraber istatistiksel olarak değerlendirildi.

Bulgular: Çalışmaya katılan gebelerin ortalama hemoglobin, hematokrit düzeyleri, serum demir, total demir bağlama kapasitesi, ferritin, folat ve B12 vitamini düzeyleri sırasıyla 12.6±1.02 g/dl, %36±4.12, 76.63±44.76 µg/dl, 302.28±93.14 ng/dl, 19.35±2043 ng/ml, 11.2±8.31 ng/ml ve 187.2±101.14 pg/ml olarak bulundu. Çalışmamızda değerlendirmeye alınan 344 gebenin 79'unda anemi saptandı. Anemi prevelansı % 22.96 olarak hesaplandı. Anemik gebelerdeki etiyoloji incelendiğinde, 35 hastada demir eksikliği (%44.3), 44 hastada B12 vitamini eksikliği (%55.7), 9 hastada ise B12 vitamini ve demir eksikliği bir arada bulundu. Hiçbir hastada folik asit eksikliğine rastlanmadı.

Sonuç: Çalışmaya dahil edilen gebelerde anemi sıklığı %22.96 olarak saptanmış olup, etiyolojide demir eksikliği kadar B12 vitamini eksikliğinin de rol oynadığı gösterilmiştir.

Anahtar sözcükler: Gebelik, anemi, mikrobesin eksikliği.

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Introduction

Healthy nutrition during pregnancy is essential in many aspects. Healthy nutrition is required for fetus development, maternal health, successful delivery and lactation process. Also, proper nutrition during pregnancy decreases postpartum obesity risk and provides a positive contribution to maternal health in the long-term.[1]

During the adaptation period at pregnancy, significant changes occur at vitamin and mineral levels in maternal blood. Vitamin B12 and folate levels increases 50% during pregnancy compared to pre-pregnancy period. Serum iron levels also tend to decrease.[1,2]

According to the data of WHO, approximately one third of women population in the world and more than half of the pregnant women are anemic. At first and second trimesters, hemoglobin value being lower than 11 g/dl and hematocrit value being lower than 33% is interpreted as anemia. At third trimester, hemoglobin value being lower than 10.5 g/dl and hematocrit value being lower than 32% is interpreted as anemia.[1,3,4]

In 50% of women not considered as anemic, and in 90% of pregnant women were found to have extremely low ferritin levels, which means iron deficiency.[5]

Deep anemia causes serious cardiac failure even in small amounts of bleeding during miscarriage or delivery, and may increase maternal mortality up to five times. It also causes fetal complications (such as preterm labor, intrauterine growth retardation, and low birth weight) as well as maternal complications (such as preeclampsia, eclampsia, and sepsis).[3,4]

Plasma volume increases about 50% during pregnancy to provide fetal development and placental blood flow. Since the increase in erythrocyte mass is lower, maternal hematocrit decreases. This is called physiologic anemia of pregnancy. Hematocrit level reaches the lowest level at third trimester, especially between 30th and 34th weeks.[6,7]

Other factors causing anemia during pregnancy are insufficient nutrition and emptied iron balance of body due to repeating and frequent pregnancies.[8,9]

In our country, there have been many regional studies aimed to present anemia prevalence. The prevalence of anemia in our country varies according to regions, and rates have been reported between 29.4% and 95.2% in various studies.[10-15] In this study, it was aimed to determine the frequency and etiology of anemia in pregnant women admitted to our clinic, and to determine demographic factors associated with anemia.

Method

Our study included 366 pregnant women below 12 weeks of gestation with age ranging between 16 and 44 who admitted to Bayrampasa State Hospital for the first time between November 2011 and February 2013. Women who had any systemic disease, vaginal bleeding for an obstetric reason in current pregnancy, and who started to have any iron and/or multi-vitamin supplement were excluded from the study. Our study is retrospective and required approval of ethics committee has been obtained.

According to the data of CDC (Centers for Disease Control), pregnant women with hemoglobin value lower than 11 g/dl and hematocrit value lower than 33% were interpreted as anemia. Values for serum folate and vitamin B12 below 3 ng/ml and 200 pg/ml, respectively, were considered as deficiencies. Informed consent forms were received from all these pregnant women and they were asked to fill a form including their demographic data. The form included information of age, hometown, obstetric history, educational status, and average income level. As a laboratory examination, patients were evaluated in terms of their hemoglobin (Hb), hematocrit (Htc), serum iron (Fe), total iron binding capacity (TIBC), ferritin, folate and vitamin B12 levels. Twenty-two patients were removed from the study since their blood had hemolysis.

Hemogram and hematocrit were studied by Swelab alpha device; serum iron and total iron binding capacity were studied by Prestige 24I device; ferritin, folate and vitamin B12 were studied by Unicel DxI 800 device.

Data obtained by forms and examinations were evaluated. Constant variables were indicated as mean and standard deviation. Data was evaluated by SPSS (Statistical Package for the Social Science) 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Pregnant women included in the study were separated into age groups for evaluation. Mean age of patients was found as 29.08±6.79. Also, gestational week, gravid, and parity of pregnant women are given in the **Table 1.**

Mean hematocrit levels and standard deviations were calculated according to the age groups. Anemia prevalence was analyzed in the basis of the age groups (**Table 2**). Accordingly, anemia prevalence was found to be high in the age groups 21-25 and 26-30 as 34.64% and 33.78%, respectively. Mean hematocrit levels were found to be coherent in age groups. Anemia was detected in 79 of 344 pregnant women included in the study. So, anemia prevalence was calculated as 22.96%.

In 21 cases in our study, serum iron levels were found to be lower than 37 µg/dl. Therefore, iron deficiency was seen in 6.1% of the pregnant women in our study.

Analyzing the etiology of anemic pregnant women, iron deficiency anemia was diagnosed in 35 patients (44.3%), vitamin B12 deficiency in 44 patients (55.7%), combination of vitamin B12 and iron deficiency was found in 9 patients (11.4%). None of the patients were found to have folic acid deficiency (**Table 3**). Age and blood parameters of pregnant women included in the study were evaluated separately in women with and without anemia (**Table 4**). The mean maternal hemoglobin, hematocrit, serum iron, total iron binding capacity, ferritin, folate, and vitamin B12 levels were respectively 12.6±1.02 g/dl, 36%±4.12, 76.63±44.76 µg/dl, 302.28±93.14 ng/dl, 19.35±20.43 ng/ml, 11.2±8.31 ng/ml and 187.2±101.14 pg/ml (**Table 3**). When hematological parameters of these women were compared, it was seen that statistically and significantly mean serum iron level was lower and total iron binding capacity was higher in pregnant with anemia.

When pregnant women with and without anemia were compared in terms of their hometowns, obstetric histories, educational status and average income level, there was statistically no significant difference between two groups.

Table 1. Age, gestational week, gravida, parity evaluation.

	Mean	Min.	Max.
Age	29.08±6.79	16	45
Gestational week	8±3	5	12
Gravida	1.5±1.2	1	9
Parity	0.8±0.9	0	5

Table 2. Anemia prevalence according to age groups.

Age	Mean hematocrit	Anemia rate
16-20	36.19±3.98	20.30
21-25	35.55±3.86	34.64
26-30	35.78±4.00	33.78
31-35	35.95±3.98	27.60
36-40	36.60±4.42	20.91
41-45	37.29±4.86	20.18

Table 3. Hemoglobin (Hb), hematocrit (Hct), folate, and vitamin B12 levels.

	Mean	Min.	Max.
Hb	12.6±1.02	6.8	17.1
Hct	%36±4.12	19.1	49.8
Folate	11.2±8.31	3.4	22.27
Vitamin B12	187.2±101.14	18	1521

Discussion

According to WHO, anemia is a health issue seen in 21-80% of women population in the world. While ane-

Table 4. Comparison of age and blood parameters in groups with and without anemia.

	Mean	With anemia	Without anemia
Age	29.08±6.79	28.66±6.39	29.22±6.93
Iron	76.63±44.76	53.54±21.61	97.23±26.41
TIBC	302.28±93.14	417.23±87.56	261.67±105.65
Ferritin	19.35±20.43	5.45±4.11	27.56±9.59
Folate	11.2±8.31	16.92±9.78	17.12±5.98
Vitamin B12	187.2±101.14	210.23±118.56	237.89±87.13

TIBC: total iron binding capacity.

mia rate of women is 14% in European countries, it is 25% in Turkey. In terms of etiology, 40-89% of anemia cases are caused by iron deficiency anemia.[16] According to the data of WHO, iron deficiency anemia affecting 30% of world population affects 51% of pregnant women.[17] Especially in underdeveloped countries, anemia is more prevalent and at more serious levels. In the study performed by Malhotra in 2002, it was found that anemia rate during pregnancy was 72.5% in India.[18] As the development level increases, anemia frequency decreases. Anemia during pregnancy in Korea was found to be 35.3% in the study performed by Choi.[19] In the studies performed in developed European countries, anemia rates were reported as 7-16%.[20,21]

Anemia was found in 79 of 344 pregnant women included into our study and therefore anemia prevalence was calculated as 22.96%. Analyzing the etiology of anemic pregnant women, iron deficiency was diagnosed in 35 patients (44.3%), vitamin B12 deficiency in 44 patients (55.7%), combination of vitamin B12 and iron deficiency was found in 9 patients (11.4%). None of the patients were found to have folic acid deficiency.

When Turkish studies performed on anemia frequency during pregnancy are analyzed, it is seen that there is no large-scale research that will represent Turkish population. Anemia frequency in Turkey varies according to the regions, and the rates range between 29.4% and 95.2%.[10-15] Compared to these rates, the anemia rate found by our study (22.96%) has been observed lower than other studies.

Al Khatib et al. reported in their study performed in Lebanon that 7.7% of women who were at fertility age but not pregnant had iron deficiency, 25.9% of them had folic acid deficiency and 39.4% of them had vitamin B12 deficiency.[22] In a study performed in Africa, only 23% of the cases had anemia due to iron deficiency, 32% of them had anemia due to iron deficiency together with the deficiency of other micronutrients (folate, vitamin B12, vitamin A), and 26% of them did not have any iron deficiency but had micronutrient deficiency.[23]

Non-existence of folic acid deficiency in our study can be explained by the sufficient folic acid supplement provided in our clinics both before pregnancy and during the first trimester. In a study performed in Adana/Turkey, the relationship between increase of pregnancy number and anemia was found statistically significant.[12] In a study performed in Elazığ/Turkey, statistically no significant relationship was found between pregnancy number and anemia frequency.[11] In our case, statistically no significant relationship was found between pregnancy number and anemia frequency.

In our study, no question was asked for nutrition. However, income levels of pregnant women that reflect their nutrition condition indirectly were asked and no relationship was found between income level and anemia frequency.

According to the Population and Health Survey of Turkey conducted in 1998, adolescent pregnancy frequency is 14% in Turkey. It was seen that mean age in the study group was 30.69±7.17 and 73% of patients were in the age group 20-35. It was observed that 3.7% of pregnant women had adolescent pregnancy.[24]

Conclusion

Consequently, anemia frequency during pregnancy was found to be lower in this study compared to the country data. Significance of the vitamin B12 deficiency as much as iron deficiency in etiology is one of the results of our study. In two third of anemic pregnant women had low vitamin B12 level. This emphasizes the importance of multi-vitamin supplement as well as the nutrition during pregnancy. Studies with larger amount of cases are required in order to present regional differences in the prevalence across the country.

Conflicts of Interest: No conflicts declared.

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Views of parents' about taking human milk of premature infants

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Abstract

Objective: This descriptive study aims to determine the views of parents that have 32-37 weeks premature babies about babies' breast feeding.

Methods: The research was conducted in Newborn Intensive Care Units in totally six hospitals including one private hospital, two university hospitals, and three state hospitals in Konya city center between July 1 and November 30, 2011. Data were obtained from 100 parents by face to face interviews or by phone. Percentage and chi-square tests were used for statistical analysis.

Results: It was determined in the study that 39% of the parents had their first baby. During the study, it was found out that 48% of babies were girl babies, 64% of babies were born by section and 60% of them were born at 32-34 weeks of gestation. It was found that 39% of the babies have other problems except prematurity and 56% of them were followed-up in incubator. It was determined that 66% of the babies were fed with human milk. It was concluded that 40% of babies took human milk by breast feeding, 21% of them by naso-gastric catheter, 15% of them by baby bottle and 24% of them by breast feeding with the support of baby bottle since breast feeding was not sufficient. It was stated by 71% of mothers and 64% of fathers that they know benefits of human milk for premature babies. Additionally, 91% of fathers stated that they want to support to mothers about breast feeding.

Conclusion: According to findings, mothers were found having more experience and knowledge than fathers on premature babies taking human milk. Additionally, it was concluded that comprehensive trainings should be given to parents about human milk and breast feeding.

Key words: Premature, breast feeding, human milk, nurse, parents.

Prematüre bebeklerin anne sütü alımı ve ebeveynlerinin görüşleri

Amaç: Araştırma, 32-37 haftalık prematüre bebeğe sahip ebeveynlerin, bebeklerinin anne sütü alması konusundaki görüşlerini belirlemek amacıyla tanımlayıcı türde yapıldı.

Yöntem: Araştırma; 1 Temmuz - 30 Kasım 2011 tarihleri arasında, Konya ili merkezinde yer alan bir özel hastane, üç devlet hastanesi, iki tıp fakültesi olmak üzere toplam altı hastanenin Yenidoğan Yoğun Bakım Ünitelerinde yapıldı. Veriler anket yöntemiyle 100 anne ve babadan yüz yüze veya telefonla görüşülerek toplandı. İstatistiksel analizlerde sayı-yüzdelik ve ki-kare testleri kullanıldı.

Bulgular: Araştırmada ebeveynlerin %39'unun ilk bebeği olduğu belirlendi. Bebeklerin %48'inin kız, %64'ünün sezaryenle dünyaya geldiği, %60'ının 32-34 haftalık olarak doğduğu bulundu. Bebeklerin %39'unun prematürite dışında başka sağlık problemlerinin olduğu ve %56'sının kuvözde takip edildiği saptandı. Bebeklerin %66'sının sadece anne sütü ile beslendiği belirlendi. Anne sütünün bebeklere %40 emzirme, %21 nazogastrik sonda, %15 biberon ve %24 oranında ise emzirmenin yeterli olmaması durumunda biberon desteği ile verildiği bulundu. Annelerin %71'i, babaların ise %64'ü prematüre bebek için anne sütünün faydalarının neler olduğunu bildiklerini ifade etti. Babaların %91'inin emzirme konusunda anneye destek vermeyi düşündükleri belirlendi.

Sonuç: Prematüre bebeklerin anne sütü alması konusunda annelerin babalara göre daha çok bilgi ve deneyim sahibi olduğu, anne sütü alımının arttırılması için ebeveynlere anne sütü ve emzirme ile ilgili kapsamlı eğitimler verilmesi gerektiği sonucuna ulaşıldı.

Anahtar sözcükler: Prematüre, emzirme, anne sütü, hemşire, ebeveyn.

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Introduction

As the growth rate is high during first years of the life, it is a critical period for a newborn for growing and development. Human milk is an ideal and natural nutrient with higher biological efficacy which is adapted for the needs of every baby.[1] UNICEF and WHO recommend parents to give only human milk to their babies during first 6 months (without any solid or liquid food and water), and to start to give supplementary food beginning from 7th month. In addition to giving supplementary food after first 6 months, it is also recommended to give human milk until two years old.[2] Human milk is not only a nutrient, but also a liquid providing a healthy start for baby and protecting against various risks that may be seen in future. Also, it supports newborn development and it is better than all artificial nutrients in terms of nutritional values.

Human milk includes growth factors providing development to many systems such as gastrointestinal system, central nervous system, respiration system etc.[3,4] Human milk includes vitamin A and essential fat acids which are required for the development of baby, and it reinforces the immune system of baby.[5,6] It is expressed that human milk cures physiologic jaundice more quickly and prevents iron deficiency anemia.[2,7] Breast feeding also increases the emotional bond between mother and baby.[5,6,8]

Premature babies have many problems since they were born before they complete their intrauterine developments and all their systems are immature. One of the most significant problems is nutrition. As Immature gastrointestinal systems of premature babies, being born between 24 and 36 weeks of gestation which has the period with the highest fetal growth rate, and having poor nutrient stores are among the factors making it difficult to get fed. Aspiration risk, weak sucking reflex and requirement of patience due to long nourishment period are also other possible difficulties during practice. In the care of premature babies, it is very essential to provide ideal nourishment.[9-12] Due to its indisputable, nutritional, immunologic, psychological and economical advantages, human milk should be of top priority for premature babies.[13] American Academy of Pediatrics stated that nourishment by human milk is preferred nourishment type also for premature babies.[14] Milk of mothers giving premature delivery is quite different than those giving normal delivery, and it includes high amounts of fat, protein, sodium, lysozyme, and low amount of lactose. These substances help premature baby to grow faster. Also, during each breast feeding period, the content of mother's milk varies according to the needs of baby, and the most appropriate milk is lactated. Human milk also decreases the retinopathy risk of premature babies.[15-17]

In our country, there are limited numbers of studies for determining human milk taken by premature babies and effective factors.[18-21] In this research, it has been aimed to determine the views of parents having premature babies about babies' breast feeding and to analyze related factors affecting these views.

Method

The research was in descriptive type in order to determine the views of parents that have premature babies about babies' breast feeding. The research was conducted in Newborn Intensive Care Units (NICUs) in totally six hospitals including one private hospital, two university hospitals, and three state hospitals in Konya city center. The data were obtained in between July 1 and November 30, 2011. The population was the parents of preterm babies between 32 and 37 weeks of gestation who had treatment and care in NICUs. Population size of the research was the parents of 100 premature babies who were 32-37 weeks of gestation between July 1 and November 30, 2011, and the study group was established from parents who were volunteers and had no problem that will prevent their participation.

As data collection method, survey form prepared by researchers was used in the light of the literature.[22-24] The survey form had two chapters of questions, which were the questions for parents, and for babies. In the first section, demographic data of parents (age, education, number of child, presence of any previous premature baby), and questions about premature baby feeding and the condition of taking human milk (feeding type of baby, feeding way, condition of taking human milk, the time for starting to take human milk, knowledge of parents about the advantages of feeding with human milk, relieving gas of baby, preventing vomiting, problems during breast feeding, opinion of father for supporting mother etc.) were asked. Some questions were open-ended, and some classifications were done according to responses. In the second section, questions about delivery and baby (delivery type, gender of baby, gestational week and current week of baby, diagnosis of baby and interventions made on baby) were asked. Data were collected by researcher at hos-

pital from parents by face to face interviews or by phone.

Preliminary practice of the research was applied to parents with babies born at 32-37 weeks of gestation (five parents) and these data were not included into the research. At the end of this practice, incomprehensible expressions were determined in the information form and reviewed. Percentage and chi square tests were applied in the statistical analysis of data by using SSPS 16.0 software, and $p<0.05$ was deemed as significant. Verbal consent was obtained from parents participated to the research, and required written consents were obtained from related hospitals.

Results

The mean age of mothers in the research group was 27.43±5.94, it was 30.94±5.74 for fathers in the group, and it was found that 69% of mothers and 51% of fathers were graduated from primary schools. 20% of parents had premature baby previously, and 40% of them had their first baby (**Table 1**). 48% of the babies were girl, 64% of them born by cesarean section and 40% of them were born at 32-33 weeks of gestation. 39% of babies had no problems other than prematurity, and 57% of them were followed-up in the incubator. 66% of the babies included to the research were fed only by human milk; 40% of babies took human milk by breast feeding, 21% of them by naso-gastric catheter, 15% of them by baby bottle and 24% of them by breast feeding with the support of baby bottle since breast feeding was not sufficient. It was found that 20% of the babies had their first breast milk when they worn, 14% of them during their first day, and 62% of them a few days after the delivery (**Table 2**).

71% of mothers and 64% of fathers stated that they were aware of the benefits of human milk for premature babies. 26% of mothers expressed that human

Table 1. Demographic data of mothers and fathers (n=100).

Data	Number	%
Maternal age (Mean age: 27.43±5.94) (yrs)		
18-24	37	37.0
25-31	36	36.0
32 and above	27	27.0
Paternal age (Mean age :30.94±5.74) (yrs)		
19-25	17	17.0
26-32	48	48.0
33 and above	35	35.0
Educational status of mother		
Primary school	69	69.0
High school	23	23.0
University	8	8.0
Educational status of father		
Primary school	51	51.0
High school	35	35.0
University	14	14.0
Having premature baby previously		
Yes	20	80
No	80	80.0
Baby number		
First baby	40	40.0
2 and above	60	60.0

Table 2. Data of premature baby and feeding (n=100).

Data	Number	%
Gender		
Girl	48	48.0
Boy	52	52.0
Delivery type		
Normal	36	36.0
Cesarean	64	64.0
Delivery week		
32-33 weeks	40	40.0
34-35 weeks	32	32.0
36-37 weeks	8	28.0
Current week		
32-34 weeks	26	26.0
35-37 weeks	55	55.0
38 week and above	19	19.0
Diagnosis		
Premature	61	61.0
Premature + Newborn jaundice	18	18.0
Premature + *Other	21	21.0
Girişimler		
Taken to incubator	57	57.0
Taken to cot	15	15.0
Connected to inhalator	28	28.0
Feeding type		
Human milk	66	66.0
Formula	4	4.0
Human milk and formula	30	30.0
Feeding method		
Breast feeding	40	40.0
Naso-gastric catheter	21	21.0
Baby bottle	15	15.0
Breast feeding + baby bottle	24	24.0
Human milk intake		
Never taken	4	4.0
Taken for a while	4	4.0
Still taking	92	92.0
Starting time of human milk intake		
As soon as born	20	20.0
During the day baby born	14	14.0
A few days after birth	62	62.0
Never taken	4	4.0

*Sepsis, congenital anomaly, diabetic mother's baby, preeclamptic mother's baby, meconium aspiration syndrome.

milk provides growth-development and strengthens immune system, while these rates were 33% and 24% for fathers, respectively. 51% of mothers and 41% of fathers stated that baby needs to have human milk until two years old. For preventing vomiting, 48% of mothers reported that they will use gas relieving and 13% of them will lay baby laterally; these rates were 24% and %3 for fathers, respectively. 39% of mothers and 73% of fathers stated that they do not know how to prevent vomiting. When gas relieving was asked, 72% of mothers said that they will hold baby over their shoulders and pat them on the back, 24% of mothers will hold baby over their shoulders and tap them on the back slightly; these rates were 35% and 22% for fathers, respectively. 43% of fathers and 4% of mothers stated that they do not know how to relieve the gas of baby. When it was asked to parents that how will they understand when their baby is fed, 29% of mothers expressed that they will understand when baby falls asleep, 54% of them understand when baby does not want to suck, 16% of them understand by urine-stool of baby; these rates were 24%, 46% and 8% for fathers, respectively. 22% of fathers stated that they will not understand whether their babies are fed or not (**Table 3**).

73% of mothers expressed that they feel sufficient themselves for applying breast feeding techniques, 28% of them have problems with breast feeding, 50% of them have no problem, 27% of them do not breast feed their babies. About breast feeding, babies of 15% of mothers fall asleep, babies of 7% of mothers cannot grab completely their breasts, and 6% of mothers have small nipples. 28% of mothers want to learn everything about breast feeding, 14% of them want to learn breast feeding techniques, 6% of mothers want to know what nutrients increase breast milk, and 11% of mothers want to know benefits of breast feeding, milk preservation conditions, prevention of vomiting etc. (**Table 4**).

In the research, 91% of fathers consider to support mother about breast feeding, and it was found that 20% of fathers consider to provide this support by taking care of mother's nourishment, 23% of them by buying nutrients increasing breast milk, 24% of them by encouraging breast feeding, and 24% of them by doing everything asked by mother.

There was a significant relationship between feeling sufficient for breast feeding techniques and maternal age (women over 25 years old), educational status (primary school graduate) and child number (having two or more children) (respectively χ^2=10.72, p=0.005; χ^2=8.30, p=0.040; χ^2=8.93, p=0.034).

Table 3. Views of mothers and fathers having premature baby on feeding and human milk (n=100).

	Mother		Father	
Topics	Number	%	Number	%
Are you aware of the benefits of human milk?				
Yes	71	71.0	64	64.0
No	29	29.0	36	36.0
What are the benefits of human milk?				
It provides growth-development.	26	26.0	33	33.0
It protects against diseases.	17	17.0	13	13.0
It strengthens immune system.	9	9.0	11	11.0
It speeds up development of intelligence.	8	8.0	4	4.0
It both speeds up the growth and protects against diseases.	11	11.0	3	3.0
I do not know.	29	29.0	36	36.0
How long do you think that your baby should take human milk?				
As long as baby lactates	21	21.0	28	28.0
Until 1 year old	5	5.0	13	13.0
Until 2 years old	51	51.0	41	41.0
As long as milk exists	23	23.0	18	18.0
What do you do to prevent vomiting?				
I relieve the gas of baby.	48	48.0	24	24.0
I lay baby laterally.	13	13.0	3	3.0
I do not know.	39	39.0	73	73.0
How do you relieve the gas of baby?				
I hold baby over my shoulder and pat him/her on the back	72	72.0	35	35.0
I hold baby over my shoulder and tap him/her on the back slightly	24	24.0	22	22.0
I do not know.	4	4.0	43	43.0
How do you understand when your baby is fed?				
When falls asleep	29	29.0	24	24.0
When does not want to lactate	54	54.0	46	46.0
By urine-stool	16	16.0	8	8.0
I do not know.	1	1.0	22	22.0

Discussion

In the research, it has been aimed to determine the views of parents having premature babies about babies' breast feeding and to analyze related factors affecting these views. Within this context, it has been considered to determine problems during breast feeding of premature baby and to contribute taking precautions for these problems by this research.

In the study, most of premature babies were born before 35th week of gestation, had many health problems and required medical care. Medical care requirements of premature babies born without completing their intrauterine development are an expected condition.[13] It was found out in the research that more than half of the premature babies (66%) take only human milk. Although this rate is not at a desirable level, it indicates that premature babies have problems with taking human milk and lactating. Almost half of the mothers (40%) participated to the research give breast milk by breast feeding. It is considered that it is caused by the developmental characteristics of the premature babies.

Human milk which is an essential nutrient for infants and babies provides immunity against childhood diseases and it fulfills the nutrient requirements by itself during the first months of a newborn.[22] In the research, differences were found among the premature babies for their first human milk intakes. TNSA-2008 results show that the time for starting to take human milk is quite late in our country. It is reported that 39%

Table 4. Competency of mothers for breast feeding and topics they want to learn (n=100).

Topics	Number	%
Do you feel sufficient yourself for breast feeding techniques?		
Yes	73	73.0
No	27	27.0
Do you have any problem during breast feeding?		
Yes	28	28.0
No	50	50.0
I do not do breast feeding	23	23.0
What problems do you have?		
I have small nipple	6	6.0
Baby cannot grab my breast	7	7.0
Baby falls asleep	15	15.0
I have no problem	72	12.0
What do you want to know about breast feeding?		
Generally everything about breast feeding	28	28.0
Breast feeding techniques	14	14.0
Benefits of breast feeding	2	2.0
Milk preservation conditions	4	4.0
Ways to prevent vomiting	5	5.0
Nutrients increasing human milk	6	6.0
I know everything	41	41

of babies who are fed with human milk are not lactated within the first hour after they are born, and 27% of babies not within first 24 hours. These rates are lower than the results of TNSA-2003 and it shows that the practice rate of early breast feeding in Turkey continues to decrease. Also, low rate of early lactating of premature babies is an expected condition.

It is reported that breast feeding period and incidence in preterm and low-birth-weight babies are lower compared to term babies. While the rate of terms babies for taking human milk is 69% in the USA, it is 50% in preterm babies.[24] The reasons for having such low breast feeding rate in these babies are reported as not receiving sufficient information, consultancy, encouragement and support from health care professionals about benefits of breast feeding, and milking and preserving the milk, hospitalizing these babies for a long time, and insufficient lactating etc.[25] Low rate of breast feeding and starting to breast feeding late are affected negatively by the concern of mother that milk will not be enough, and false beliefs and practices about unprepared delivery and breast feeding.[23] Even though premature babies lactate insufficiently, it is recommended to encourage breast feeding babies if they are available to lactate.[21]

In the research, it was found out that mothers have more knowledge about the benefits of human milk compared to fathers. Same results are observed also about relieving the gas of baby, preventing vomiting and understanding that baby is fed. These results show that mother is more efficient and well-informed about the primary care of premature baby compared to father. It was found by the research that a major part of mothers (73%) feels sufficient themselves for applying breast feeding techniques. In the study of Eker and Yurdakul (2006), it was reported that most of mothers carry out breast feeding techniques properly.[20] In our study, for some reasons (mothers having small nipple, babies cannot grab breasts, baby falls asleep), half of the mothers had problems during breast feeding. It was shown in various studies that similar problems may occur in premature baby feeding.[18-21] Newborn nurse has an active role in resolving and preventing such problems.

In our research, it was observed that mothers are willing to learn some baby feeding topics (everything about breast feeding, breast feeding techniques, nutrients increasing breast milk, benefits of breast feeding milk preservation conditions, prevention of vomiting). These results also determine the extent and borders of trainings to be applied for baby feeding. Therefore, it is required to inform mothers beginning before delivery. It was reported in a study that the training and support given to mothers having term and preterm babies had significant consequences in terms of the continuity of human milk.[20-26] It is reported that breast feeding and human milk trainings given to mother by nurse contribute to maintaining breast feeding and preventing breast complications.[27] Before baby is discharged from NICU, nurse should provide these services to parents within the context of family-oriented approach. Also it is required to perform regular follow-up on mother during postnatal period, the control whether breast feeding trainings are practiced or not, and to response questions of parents with premature baby.

In the research, almost all of the fathers stated that they will support mother about breast feeding. It has been seen that this support has many fields. Supports of fathers on breast feeding and other baby care issues (relieving gas, bathing etc.) will also make positive contribution to maternal health, and also it will help to create deeper bond between father and baby.[28] For that purpose, taking baby on lap by father and visiting mother at hospital frequently will help to strengthen the bond with baby. A significant relationship was found in the research between the condition of mothers for feeling sufficient in breast feeding techniques and maternal age, educational status and child number. Mothers graduated from primary school feels sufficient themselves and this may be caused by having two or more children. In our country, it is a well-known fact that number of child decreases as educational level increases. The increase of baby feeding capabilities in parallel to the increase of child number is an expected condition. The experience may help mothers to feel more comfortable, to resolve problems easily and to feel themselves more sufficient.

Conclusion

Human milk has an essential role on the feeding of premature babies. In order to increase human milk intake, it is required to remedy the concerns of parents having premature babies about feeding, and to inform parents about human milk and breast feeding. It has been found by the research that mothers are more knowledgeable and experienced than fathers about human milk intake of premature babies. It can be recommended to give trainings on feeding premature baby for both fathers and mothers.

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Case Report

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Prenatal diagnosis of congenital mesoblastic nephroma

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Abstract

Objective: Although congenital mesoblastic nephroma is a quite rare tumor, it is the most common renal tumor during fetal and neonatal period. It is usually benign and curable by just a surgical approach consisting of nephroureterectomy. Hence, the prenatal diagnosis of congenital mesoblastic nephroma and distinguishing it from other tumors are essential. In this study, we have aimed to present a case of congenital mesoblastic nephroma which was diagnosed prenatally only by ultrasound in our clinic.

Case: A twenty-five-year-old, 35 weeks pregnant woman was referred to our clinic because of fetal intraabdominal mass. Ultrasonographically, a homogeneous solid mass was detected at the right renal fossa of the fetus. The mass was thought to be congenital mesoblastic nephroma and weekly follow-up was planned.

Conclusion: Prenatal diagnosis of congenital mesoblastic nephroma is possible by a careful ultrasonographic evaluation.

Key words: Congenital mesoblastic nephroma, prenatal diagnosis, ultrasonography.

Konjenital mezoblastik nefromun prenatal tanısı

Amaç: Konjenital mezoblastik nefrom oldukça nadir rastlanan bir tümör olmasına rağmen, fetal ve neonatal dönemin en sık görülen renal tümörüdür. Genelde benign karakterlidir ve sadece nefroüreterektomiden oluşan bir cerrahi yaklaşım ile kür sağlanabilir. Bu durum, konjenital mezoblastik nefromun prenatal tanısını koymayı ve diğer tümörlerden ayırmayı önemli kılmaktadır. Bu makalede, sadece ultrasonografi ile konjenital mezoblastik nefromun prenatal tanısını koyduğumuz bir olguyu sunmayı hedefledik.

Olgu: Yirmi beş yaşında, 35 haftalık gebe, dış merkezden fetal intraabdominal kitle nedeniyle sevk edildi. Ultrasonda, fetüsün sağ böbrek lojunda homojen ekojeniteye sahip solid kitle saptandı. Kitlenin konjenital mezoblastik nefrom olabileceği düşünüldü ve haftalık takibe alındı.

Sonuç: Dikkatli bir ultrasonografik inceleme ile konjenital mezoblastik nefromun prenatal tanısını koymak mümkündür.

Anahtar sözcükler: Konjenital mezoblastik nefrom, prenatal tanı, ultrasonografi.

Introduction

Approximately 2/3 of abdominal masses during fetal and infantile periods are related with renal problems, and most of them are hydronephrosis and multicystic dysplastic kidneys.[1] Although congenital mesoblastic nephroma (CMN) is less than 5% of infantile renal tumors, it is the most frequently seen renal tumor in the first three months of life.[2] Also, it is 80% of renal tumors reported during neonatal period.[3] Congenital mesoblastic nephroma consists of mesenchymal cells and they are generally benign.[4] In this study, we aimed to present and discuss a case that was diagnosed with prenatal CMN in the 35-week-old fetus in our clinic.

Case Report

Twenty-five years old, G2P1 patient who was on her 35 weeks of gestation according to her last menstrual period (LMP) was referred to our clinic due to fetal

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intra-abdominal mass. Her ultrasound imaging was consistent with her LMP, her placenta and amniotic fluid amount was normal, and a single living fetus was observed. A solid mass (47x51x54 mm) which was generally homogeneous, displaying heterogeneity due to necrosis on the center, including some cystic areas, and could not be distinguished from renal parenchyma clearly was observed on the right renal canal of the fetus. In the color Doppler imaging, it was conspicuous that the mass had intense vascularization and these vessels were in circle forms on the periphery (**Figs. 1a** and **1b**). Left kidney, both surrenal glands and other organs were normal. Based on these findings, it was considered that the mass could be congenital mesoblastic nephroma and weekly follow-up was planned.

The size of the mass did not change during follow-ups. The labor began at 38th week and she vaginally delivered a female baby (Apgar score: 8-9; birth weight: 2770 g). In the tomography imaging when infant was 8-day-old, a solid massive lesion originating from the center of right kidney, reaching 5x.5 cm axial size and cannot be distinguished from kidney clearly, coherent with congenital mesoblastic nephroma was found. Right nephroureterectomy was applied to baby when she was two weeks old.

During the macroscopic pathologic examination, a solid, gray-whitish lesion which was partly including thin fibrous septums and was 6x5 cm on renal tissue compressed in a narrow area and material was observed on the right nephrectomy surgery material. When lesion was examined microscopically, fusiform cells creating fascicles beside some normal renal elements, and cellular mesoblastic nephroma focuses with increased cellularity near classical nephroblastoma area were found (**Figs. 2a** and **2b**). In the immunohistochemical analysis of the material, proliferation index was found to be high in SMA (smooth muscle actin) focal positive, desmin-negative and Ki67, and cellular fields. Therefore, it was considered that the mass was a mixed type congenital mesoblastic nephroma. Surgical borders of ureter, renal capsule, perinephritic adipose tissues and vessels were intact. It was only decided to do follow-up and baby was discharged healthily.

Discussion

Perinatal renal tumors are rare and seen about 5% of the cases.[3] Although CMN is less than 5% of infantile renal tumors, it is the most frequently seen renal tumor during fetal and neonatal periods.[2,3,5] CMN can be suspected when solid renal mass found in prenatal sonography is unilateral and in an echogenicity reminding myoma.[4,6,7] Polyhydramniosis accompanies to 70% of cases.[7] Even though the formation mechanism of polyhydramniosis is not known well, mass pressuring gastrointestinal system, polyuria created by renal perfusion increased due to hyperdynamic circulation of tumor, and fetal polyuria triggered by hypercalcemia

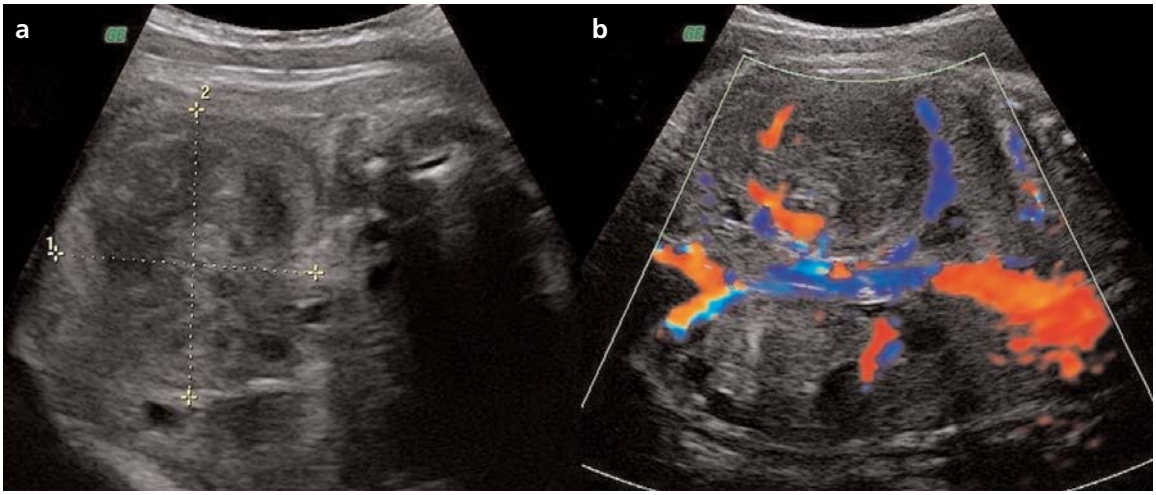

Fig. 1. Axial image of the tumoral mass appearing at the right renal fossa of the fetus (**a**) and the ring view of the highly vascular mass at the color Doppler sonography (**b**).

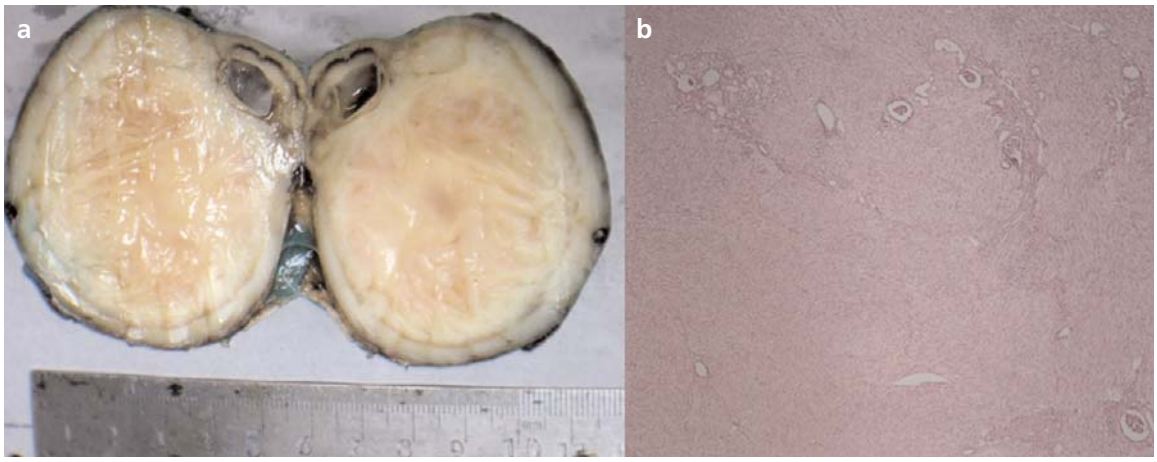

Fig. 2. Macroscopic (**a**) and microscopic (**b**) images of the right nephrectomy material. Microscopy reveals fascicles of spindle-shaped cells and small number of regular renal elements (HE x100).

associated with prostaglandins released from tumor are among the suggested mechanisms.[3,8,9]

Hyperdynamic circulation may cause cardiac failure and hydrops fetalis except polyurea.[4] Four CMN cases which developed hydrops fetalis, took place in the literature where two were diagnosed prenatally were all resulted in death. Therefore, in cases developing hydrops fetalis, it is recommended to deliver baby immediately.[3] In our case, despite the intense vascularization, no polyhydramniosis or hydrops fetalis was developed.

The most important step of the prenatal diagnosis of congenital mesoblastic nephroma is to carry out differential diagnosis of Wilms tumor from adrenal neuroblastoma. Neuroblastoma has a mixed echogenity appearance originating from adrenal gland and seemed to have solid and cystic components in ultrasound imaging. On the other hand, its margins are apparent and it is a mass separate from kidney, direct renal parenchyma invasion is not observed, and it moves asynchronous with kidney during fetal respiration; all these helps to do differential diagnosis of CMN from neuroblastoma.[3,5,6] Wilms tumor is generally surrounded with a capsule having clear margins and invades renal parenchyma completely. In congenital mesoblastic nephroma, as in our case, the margins of the mass may not be distinguished from renal parenchyma clearly.[3,6] Also CMN is an angiomatosis tumor characterized by arteriovenous shunts that may be reflected to color Doppler with intense vascularization and ring appearances.[4,10] Differential diagnosis of the mass can be performed considering that Wilms tumor is rarely seen at prenatal period and during early months of life. Yet, histopathology is inevitable for final diagnosis.[3,6]

Some authors recommend delivery by cesarean section with the concern that rupture of mass may occur during vaginal deliveries.[9] In our case, no traumatic complication occurred during vaginal delivery at term.

Conclusion

With a careful ultrasonographic examination, it is possible to establish prenatal diagnosis of CMN. When CMN is detected during perinatal period, as long as hydrops does not occur, it should be followed up considering that it is a tumor in benign nature. At least, anticipatory approach allowing fetal lung maturity should be preferred. The delivery should be carried out at a tertiary institution which has obstetrician, neonatologist, pediatric surgeon and pediatric oncologist.

Conflicts of Interest: No conflicts declared.

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PERINATAL JOURNAL

Case Report

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A diprosopus monocephalus tetrophthalmos: a case report and review of literature

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Abstract

Objective: The aim of this paper was to present and discuss a case of double-face or diprosopus of a rare variant of conjoined twins.

Case: A 24-year-old patient at 21 weeks of gestation having gravida 3, 2 living children and no significant family history was referred to our clinic with the diagnosis of hydrocephaly. Intrauterine assessment of the obstetric ultrasonography showed the fetus with one head, two faces, one body, two arms and legs, a single, unified spinal cord and vertebral column compatible with 21 weeks of gestation.

Conclusion: With the spread of prenatal follow-up, early detection of cases with conjoined twins, such as diprosopus, is essential in terms of social, economic and ethical aspects, and it will enable parents to decide at early weeks.

Key words: Diprosopus, monocephalus, tetroftalmus.

Bir diprosopus monosefalus tetroftalmus olgusu ve literatürün gözden geçirilmesi

Amaç: Bu makalede yapışık ikizin nadir bir varyantı olan çift yüz veya diprosopus olgusunu sunmak ve tartışmak amaçlanmıştır.

Olgu: Yirmi dört yaşında gravidası 3 yaşayanı 2, özgeçmiş ve soygeçmişinde özellik bulunmayan hasta 21. gebelik haftasında hidrosefali ön tanısıyla dış merkezden kliniğimize refere edildi. Yapılan obstetrik ultrasonografi değerlendirilmesinde intrauterin 21 hafta ile uyumlu, tek baş, iki yüz, dört göz, tek gövde, iki kol ve bacak, hidrosefalisi bulunan fetüs tespit edildi.

Sonuç: Prenatal takibin yaygınlaşması ile diprosopus gibi yapışık ikiz olgularının erken dönemde tespit edilmesi, sosyal, ekonomik ve etik açıdan önemli olup, ebeveynlerin erken haftalarda karar vermesini sağlayacaktır.

Anahtar sözcükler: Diprosopus, monosefalus, tetraftalmus.

Introduction

Conjoined twins are rare and interesting phenomenon, and the incidence reported for craniofacial duplication or diprosopus (two face, single head and single body) is 180,000/15,000,000.[1] Conjoined twins have high mortality rate. Approximately 40% of them results in abortus, and 1/3 of the cases die less than 24 hours after birth.[2,3] Although its etiology is not known well, they have a wide spectrum from double nasal structure to double face, four eyes (tetrophthalmos) and single head (diprosopus monocephalus).[4]

The oldest diprosopus case known was first stated in the works of Ambroise Pare in 16th century. Many diprospus cases with single body and normal extremities are complete duplication and there are severe defects in the central nervous system. On the other hand, incomplete diprosopus cases (duplication of maxilla, mandible and oral cavity) have normal central nervous system.[5] In this study, we aimed to evaluate prenatal diagnosis and management of a diprosopus case diagnosed on 21st week of gestation, through the literature.

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Case Report

A 24-year-old patient at 21 weeks of gestation having gravida 3, 2 living children and no significant family history was referred to our clinic with the diagnosis of hydrocephaly from another clinic. In the intrauterine assessment by the obstetric ultrasonography (Voluson 730 PRO, General Electric, Fairfield, Connecticut, USA) of the patient at 21 weeks of gestation showed the fetus with one head, two faces, four eyes (**Fig. 1**), one body, two arms and legs, hydrocephaly, and compatible with intrauterine 21 weeks of gestation. The findings were confirmed by MRI (**Figs. 2** and **3**).

In the transverse and longitudinal views, it was found that fetus had one heart, one stomach, one bladder, one placenta and one umbilical cord. The patient and her husband were informed about the condition. The case was discussed in the ethics committee of our clinic. After the written consent of the patient and her husband was obtained, termination was decided. After termination, it was observed in the macroscopic examination that fetus had one head, two faces, one body, two arms and legs (**Fig. 4**). The parent did not allow an examination on fetus after delivery.

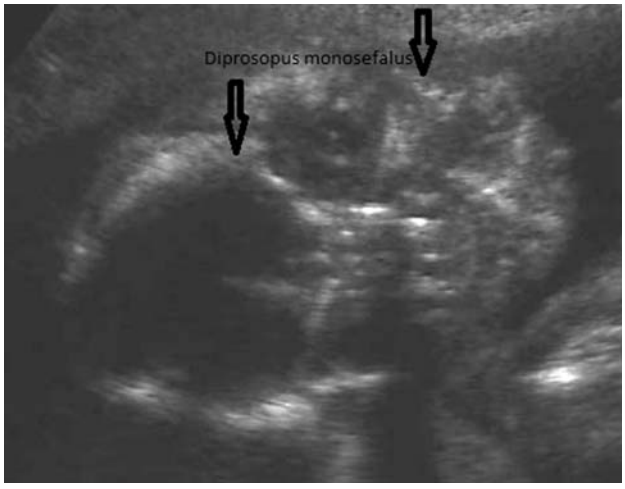

Fig. 1. Ultrasonographic view of double-face, single head.

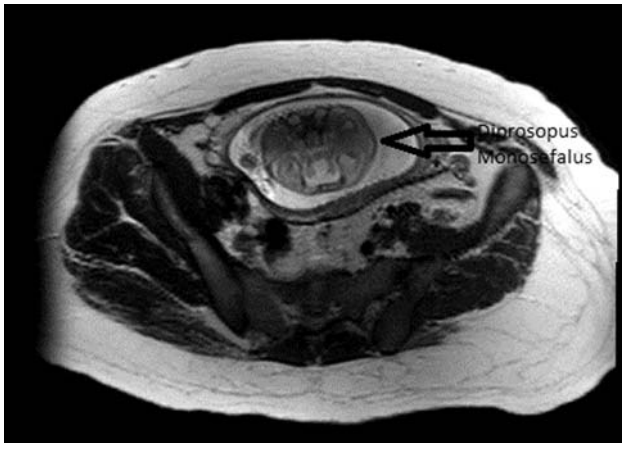

Fig. 2. MRI view of double-face, single head.

Discussion

Conjoined twins are quite rare congenital anomaly seen in 1/50,000-1/100,000 cases.[6] Our case was a craniofacial duplication or diprosopus case which is a variant of conjoined twins. The conjoined twins are independent from race, heredity, delivery number or kinship.[7] Although the etiology of conjoined twins is not known well, there are two theories proposed: According to the first theory, monovular embryo is divided incompletely on 13th-15th days of conception. In fusion theory, a secondary fusion occurs among two monovular embryonic disks.[8]

When fusions with different pattern are compared, central-located conjoined twins are seen more frequently.[9] Although complex problems within a wide

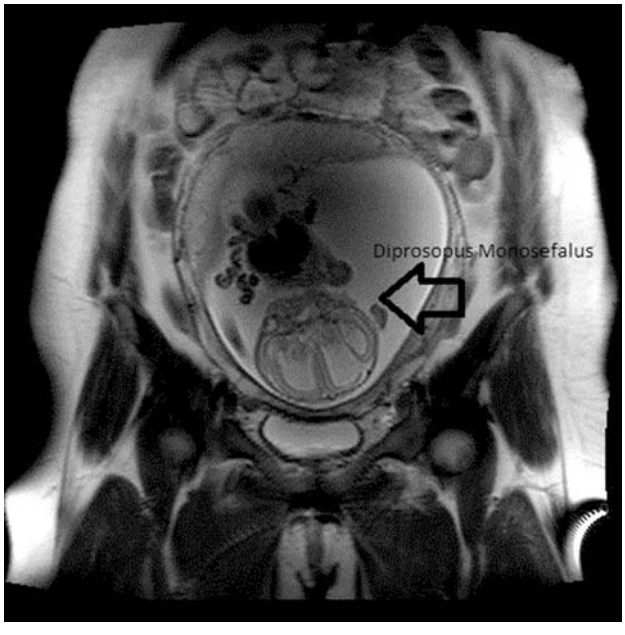

Fig. 3. MRI view of double-face, single head.

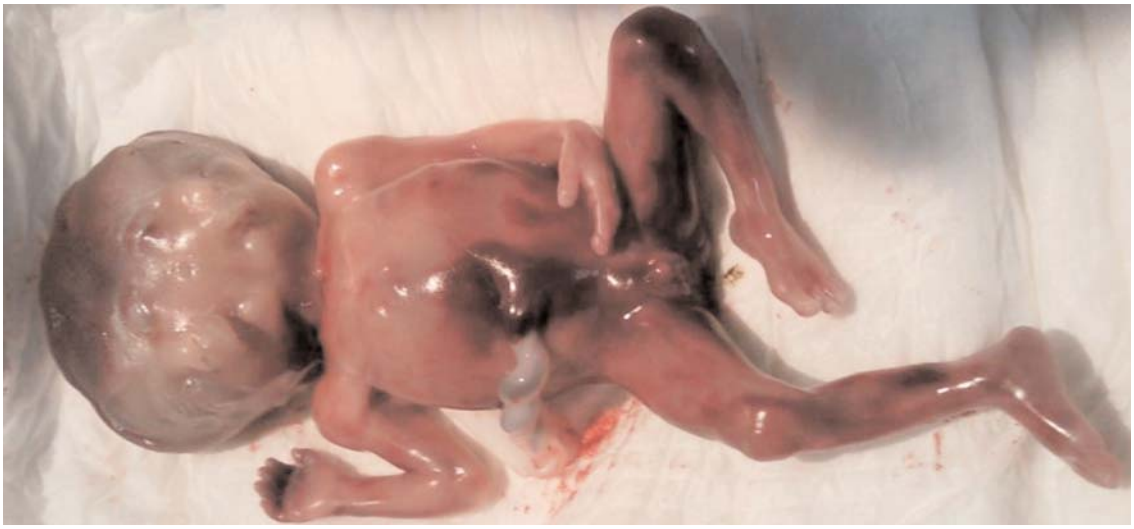

Fig. 4. Diprosopus monocephalus.

spectrum which may include all organ systems are observed in conjoined twins, the most severe anomalies are seen on fusion location. Diprosopus shows full duplication of face structures. Cleft palate and lip anomalies as well as central nervous system, cardiac, gastrointestinal and respiratory system anomalies are observed at a high rate. In our case, there was hydrocephaly. As in our case, generally female gender is dominant.[10] Chromosomal analysis results of such cases are generally normal. We could not conduct a chromosomal analysis in our case since the parent did not allow.

It is believed that diprosopus occurs as a result of a fault in the neurulation of embryo. Notochord defines the axis of embryo and induces neurulation. Peripheral neural crest cells create mesenchymal connective tissue of face and mouth areas, and pharyngeal arch.[10] A fault in the neurulation causes neural tube to fail to be closed.[11] Central nervous system anomalies frequently accompany.[12] In our case, hydrocephaly was observed as neural tube defect.

Prenatal diagnosis of cases with diprosopus was reported in the first trimester. Maternal alphafetoprotein levels were found to be high in some cases. Low fetoprotein was reported only in a case with cranioschisis.[13,14] Although polyhydramnios is observed in conjoined twins more frequently as a prenatal sonographic finding compared to normal twins, amniotic fluid was normal in our case. Interestingly, Onuf mentioned excessive amount of amniotic fluid by the examination before ultrasound.[15] Other sonographic findings are irregular cranium, enlargement of vertebra, and head in heart shape or with two equal parts.[13] Facial duplication is shown clearly by sonography.

Central nervous system anomalies were detected in all reported cases with diprosopus. In our case, hydrocephaly and double faces were seen prenatally. Conjoined twins can be recognized at first trimester easily by ultrasonography. If a single yolk sac and two fetuses or monoamniotic twins are observed by ultrasonography, the possibility of conjoined twins should be kept in mind. Cases which have advanced fusion like diprosopus can be recognized in advanced weeks.

Conclusion

Consequently, diprosopus is one of the conjoined twin types and usually central nervous system anomalies accompany it. In our region, diagnosing such cases occur only in advanced weeks of gestation due to irregular prenatal follow-up. With the spread of prenatal follow-up, early detection of cases with conjoined twins, such as diprosopus, is essential in terms of social, economic and ethical aspects, and it will enable parents to decide at early weeks.

Conflicts of Interest: No conflicts declared.

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PERINATAL JOURNAL

Case Report

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A case of postpartum cerebral venous thrombosis presented by convulsions

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Abstract

Objective: Cerebral venous thrombosis is a disease with high mortality. The incidence of the disease increases in pregnancy and puerperium. It may be associated with headache, convulsions, focal deficits, coma and death. Here, we report a case of puerperal cerebral venous thrombosis, presented by convulsions and successfully treated by heparinization despite the concomitant hemorrhagic infarct.

Case: Twenty-eight-year-old patient was admitted to Obstetrics and Gynecology emergency service, Gaziantep Maternity Hospital with convulsions, following severe headache. The patient (G2P2) had a cesarean section 10 days ago with the diagnosis of 32 gestational weeks of monochorionic diamniotic twin pregnancy and fetal distress. Cerebral venous thrombosis was detected in transverse and sigmoid sinus with concomitant hemorrhagic infarct at the thalamic region. The patient was successfully treated by heparinization.

Conclusion: Cerebral venous thrombosis should be bear in mind, because of pitfalls in the diagnosis, high incidence in the postpartum period and the importance of the differential diagnosis with eclampsia. The mortality is still high, despite the advances in diagnosis and treatment. We report this case, because of its rarity, presentation type and the treatment success.

Key words: Cerebral venous thrombosis, postpartum, heparin.

Postpartum dönemde konvülsiyon ile prezente olan serebral venöz tromboz olgusu

Amaç: Serebral ven trombozu özellikle gebelik ve puerperiumda artış gösteren, mortalitesi yüksek bir rahatsızlıktır. Baş ağrısı, konvülsiyonlar, fokal defisitler, koma veya ölüm ile ilişkili olabilir. Biz burada postpartum dönemde konvülsiyon ile prezente olan olgumuzu ve eşlik eden hemorajik infarkta rağmen heparinizasyon ile başarılı tedavisini sunduk.

Olgu: Yirmi sekiz yaşındaki hasta, şiddetli baş ağrısını takiben başlayan konvülsiyon şikayetleriyle Gaziantep Doğum ve Kadın Hastalıkları Hastanesi, Kadın-Doğum Acil Polikliniğine başvurdu. G2P2 hasta, 32 haftalık monokoryonik diamniyotik ikiz gebelik ve fetal distress tanılarıyla 10 gün önce sezaryen ile doğum yapmıştı. Transvers ve sigmoid sinüste tromboz ve talamik bölgede hemorajik infarkt saptanan hasta, heparinizasyon ile başarılı bir şekilde tedavi edildi.

Sonuç: Serebral venöz tromboz tanıda karşılaşılabilen zorluklar, lohusalıkla artan sıklık ve eklampsi ile karışabilmesi nedeniyle akılda tutulması zorunlu olan bir hastalıktır. Tanı ve tedavideki ilerlemelere rağmen mortalitedeki yükseklik unutulmamalıdır. Biz bu olguyu nadir görülmesi, postpartum dönmede konvülsiyon ile prezante olması ve heparinizasyon ile başarılı tedavisi nedeniyle tartışmak istedik.

Anahtar sözcükler: Serebral venöz tromboz, postpartum, heparin.

Introduction

Obstetrical thromboembolic disease incidence is 0.13%, and it is an essential reason for maternal morbidity and mortality in developed countries, and the mortality rate is 10% despite the treatment.[1] Pregnancy and puerperal period are accepted as a predisposing factor for cerebral venous thrombosis and the risk increases 5-6 times during pregnancy.[2] Most of the cerebral venous thrombosis cases during pregnancy occur during puerperal period, especially in the

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first three postpartum weeks. The structure mostly affected by thrombosis is superior sagittal sinus.[3] Then, transverse sinus, sigmoid sinus and cavernous sinus involvement at a less rate are observed.[3,4] Cortical and cerebellar veins may also be involved.[3,5] Here, we report transverse-sigmoid sinus thrombosis case developed in puerperal period due to its rarity, and significance of its presentation and treatment.

Case Report

Our 28-year-old patient admitted to the Maternity Emergency Polyclinic of Department of Obstetrics and Gynecology of Gaziantep Hospital with complaints of blackout, contraction, trembling, and foaming at the mouth following severe headache. The patient (G2P2) had a cesarean section 10 days ago with the diagnosis of 32 gestational weeks of monochorionic diamniotic twin pregnancy and fetal distress. The patient had a severe headache starting a few days after the delivery. There was no problem in the back story and family history of the patient, and also there was no disease or medication history during the gestational period. The first pregnancy of patient had no problem, and she had cesarean section due to breech presentation at term, and had no problem during postpartum period.

In physical examination, general condition was worse, she was unconscious, had no response to verbal and painful stimulations, there were tonic-clonic contractions and Babinski's sign was absent. Her fundus examination was natural. Her gynecologic examination was compatible with postpartum period, no additional diagnosis was observed. Tension arterial was 140/80 mmHg.

Laboratory findings were; Hct: 28%, FBG: 116 mg/dl, LDH: 874 U, SGOT: 43 IU, SGPT: 32 IU, Na: 129 mEq/l, K: 3.9 mEq/l, Ca: 8.2 mEq/l. The patient was immediately transferred to neurology clinic with the diagnosis of eclampsia due to being on postpartum 10th day. In the emergency CT, hypodense areas on the left were observed. Then, in the cranial MR imaging, left transverse sinus and sigmoid sinus had a view compatible with subacute period thrombus, and hemorrhagic infarct was observed on the left temporal and left thalamus. Due to ongoing convulsions of the patient, neurology clinic initiated antiepileptic treatment and low molecular weight heparin. The patient was followed up in neurology intense care unit for 72 hours, and then taken to the service. The neurological findings of the patient gradually regressed, and she was discharged on the 15th day. Low molecular weight heparin treatment was continued and it was seen in the MR taken on the postpartum second month that her findings regressed. No characteristic was observed in the thrombophilia panel of the patient.

Discussion

Cerebral vein thrombosis (CVT) is an entity which may cause problems during its diagnosis due to its wide clinical spectrum, and may have increased rate especially in women during contraceptive drug use and puerperal period. While headache has been found as the most frequent reason in the studies, superior sagittal sinus has been observed as the mostly involved region.[5,6] Focal and generalized seizures are seen with a rate of 35-40%, and this rate increases in puerperium.[7-9] With these clinical characteristics, it is highly possible to confuse mild CVT cases with eclampsia cases. In case of clinical suspicion, CT (with or without contrast) in differential diagnosis is the first imaging method required. However, it should be kept in mind that CT may result normal in 20-25% of cases.[10] In cases without pathognomonic CT changes, MRI and MRI venography are the most significant tools for diagnosis. Especially, it is easy to diagnose superior sagittal sinus thrombosis by MRI.[11]

Cerebral venous thrombosis certainly should be kept in mind and required consultations should be requested especially in the cases coming with postpartum convulsion, in the presence of neurological findings developing during pregnancy and postpartum period, and in unexpected cerebral hemorrhage cases. Use of imaging methods is essential, differential diagnosis cannot be established only by clinical and laboratory findings.

Anticoagulants are the first option in the treatment of cerebral venous thrombosis.[12] Unfractionated heparin is accepted as an efficient and safe treatment in CVT.[7,8] Therefore, anticoagulants are primarily used in the treatment of CVT developed during puerperal period.[4,9]

Unlike arterial infarct and ischemic necrosis as its concomitant, venous infarcts are frequently hemorrhagic and consist of erythrocytes and fibrin filaments, not of platelet plug. There is hemorrhage risk. Some of cerebral thrombosis cases have hemorrhagic infarct. In the presence of hemorrhagic infarct, there are some

risks about the anticoagulant use in terms of hemorrhage risk. In a study analyzing cerebral venous thrombosis cases, venous infarct developed in 59.38% of the cases. In other patients (40.63%), brain parenchyma was found natural.[6] The presence of hemorrhagic infarct is associated with increased hemorrhage risk. Hemorrhagic infarct was developed also in our case. Yet, we started to give low molecular weight heparin to the patient. Even though the increase of intracranial bleeding risk and the conflict about the indications, heparin is the first option as an anticoagulant treatment despite the presence of intracranial bleeding. Although there is no certain consensus about the continuity and duration of the treatment, general tendency is to maintain the anticoagulant treatment for 3-6 months unless there is an underlying thrombophilia.[13,14]

Conclusion

Cerebral venous thrombosis is a disease which should be kept in mind due to the difficulties during diagnosis, increase during postpartum period and confusion with eclampsia. Despite the developments in diagnosis and treatment, the high rate of mortality should be kept in mind.

Conflicts of Interest: No conflicts declared.

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PERINATAL JOURNAL

Case Report

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Prenatal diagnosis and postnatal treatment with bleomycin of fetal axillary cystic hygroma

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Abstract

Objective: Fetal cystic hygroma is a rare congenital malformation of the lymphatic system, characterized by the formation of a multilocular cystic mass in different parts of the fetal body. Expectant management, aspiration, surgery and the use of sclerosing agents are the current treatment options available today. Herein, we discussed a case of fetal axillary cystic hygroma with its antenatal follow-up and successful postnatal treatment with sclerotherapy.

Case: In this report, we present a case of fetal axillary cystic hygroma diagnosed antenatally at 32nd weeks of gestation followed by full-term delivery in a 30-year-old woman. During postnatal follow up, bleomycin sclerotherapy was performed. The result was excellent with good cosmetic result.

Conclusion: Since it affects the timing of birth and requires tertiary postnatal care, prenatal diagnosis of fetal cystic hygroma is very important.

Key words: Fetal cystic hygroma, prenatal diagnosis, bleomycin sclerotherapy.

Prenatal diagnosis and postnatal treatment with bleomycin of fetal axillary cystic hygroma

Amaç: Fetal kistik higroma, lenfatik sistemin nadir bir konjenital malformasyonu olup fetal vücudun değişik kısımlarında multiloküle kistik kitle oluşumu ile karakterizedir. Beklegör yönetimi, aspirasyon, cerrahi ve sklerozan ajan kullanımı günümüzde mevcut tedavi seçenekleri arasında yer almaktadır. Burada, bir fetal aksiller kistik higroma olgusunun antenatal takibi ve postnatal dönemde skleroterapi ile başarılı tedavisi tartışılması amaçlanmıştır.

Olgu: Otuz yaşındaki gebenin, gebeliğinin 32. haftasında tanı alan bir fetal aksiller kistik higroma olgusu saptandı. Postnatal izlemde bleomisin ile skleroterapi uygulandı. Sonuç, iyi kozmetik sonuç ile birlikte mükemmeldi.

Sonuç: Doğum zamanlamasını etkilemesi ve tersiyer postnatal bakım gerektirmesi nedeniyle, fetal kistik higromanın prenatal tanısı önem taşımaktadır.

Anahtar sözcükler: Fetal kistik higroma, prenatal tanı, bleomisin skleroterapi.

Introduction

Cystic hygroma is a congenital malformation of the lymphatic system appearing as large multiloculated fluid-filled cavities located predominantly in the neck region.[1,2] It has been associated with fetal chromosomal abnormalities, Turner's syndrome being the most common, hydrops fetalis and structural malformations.[3]

The treatment modality depends on the clinical picture, lesion size, anatomic location and related complications. While surgery is the treatment of choice, this is very difficult to perform in some cases due to the infiltrative nature of the lesion to adjacent vital structures. Complete excision can not always be accomplished and recurrences commonly occur after surgery.[4] The patient can be affected by several morbid conditions such as nerve injuries, prolonged lymphatic drainage, recurrence, wound infections, unacceptable scar formation and incomplete resection due to infiltration of surrounding vital structures.[2] In recent years, two sclerosing agents, bleomycin and OK-432,

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have been favored by some surgeons for the treatment of cystic hygroma.[4]

Herein, we present a case of antenatally diagnosed fetal axillary cystic hygroma, postnatal treatment with bleomycin sclerotherapy and excellent post-treatment result.

Case Report

A 30-year-old woman, gravida 3, parity 2 was referred to our hospital at 32 weeks of gestation because of a mass on the left fetal axilla detected by routine ultrasonography performed at a hospital. The patient's family history and previous medical history were unremarkable and there were no consanguinity between parents. In the current pregnancy, 1st trimester biochemical screening and the maternal serum α-fetoprotein checked at 16 weeks of gestation were both normal. Second trimester fetal anomaly screening ultrasound performed at 20 weeks of gestation was also normal.

Ultrasound examination, performed in our hospital at 32 weeks of gestation, revealed a 5x6 cm-sized, multiseptated cystic mass which was extending to the anterior and posterior thoracic wall in the left axillary region of the fetus. There was no evidence of intrathoracic extension of mass. Other fetal sonographic biometric indices and amniotic fluid amount were normal and no other structural abnormalities were found with normal echocardiography in the fetus. Prenatal karyotyping was not offered due to the advanced gestational age at admission. A provisional diagnosis of cystic hygroma was made.

Sonography was repeated at 36 weeks of gestation and revealed a normal fetal growth and no change in size of the mass. Cesarean section was performed at 38 weeks of gestation due to rupture of membranes accompanying breech presentation and hyperabduction of the left arm. A 3210 grams of weight female infant was delivered with Apgar scores of 9 and 10 at 1 min and 5 min, respectively. On delivery, the baby demonstrated a 5x5 cm-sized, soft cystic mass in the left axillary region (**Fig. 1**). The baby did not have any other structural anomalies. Peripheral blood karyotype was normal, 46,XX. Postnatal chest magnetic resonance imaging was performed a month after delivery and revealed a 8x3x5 cm-sized macrocystic mass which was extending to the anterior and posterior thoracic wall, with contrast-enhancing septa (**Fig. 2**). The mass did not have intrathoracic extension but had close proximity brachial

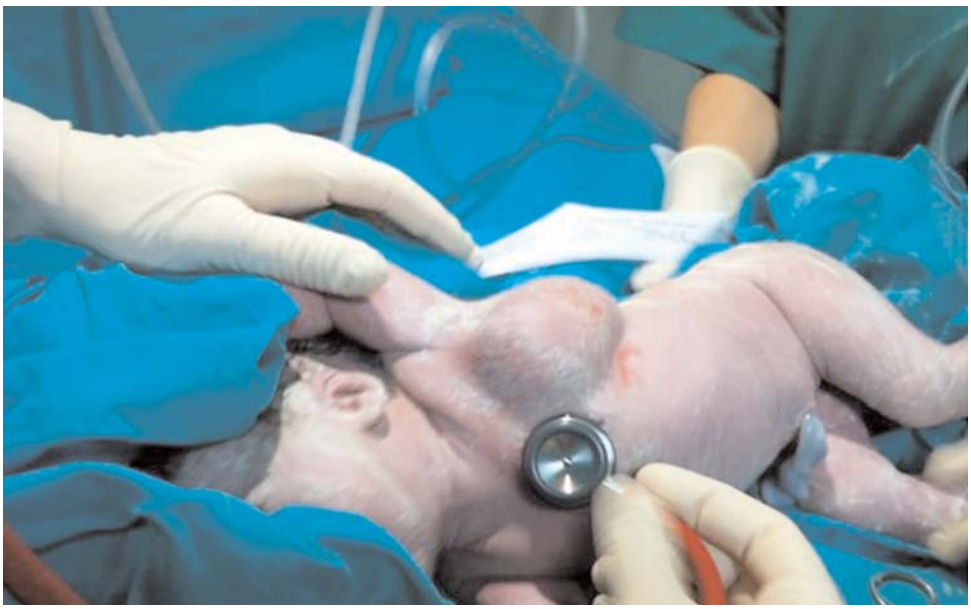

Fig. 1. The fetus during delivery. In the clinical picture taken during delivery, 5x5 cm sized, soft cystic mass causing hyperabduction of the arm is seen on the left axillary region.

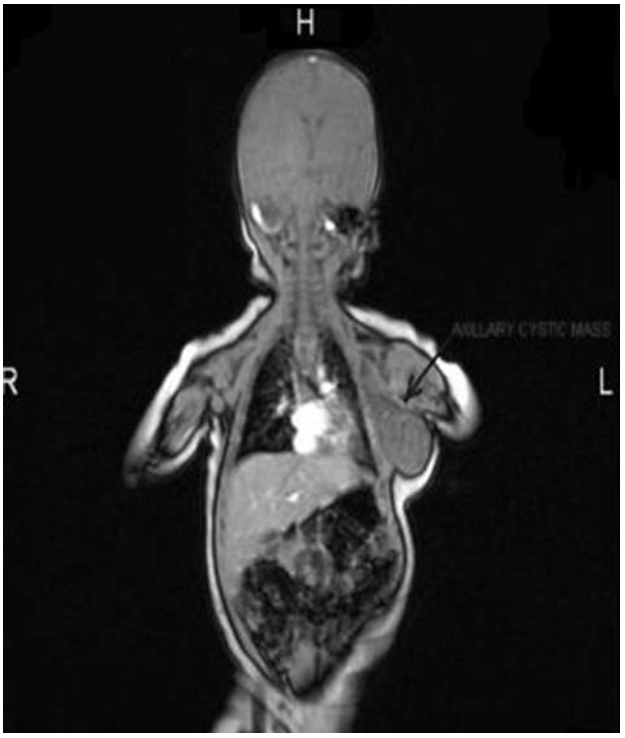

Fig. 2. Axillary mass in fetal MRI. Coronal MR images with contrast reveals a 8x3x5 cm-sized macrocystic mass which is extending to the anterior and posterior thoracic wall, with contrast-enhancing septa.

plexus. Due to the nature of the cystic mass, the probability of incomplete resection, related recurrences and nerve injury, pediatric surgeons performed bleomycin sclerotherapy. The result was excellent, no complications related to bleomycin were seen and the patient has no residual disease 6 months after therapy.

Discussion

Fetal cystic hygroma is a congenital malformation in which distended fluid-filled cavities develop, mostly in the fetal neck region, resulting from developmental anomaly of the lymphatic system.[3] The incidence of cystic hygroma is 1 in 6,000 births, but it is a relatively common anomaly in miscarried fetuses, with a frequency of 1:875.[5]

Cystic hygroma shows postnatal anatomic variability. 75% found in the neck, mainly the posterior triangle, with a predilection for the left side, and 20% localized in the axillary region.[2] The other rare locations are mediastinum, groin and retroperitoneum.

The frequency of chromosomal abnormalities associated with cystic hygroma is high (78%), the most common one is Turner's syndrome.[5] Trisomies, cardiac anomalies, hydrops fetalis and Noonan syndrome also have association with this congenital malformation.[6] Our case showed a normal karyotype. When a cystic hygroma diagnosed antenatally, serial ultrasound examination is recommended.[5] Other recommendations are the research for cardiac, renal anomalies and signs of hydrops fetalis.

The prognosis depends on several variables such as karyotype, location of the mass, gestational week of diagnosis, depth of invasion, and presence of septations.[3,5] Our case was first established in the late third trimester, with a fist-sized septated cystic mass localized to the axillary region without intrathoracic extension. Since these benign lesions have a potential of growth, serial ultrasonographic measurements are important in timing and mode of delivery. In small isolated cystic hygroma cases, there is no need to modify standard obstetrical management.[3] When large lesions are present, a cesarean section may be advisable.[3] Masood et al. reported dystocia during birth of the fetal body.[6] Since our case had a large mass along with the abduction of arm, the patient was counseled about dystocia and cesarean section was performed.

In the medical literature, there are many different treatment options, but among these, surgery and the use of sclerosing agents should be mentioned. Since these lesions usually infiltrates the adjacent vital structures such as nerves and vessels, surgical excision would result in inadvertent nerve and vessel injury and residual disease. Afterward, residual disease may lead to wound infections, recurrences and bad cosmetic results. Another treatment option, intralesional sclerosing agents have been suggested for cystic hygroma. In 1966, Umezawa discovered the chemotherapeutic agent, bleomycin.[4] Yura et al. reported the first satisfactory results of intralesional bleomycin injection in 1977.[7] Niramis et al. also suggested that bleomycin would be more effective in single superficial and large cystic lesions allowing easy aspiration.[4] Partial reduction is also valuable, since reduction in the mass, simplifies the excisional surgery.[8] Niramis et al. reported transient swelling, pain, fever, redness at the side of injection and leukopenia within 24-48 hours after injection.[4] Because of temporary bone marrow suppression, dose reduction in infants may be advisable.

Conclusion

Prenatal diagnosis of fetal cystic hygroma is very important in the management of these patients. Timed delivery and postnatal follow up are crucial in prognosis. Surgeons should keep in mind not only the alternative therapy with intralesional bleomycin injection in selected cases but also the treatment-related side effects.

Conflicts of Interest: No conflicts declared.

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