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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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# Perinatal Journal

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# Analysis Of Seven-Year Second Trimester Genetic Amniocentesis Results Of Our Clinic

Oluş Api, Ayşe Gül Özyapı, Birol Cengizoğlu, Orhan Ünal, Mehmet Cem Turan

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**Abstract**

**Objective:** To evaluate the second trimester amniocentesis procedures in last seven years performed in our clinic.

**Methods:** Indications of 594 amniocentesis procedures are high risk in triple test (38%), advanced maternal age (24.9%), high risk in first trimester screening test (14.8%), advanced maternal age together with high risk in triple test (10.9%), major anomaly (3.7%), minor anomaly (3%), previous fetus with Down syndrome (2%), history of trisomy in the family (0.5%), maternal anxiety (2.2%). There were trisomy 21 in 18 patients, trisomy 13 in two patients, trisomy 18 in two patients, other aneuploidies in 12 patients. The frequency of major chromosomal anomalies was 3.7%. This resulted in an abortion rate of 1.18% in the first two weeks following the procedure. Additionally, there occurred four other fetal deaths in the coming next two weeks. Totally, the fetal loss rate follow-ing the second-trimester amniocentesis in the first four weeks was calculated to be 1.9%. To obtain one chromosome anomaly, the least number of amniocentesis was performed by the indication of high risk in first trimester test .

**Results:** Indications of amniocentesis, karyotype anomalies, fetal loss ratios between the years of 2001-2008 have been reviewed retrospectively.

**Conclusion:** In last seven years , amniocentesis was performed mostly by the indication of high risk in triple test. The frequency of major chromosomal anomalies and fetal loss rate was compatible with the litreture. To obtain one chromosome anomaly, the least number of amniocentesis was performed by the indication of high risk in first trimester test . As first trimester screening test is more commonly used, the number of procedures to obtain one chromosome anomaly will decrease.

**Keywords:** Amniocentesis, chromosomal anomaly, fetal loss.

## *Yedi yıllık ikinci trimester genetik amniyosentez sonuçlarımız*

**Amaç:** Kliniğimizde son yedi yılda yapılan ikinci trimester amniyosentez işlemlerini değerlendirmek.

**Yöntem:** 2001-2008 yılları arasında yapılan amniyosentez işlemlerinin endikasyonları, saptanan karyotip anomalileri, karyotip anomalisi saptanan olguların özellikleri, ve işleme bağlı fetal kayıp oranları retrospektif olarak değerlendirildi.

**Bulgular:** 594 amniyosentez işleminin endikasyonları, üçlü testte yüksek risk (%38), ileri anne yaşı (%24,9), birinci trimester taramada yüksek risk (%14,8), ileri anne yaşı ve üçlü testte yüksek risk (%10,9), major anomali (%3,7), minor anomali (%3), Down sendromlu bebek doğurma öyküsü (%2), ailede trizomi öyküsü (%0,5), maternal anksiyete (%2,2) idi. Toplam 18 hastada trizomi 21, iki hastada trizomi 13, iki hastada trizomi 18, 12 hastada diğer anöploidiler tespit edilmiş olup, major kromozom anomalisi sıklığı %3,7 olarak tespit edildi. İşlemi takip eden 15 gün içinde, toplam abortus oranı %1,18 olarak hesaplandı. Ayrıca işlemi takip eden bir ila dört hafta içinde dört olguda in utero fetal ölüm saptandı. İşlemi takip eden bir ila dört hafta içinde toplam fetal kayıp oranı % 1,9 olarak bulundu. Bir anomali saptamak için en az işlemin ikili testte yüksek risk grubunda yapıldığı saptandı.

**Sonuç:** Amniosentez işlemi, son yedi yılda kliniğimizde en sık üçlü testte yüksek risk endikasyonu ile yapılmış olup, major kromozom anomali sıklığı ve fetal kayıp oranı literatürle uyumlu bulunmuştur. Bir anomali saptamak için en az işlemin birinci trimester tarama testinde yüksek risk grubunda olması nedeniyle, birinci trimester tarama testinin yaygınlaşması ile kromozom anomalisi saptayabilmek için yapılan işlem sayısı azalacaktır.

**Anahtar Sözcükler:** Amniyosentez, kromozom anomalisi, fetal kayıp

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## Introduction

First amniocentesis had been performed in 1881 for the treatment of polyhydramnios. Steele and Breg defined cell culture and chromosome analysis in 1966, after that amniocentesis performed for prenatal diagnosis.[1,2]

As prenatal diagnostic procedures progress, the diagnosis of numeric and structural chromosomal anomalies, single gene disorders, hemoglobinopathies, enzyme deficiencies, congenital infections become possible. Chromosomal anomalies are responsible for 50% of early pregnancy loss, 6-11% of all fetal death and neonatal death.[3,4] Invasive antenatal procedures are performed more common due to widespread use of biochemical screening tests and development of ultrasonographic technology. Whereupon, amniocentesis is the most common invasive prenatal diagnostic procedure.[5] The aim of this retrospective study is to evaluate the second trimester amniocentesis procedures performed in last seven years of our clinic.

## Methods

732 amniocentesis procedures were performed between the years of 2001-2008 with the indications of high risk in first trimester screening test and triple test (>1/300), advanced maternal age (>35), advanced maternal age together with high risk in triple test, major anomaly, minor anomaly (hyperechogenic bowel, echogenic intracardiac focus, single umblical artery, coroid plexus cyst, pyelectasis), previous fetus with Down syndrome, history of trisomy in the family, maternal anxiety.

Informed consent were signed by the patient and her husband. Fetal heart activity and biometry was evaluated before the procedure and the procedure was performed between 16-20 gestational weeks. All procedures were performed by 20 Gauge spinal needle, from a point as far as possible from placenta and fetal face and body via abdominal route with the aid of Logiq 200 Pro Series ultrasonography. First 1-2 ml of amniotic fluid was discarded and 1 ml sample for each gestational week was taken. Cytogenetic analysis of amniotic fluid was performed by a special genetic laboratory via Giemsa band technique. Mean duration for cell culture was 14-20 days. After amniocentesis, the patients were followed in perinatology clinic. 594 patients with full records and followed up to delivery were included to the study. The indications of amniocentesis, results of the chromosome analysis, complications of procedure and results of the pregnancy were studied.

## Results

732 amniocentesis procedures were performed in our clinic in last seven years. 138 patients with incomplete records were excluded from the study. 594 patients were studied retrospectively. When we look at demographic characteristics of the patients, the mean age was found to be 32.2 (17-47).

The most common indication was high risk in triple test ( %38, n=226). Other indications were advanced maternal age (% 24.9, n=147), high risk in first trimester screening test (%14.8, n=88), advanced maternal age together with high risk in triple test (%10.9, n=65), major anomaly (%3.7, n=22), minor anomaly ( %3, n=18), previous fetus with Down syndrome (%2, n=12), history of trisomy in the family (%0.5, n=3), family anxiety (%2.2, n=13) (Table 1).

We obtained Trisomy 21 in 18 patients, trisomy 13 in two patients, trisomy 18 in two patients, other aneuploidies in 12 patients and the frequency of major chromosome anomaly was calculated as %3.7 (Table 2).

When we evaluate the rate of chromosomal anomaly according to the indications high risk in first trimester screening test was in the first term (5.6%), advanced maternal age together with high risk in triple test was in the second term (4.6%), high risk in triple test was in the third term (3.5%). When the indication was only advanced maternal age, chromosomal anomaly was obtained 2.7% of the cases.

There were no amnion cell culture failure reported.

We suggested termination to 25 patients with major aneuploidies, all preferred termination despite one (Table 3). Complications that occurred in 15 days after the procedure were spontaneous abortion in four patients, amniorexis in three patients and total rate of abortion was 1.18%. Furthermore, intrauterine fetal death occurred one to four weeks after the procedure in four patients, after four weeks in three patients. Total fetal loss ratio that occurred one to four weeks after the procedure was 1.9%. Twenty patients (3.5%) delivered between 30-34 weeks.

Number of procedures to obtain one anomaly is calculated according to the indications. The least number of procedures to obtain one anomaly is in high risk in first trimester screening test group and the most number of procedures is in advanced maternal age group (Table 2).

## Discussion

There has been no significant decrease in the number of invasive procedures performed for prenatal diagnosis although developments in ultrasonographic technology and variability in serum biochemical screening tests. Due to widespread use of rapid genetic assessment methods like polimerase chain reaction (PCR) and flouresance insitu hybridization (FISH), invasive procedures like amniocentesis are more frequently performed. Advanced maternal age, high risk in first trimester screening test and triple test, fetal anomaly, parental reciprocal translocation, habituel abortion and history of previous fetus with chromosomal anomaly are classical indications for amniocentesis.[6]

**Table 1.** The distribution of indications for amniocentesis.

| Indication | % | n |
|---|---|---|
| High risk in triple test | 38 | 226 |
| Advanced maternal age | 24,7 | 147 |
| First-trimester screening high-risk | 14,8 | 88 |
| Advanced maternal age + High risk in triple test | 10,9 | 65 |
| Major anomaly | 3,7 | 22 |
| Minor anomaly | 3 | 18 |
| History of trisomy | 2 | 12 |
| A family history of trisomy | 2 | 12 |
| Maternal anxiety | 2,2 | 13 |
| Total | 100 | 594 |

**Table 2.** Amniocentesis is the distribution of businesses detected karyotype anomalies

| Indication | n (%) | Normal | Trizomi 21 | Trizomi 18 | Trizomi 13 | Other Aneuploidy | Aneuploidy, the number of transactions required to determine |
|---|---|---|---|---|---|---|---|
| Advanced maternal age | 147 (24,7) | 140 | 3 | - | 1 | 3 | 37 |
| Advanced maternal age+ High risk in triple test | 65 (10,9) | 61 | 3 | - | - | 1 | 21 |
| High risk in triple test | 226 (38) | 215 | 7 | - | - | 4 | 32 |
| First-trimester screening high-risk | 88 (14,8) | 82 | 4 | 1 | - | 1 | 17 |

**Table 3.** The results of amniocentesis karyotype anomaly.

| Karyotype | Age | Indication | Ultrasound findings | Week on | Prognoz |
|---|---|---|---|---|---|
| 46, XX, 15p | 39 | Advanced maternal age | No | 37 | normal phenotype |
| 46, XY, inv (9) (p1q1) | 43 | Advanced maternal age + Triple test-High risk | No | 39 | normal phenotype |
| 46, XX, inv dup (9) | 25 | Triple test-High risk | No | 39 | Normal phenotype (mother carrier) |
| 46, XY, t (1;3) dengeli | 42 | Advanced maternal age | No | 39 | Normal phenotype (father carrier) |
| 46, --, t (3;12) (q12;p13) | 27 | Major anomaly | Dandy-Walker malformasyon | - | Ended |
| 46,--,t (2;7) (p11.1;q22.1) | 28 | Binary test-high risk | No | 38 | normal phenotype |
| 46,--,t (11;12) (p11;q11) | 34 | Triple test-High risk | No | 38 | normal phenotype |
| 46,--, 1qh+,1qh+ | 30 | Triple test-High risk | No | 39 | normal phenotype |
| 45,--,der(18)(21qter-21q11:18p11.1-18qter) | 26 | Triple test-High risk | Increased nuchal pilisi | 39 | normal phenotype |
| 47,--,idic(15;15) (q12;p12) | 41 | Advanced maternal age + Triple test-High risk | No | 39 | normal phenotype |
| 69,-- | 26 | Triple test-High risk | Symmetrical IUGR + syndactyly | - | Ended |
| 47, XX+9 | 32 | Major anomaly | Dandy-Walker malformation + micrognathia + VSD + double-outlet right ventricle +symmetrical IUGR | - | Ended |
| 47, XX+13 | 40 | Major anomaly | omphalocele | - | Ended |
| 47, XX+13 | 25 | Major anomaly | Dandy-Walker malf + hyperechoic bowel + Polydactyly | - | Ended |
| 47,--,+18 | 30 | Major anomaly | Omfolosel + bilateral. Choroid plexus cyst + single umbilical artery + hyperechoic bowel | - | Ended |
| 47,--,+18 | 33 | Binary test-high risk | Early symmetrical IUGR | - | Ended |
| 47, XX+21 | 35,43 | Advanced maternal age | No | - | Ended |
| 47, XX+21 | 22 | Binary test-high risk | duodenal atresia | - | Ended |
| 47, XX+21 | 36 | Binary test-high risk | No | - | Ended |
| 47, XX+21 | 36 | Binary test-high risk | Large cisterna magna + thickened nuchal pilisi + hypertelorism + hyperechoic focus cardiogenic | - | Ended |
| 47, XX+21 | 41 | Advanced maternal age + Triple test-High risk | Nonimmun hydrops fetalis | - | Ended |
| 47, XY+21 | 37,40 | Advanced maternal age + Triple test-High risk | No | - | Ended |
| 47, XX+21 | 19,23, 29,29 | Triple test-High risk | No | - | Ended |
| 47, XY+21 | 38 | Binary test-high risk | Thickened nuchal pilisi + VSD | - | Ended |
| 47, XY+21 | 23 | Minor anomaly | bilateral pyelectasis | - | Ended |
| 47, XX+21 | 24,28 | Triple test-High risk | hyperechoic bowel | - | Ended |
| 47, XX+21 | 38 | Advanced maternal age | hyperechoic bowel | - | Ended |
| 47, XY+21 | 23 | Triple test-High risk | No | - | Did not accept termination |

In this study as we look at the indications for amniocentesis, high risk in triple test is in the first term and advanced maternal age is in the second term. Other indications are as follows high risk in first trimester screening test, advanced maternal age together with high risk in triple test, pathological findings in ultrasonography. Since we did not have the facilites of genetic laboratory for karyotype analysis from chorion villus sampling (CVS), our patients mainly preferred amniocentesis as the invasive test of choice. In the literature there are different ratios by years in the studies that evaluate indications of amniocentesis. Especially, in previous years the most common indication was advanced maternal age. In one study the most common indication is advanced maternal age (%86.3).[7] In the study of Şener et al. the most common indication is high risk in triple test the same as our study.[8]

When we evaluate amniocentesis results numerical chromosomal anomalies were obtained in 3.9% of cases, minor structural chromosomal anomalies were obtained in 1.9% of cases. According to the literature the rate of catching chromosomal anomaly by amniocentesis is between 2.3%- 4.5%. For example, this ratio is found to be 2.3% by Şener et. al, 3.6% by Yayla et. al., 3.5% by Başaran et. al., 4.5% by Cengizoğlu et. al.[8-11]

The ratio of catching chromosomal anomaly of our clinic is similar to that of various clinics in Turkey.

Although widespreadly used in practice, advanced maternal age as an indication of invasive prenatal diagnostic test is contraversial. Although once used widespread, the use of advanced maternal age as an indication for invasive test has been controversial. With the extended use of first trimester Down syndrome screening during the last 10 years, advanced maternal age is no more accepted as an indication for amniocentesis. However,in this study, advanced maternal age was the second most common indication of amniocentesis. The main reasons for this were women with advanced age who could not make use of Down syndrome screening tests, maternal anxiety due to age factor and referral of advanced age pregnant women due to unawareness of the clinicians about the knowledge of exclusion of these women for amniocentesis. We caught chromosomal anomaly in 2.7% of 147 cases with maternal age more than 35 which is found to be 3% by Cruikshank et. al, 3.7% by Hassold et al. Sjögren et al. found that ratio as 2.2% when maternal age was more than 35 and 5.3% when maternal age was more than 40.[12-14] In the literature of our country, chromosomal anomaly ratio was found to be 4% by Yayla et al., 6.1% by Cengizoğlu et al., 13.3% by Bal et al. among similar cases.[9,11,15] In the study of Dommerguez et al. it is reported that amniocentesis should not be suggested as a routine procedure in advanced maternal age (>38) but as a result of noninvasive screening tests selectively.[16] In their study, no woman in 359 patients between the ages of 38-47 delivered baby with chromosomal anomaly when nuchal translucency in first trimester was less than 3 mm and second trimester ultrasonography was normal although down synrome risk in triple test was less than 1/250. Thus first trimester screening test, triple/quater screening tests and detailed ultrasonography in second trimester have higher rates of catching anomaly it seems to be logical to avoid invasive tests performed only by advanced maternal age.

In this study when we analyse the number of procedures to obtain one chromosomal anomaly, the least number of procedures performed

with the indication of high risk in first trimester screening (17 procedures) and the most number of procedures performed by the indication of only advanced maternal age (37 procedures). In the study of Güven et al. no karyotype anomaly was obtained in 49 amniocentesis procedures although Kutlu Dilek et al. obtained five karyotype anomaly in 341 procedures performed by the indication of only advanced maternal age.[17,18] In our series, 27 procedures performed to obtain one chromosomal anomaly in terms of all indications. When it is compared with the literature, this number was reported as 25 by Önderoğlu et al., 63 by Bal et al., 49 by Kutlu Dilek et al.[19,15,18]

The most important complication of amniocentesis is fetal loss. The definition of fetal loss related to the procedure and complications in which period can be included to this definion is contraversial in the literature. When we analyse spontaneous abortion and fetal death rates together, total fetal loss rate was calculated as 1.9% in one month after the procedure. In the literature, the risk of fetal loss related to the procedure is reported between 0.2-2.1% in broad series.[5] The fetal loss rate in our series is compatible with the literature.

## Conclusion

Consequently, amniocentesis was performed mostly by the indication of high risk in triple test in last seven years of our clinic. The frequency of major chromosomal anomalies and fetal loss rate was compatible with the litreture. Thus, the least number of procedures performed in the group of high risk in first trimester screening test, as first trimester screening test is more commonly used, the number of procedures to obtain one chromosome anomaly will decrease.

**References**


1. Lambl D. Ein seltener Fall von Hydramnios. *Zentralblatt Gynaekologie* 1881; 5: 329.
2. Steele MW, Breg WR. Chromosome analysis of human amniotic fluid cells. *Lancet* 1996; 383-5.
3. Gardner RJM, Sutherland GR. Pregnancy loss and infertility: In: "Chromosomal abnormalities and genetic counselling" Oxford Monographs on Medical Genetics. Oxford: Oxford University Press; 1996; p: 311-21.
4. Alberman ED, Creasy MR. Frequency of chromosomal abnormalities in miscarriages and perinatal deaths. *J Med Genet* 1977; 14: 313-5.
5. ACOG Practice Bulletin No: 27. Prenatal diagnosis of chromosomal abnormalities. New York: Obstete Gynecol; 2001.
6. Fostner KB, Szymanski LM, Fox HE, Wallach EE. Çeviri Editörü Oral E. Johns Hopkins Jinekoloji ve Obstetri El Kitabı. Ankara: Güneş Tıp Kitapevi; 2008; p: 73.
7. Tongsong T, Wanapirak C, Sirivatanapa P. Amniocentesis-related fetal loss; a cohort study. *Obstet Gynecol* 1998; 92: 64-7.
8. Şener KT. Kliniğimizde 7 yıllık amniosentez sonuçları. *Perinatoloji Dergisi* 2006; 14: 170–5.
9. Yayla M, Bayhan G, Yalınkaya A, Alp N. Fetal Karyotyping with amniosentesis and cordoncentesis: Results of 250 cases. *Perinatal Journal* 1999; 7: 255–8.
10. Başaran S, Karaman B, Aydınlı K, Yüksel A. Amniyotik sıvı, trofoblast dokusu ve fetal kan örneğinde sitogenetik incelemeler. 527 olguluk seri sonuçları. *Jinekoloji Obstetrik Dergisi* 1992, 6: 81-9.
11. Cengizoğlu B, Karageyim Y, Kars B, Altundağ M, Turan C, Ünal O. he results of amniocentesis for three years. *Perinatal Journal* 2002; 10: 14-17
12. Cruikshank DP, Varner MW, Grant SS, Donnely E. Midtrimester amniocentesis; an analysis of 923 cases with neonatal follow-up. *AmJ Obstet Gynecol* 1991; 146: 204-10.
13. Hassold T, Chen N, Funkhouser J, Matsuyama A, Wilson C. Cytogenetic study of 1000 spontaneus abortions. *Ann Hum Genet* 1980; 44: 15-64.
14. Sjögren B, Uddenberg N. Decision making during the pre natal diagnostic procedure. A questionnaire and interview study of 211 women paıticipating in prenatal diagnosis. *Prenat Diagn* 1989; 9: 263-73.
15. Bal F, Uğur G, Yıldız A, Şahin İ, Menekşe A. 2. Trimester riskli gebeliklerinde amniyosentez uygulamaları. *Türkiye Klinikleri Jinekoloji Obstetrik Dergisi* 1995; 5: 249-56.

16. Dommergues M, Audibert F, Benartter C, Champagne C, Gomel V, Frydman R. Is routine amniocentesis for advanced maternal age still indicated? *Fetal Diagn Ther* 2001; 16: 372-2.
17. Güven MA, Ceylaner S. Prenatal diagnoses with amniocentesis and cordocentesis: Evaluation of 181 cases *Perinatal Journal* 2005; 13: 25-9.
18. Kutlu Dilek TU, Pata Ö, Yazıcı G. 2000-2005 yılları arasında gerçekleştirdiğimiz genetik amniyosentez işlemlerinin sonuçları, verim ve maaliyet analizi. *J Turkish-German Gynecol Assoc* 2005; 6: 285–9.
19. Önderoğlu L, Kabukçu A, Aktaş D, Kaşifoğlu MA, Balcı S, Gökşin E. Prenatal screening for down syndrome with use of second trimester maternal serum alphafetoprotein, human chorionia ganadotropin, and unconjugated estriol. *Perinatal Journal* 1996; 4: 117-20.

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# Multicentric Multiple Pregnancy Study II: Perinatal Mortality in Twins

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**Abstract**

**Objective:** The aim of the study is to determine the relationship between perinatal mortality and clinical demographic characteristics in twin pregnancies.

**Methods:** A questionnary and data obtained from 15 obstetrics centers was used to show the relationship between perinatal mortality and maternal age, parity, maternal morbidity, gestational week at delivery, mode of delivery, fetal or newborn's weight and sex in twin pregnancies, delivered between the period of 2003 and 2004. Chi-square, Fischer's exact and Student's t tests are used for statistical analyses.

**Results:** Perinatal mortality ratio was 107 per thousand in twins. A chance of delivery without fetal or neonatal mortality was assessed in 85% of the twin pregnancies. Mortality was high in cases born before 30th gestational week, and less than 1000g, also in twins with the same sex, in females, in discordant for growth and in small ones.

**Conclusion:** According to the results of 15 different national obstetrics centers, mortality is found in 15% of the twin pregnancies at least in one of the twin pairs. Perinatal mortality ratio is 107 per thousand. Discordant females born before the 30th gestational week have the highest risk.

**Keywords:** Twin pregnancy, perinatal mortality, multicentric study.

## *Çok merkezli çoğul gebelik çalışması II: ikizlerde perinatal mortalite*

**Amaç:** Çalışmanın amacı ülkemizdeki ikiz gebeliklerde perinatal mortalite oranını ve bu oranın klinik bulgular ile ilişkisini araştırmak.

**Yöntem:** Onbeş değişik Kadın Hastalıkları ve Doğum Kliniğinden elde edilen anket ve veri formlarının yardımı ile 2003-2004 yıllarındaki ikiz gebeliklerde perinatal mortalite ile anne yaşı, gebelik ve doğum sayıları, anne morbiditesi, doğum haftası ve şekli, yenidoğan ağırlığı ve cinsiyeti arasındaki ilişki araştırıldı. İstatistiksel yöntem olarak Chi-square, Fisher's exact ve Student t testleri kullanıldı.

**Bulgular:** İkizlerde perinatal mortalite binde 107, ikiz gebeliklerde kayıpsız doğum şansı %85 olarak belirlendi. Gebeliğin 30. haftasından önce veya 1000 g'ın altında doğanlarda, aynı cinsiyetteki ikizlerde, kızlarda, uyumsuz gelişen ve küçük olan ikiz eşlerinde mortalite daha yüksek oranda bulundu.

**Sonuç:** Ülkemizdeki onbeş ayrı merkezimizin verilerine göre ikiz gebeliklerin %15'inde bir veya her iki ikiz eşini de ilgilendiren kayıp söz konusudur ve perinatal mortalite oranı binde 107'dir. Gebeliğin 30 haftasından önce doğan uyumsuz kız ikizler en yüksek riske sahip olan gruptur.

**Anahtar Sözcükler:** İkiz gebelik, perinatal mortalite, çok merkezli çalışma.

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## Introduction

According to the general result of all studies in the world, multiple pregnancies are responsible for approximately 10% of perinatal deaths. Similarly, 8% of fetal deaths and 14% of neonatal deaths are related with multiple pregnancies. When compared to single pregnancies, perinatal mortality rate is four times higher in twin pregnancies and nine times higher in triplet and above pregnancies.[1] For example, monozygotic monochorionic twins are the group under the highest risk depending on cell division causing chromosomal or other lethal formations. Again, abnormal placenta exchanges and improper growth in fetuses among complications peculiar to monochorionic twins cause increase in morbidity and mortality.[1-3]

Though it has been expressed in many scientific meetings that there is an increase in multiple pregnancies recently in Turkey, no study has been performed for factors affecting multiple pregnancy rates, maternal and fetal morbidity and mortality related with multiple pregnancies. The widest research including many centers on this subject was published by current study group.[4]

Our goal in this multicentric cross-sectional study is to present perinatal mortality rates of twin pregnancies in some centers in our country and some basic epidemiological parameters which may be related with them.

## Methods

This study was done by questionnaire and clinical information forms sent to 15 different clinics of obstetrics and gynecology within universities and training research hospitals around Turkey between 2003 and 2004. Maternal age, gestation and delivery counts, conception type, delivery week and type, newborn weight and gender and mortality, and maternal mortality-morbidity parameters were questioned in the questionnaire. Some data not reported in the questionnaire form were questioned again and missing data were completed. Data in the group where mortality was detected in perinatal period (deliveries over 20th gestational week and first week after delivery) was compared with data in multiple pregnancy group without mortality by applying Chi square, Fisher's exact and Student T tests. $p<0.05$ was taken as a statistical significance limit.

Stillbirth was accepted as the death of fetuses who completed 20th gestational week and are at least 400gr before delivery or being unable to breath after delivery or having no heart beating while early neonatal death was accepted as newborn deaths within first 7 days after delivery; incompatible twin development was accepted as 20% difference between weights of newborns.

## Results

Total deliveries of 15 centers included into the study were 70.091 between 2003 and 2004, and 1310 of them were twins. According to this, twin delivery prevalence was found as 18.6 per thousand. Twins constituted 96% of multiple pregnancies. Delivery number of 10 centers who sent detailed twin data was 43258 and 818 of them were twin and it is suitable to the general rate (18.6 per thousand). Among them, 792 twin pregnancies formed the perinatal mortality study group since 26 cases had insufficient data. Demographical data of this group was shown in Table 1.

In multiple pregnancies, the risk of losing all pregnancy products was found as 7.07% (Table 2). In twin pregnancies, perinatal mortality rate was 106.9 per thousand (136/1272). There was one or more fetus-newborn loss in 14.3% of

twin pregnancies (Table 2). The chance of twin pregnancy without loss was 85.7%.

The weight of living one in twins with one lost was found averagely 782g higher than stillborn and 325g less than the mean birth weight of those both born alive. Mean weight of dead fetus in those with single loss was 355g higher than those with double loss (Table 3). Cesarean operation was mostly applied to twins who were both alive.

It was observed that prognosis was bad if delivery week for pregnants were under week 28, and that mortality decreased significantly when delivery week was above 30th week (p<0.001) (Table 4) (Figure 1).

In twins, surviving chance of fetuses over 1000 g was statistically higher than those below 1000g with a significant rate (p<0.001). Mortality rate of those with 1001-1500g weight was 20%. Mortality rate decreased to 7% in those with 1500g newborn weight and to 1.7% in those with over 2000g newborn weight (Table 5) (Figure 2).

When gender and weight ranges of twins were analyzed generally, it was seen that mean birth weight of boys (2243±673g) was higher than girls (2089±666g). When we analyzed the association between mortality and gender, we found that mortality was 14% in girls (82/582) while it was 8.5% in boys (55/650) (p<0.01). Mortality rate was found 22% in girl/girl twins (42/192), 12% in boy/boy twins (28/227), and 11% in mixed twins (21/197). Increased mortality in girl/girl twins was found statistically significant (p<0.01). Mortality risk in twins with same gender (70/419: 17%) was higher than twins with different gender (27/203: 13%) (p<0.05) (Table 6).

**Table 1.** Demographical and clinical data of twin pregnancies in the study group.

| | Twin (n: 792) |
|---|---|
| Age | 27.91 ± 5.36 |
| Pregnancy number | 2.40±1.90 |
| Pregnancy week | 1.10±1.66 |
| Delivery week | 34.41±3.28 |
| Fetal neonatal weight | 2172±674 g |

*Values are expressed as Mean± Standard Deviation.*

**Table 2.** Perinatal mortality in twin pregnancies.

| | Twin (n: 636) |
|---|---|
| All lost | 45 (7.07%) |
| One is alive | 46 (7.23%) |
| Both alive | 545 (85.69%) |
| At least one lost | 91 (14.30%) |

**Table 3.** Comparison of groups with and without perinatal mortality in twins (n:636).

| | Single mortality (d) | Double mortality (n: 46) | At least one mortality (n: 91) | No mortality (n: 545) | p |
|---|---|---|---|---|---|
| Age | 27.30±5.32 | 26.84±5.26 | 27.07±5.26 | 28.07±5.44 | >0.05 |
| Gestation | 2.71±1.92 | 2.62±2.24 | 2.67±2.06 | 2.39±1.92 | >0.05 |
| Parity | 1.26±1.74 | 1.00±1.54 | 1.14±1.64 | 1.09±1.72 | >0.05 |
| Delivery week | 32.57±4.03 | 26.89±3.62 | 29.66±4.78 | 35.07±2.56 | <0.001 |
| Cesarean | 29/45 (64%) | 10/46 (22%) | 39/91 (43%) | 398/545 (73%) | <0.001 |
| Weight of surviving one | 1972±807g | – | 1972±807g | 2297±539g | <0.01 |
| Weight of lost one | 1201±615g | 846±462g | 1190±782g | – | <0.01 |
| P | <0.001 | – | <0.001 | – | |

*Values are expressed as Mean± Standard Deviation.*


**Figure 1.** Delivery week and mortality in twins (%).

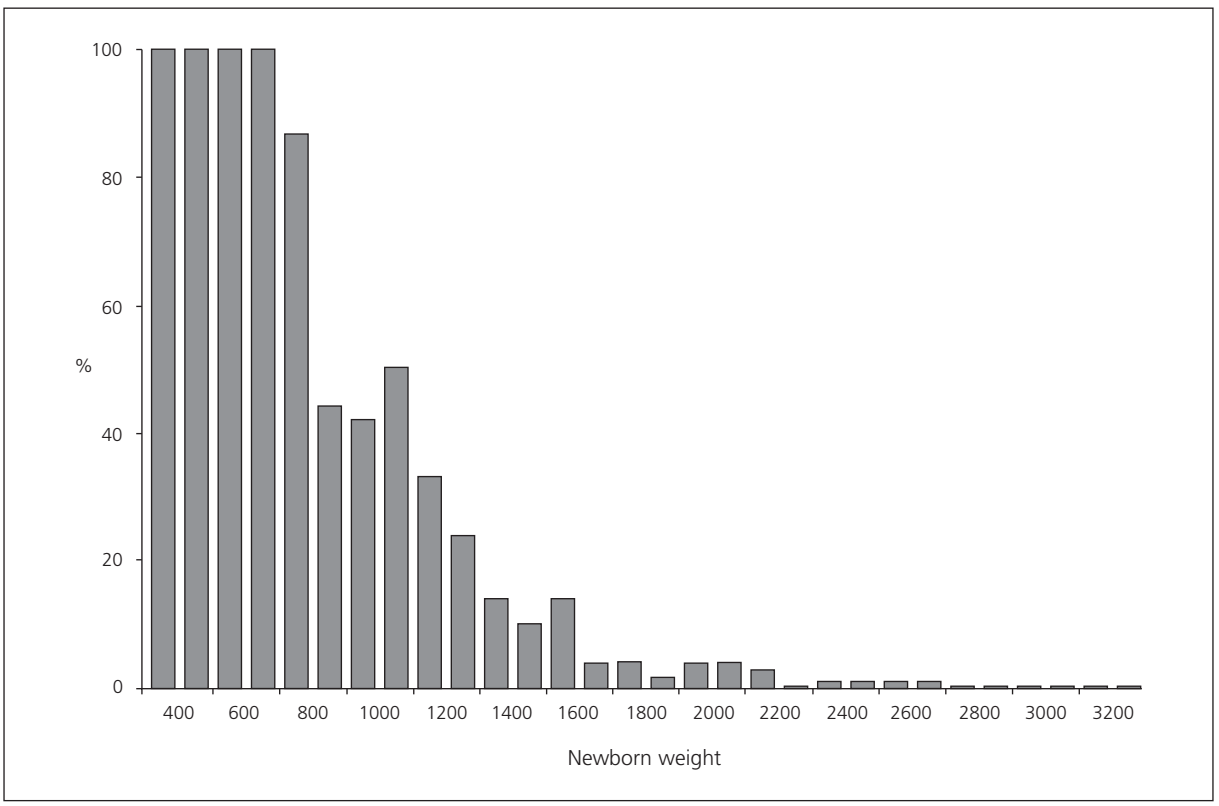


**Figure 2.** Newborn weight (g) and mortality (%) in twins.

**Table 4.** The relation of perinatal morbidity with gestational week in twin pregnancies (n:636)..

| | No mortality | ≥Mortality Exists | Total | Mortality (%) |
|---|---|---|---|---|
| Week 20-24 | 0 | 14 | 14 | 100 |
| Week 25-27 | 2 | 23 | 25 | 92.0 |
| Week 28-30 | 30 | 17 | 47 | 36.2 |
| Week 30-31 | 128 | 15 | 143 | 10.5 |
| Week 34-36 | 206 | 15 | 221 | 6.8 |
| Week >36 | 176 | 9 | 185 | 4.9 |
| Total | 545 | 91 | 636 | 14 |

**Table 5.** The relation of perinatal morbidity with birth weight in twins (n:636x2=1272).

| | No mortality | Mortality Exists | Total | Mortality (%) |
|---|---|---|---|---|
| Week 20-24 | 0 | 18 | 18 | 100 |
| Week 25-27 | 21 | 65 | 86 | 75.6 |
| Week 28-30 | 89 | 23 | 112 | 20.5 |
| Week 30-31 | 252 | 19 | 271 | 7.0 |
| Week 34-36 | 681 | 12 | 693 | 1.7 |
| Week >36 | 92 | 0 | 92 | 0 |
| Total | 1135 | 137 | 1272 | 10.8 |

**Table 6.** Relationship between gender and mortality in twins with known gender (n:616) (Girl: 582; Boy: 650).

| | Single mortality (n: 45x2) | Double mortality (n: 46x2) | At least one mortality (n: 91x2) | No mortality (n: 525x2) | Total 1232 |
|---|---|---|---|---|---|
| Dead girl | 23 | 59 | 82 | – | 82 |
| Dead boy | 22 | 33 | 55 | – | 55 |
| Living girl | 23 | – | 23 | 477 | 500 |
| Living boy | 22 | – | 22 | 573 | 595 |
| Girl + girl | 15 single | 27 double | 42 | 150 | 192 |
| Boy + Boy | 14 single | 14 double | 28 | 199 | 227 |
| Girl + Boy | 16 single | 5 double | 21 | 176 | 197 |
| Total | 90 | 92 | 192 | 1050 | 1232 |

When twin pregnancies which have at least one living fetus were analyzed, it was found that younger fetus was lost in 78% (35/45) of them. 51.64% (47/91) of twins with perinatal loss were discordant twins. Discordant twin rate in the group without loss was 21.28% (116/545). When discordant twins were examined in terms of mortality, 64% of losses occurred in younger one of twin. Mortality of 28.83% in discordant twin pregnancies was statistically and significantly three times higher than mortality of 9.30% in concordant twin pregnancies ($p<0.001$) (Table 7).

When the relationship between mortality and antenatal maternal disease in twins was evaluated, it was seen that hypertensive problems (preeclampsia, eclampsia), early membrane rupture and systemic diseases (diabetes,

**Table 7.** Discordance and perinatal mortality in twins.

| | Younger twin mortality | Elder twin mortality | Dual mortality | Those with mortality | Those without mortalit | p |
|---|---|---|---|---|---|---|
| Discordant twin (n:163) | 30 | 3 | 14 | 47 (28.83%) | 116 (71.17%) | <0.001 |
| Concordant twin (n:473) | 9 | 4 | 31 | 44 (9.30%) | 429 (90.70%) | |
| Total (n:1172) | 39 | 7 | 45 | 91 (7.76%) | 545 (92.24%) | |

blood diseases) were the first three issues. In twins with losses, only the existence of early membrane rupture (EMR) was statistically significantly high than other findings. While morbidity factors belonging to mother were higher in pregnancies where perinatal mortality was observed generally, statistically no significant difference was found (Table 8).

**Table 8.** The relationship between maternal morbidity and perinatal mortality in twins.

| | Twins without mortality (n: 545) | Twins with mortality (n:91) | P |
|---|---|---|---|
| Hypertensive diseases | 44 (8.1%) | 5 (5.5%) | >005 |
| EMR | 10 (1.8%) | 7 (7.7%) | <0.01* |
| Systemic disease | 10 (1.8%) | 2 (2.2%) | >005 |
| Other | 5 (0.9%) | 3 (3.3%) | >005 |
| Total | 69 (12.6%) | 17 (18.7%) | >005 |

## Discussion

Twin pregnancies recently have become as frequent as gestational diabetes or chronic hypertension in pregnancy. Therefore, when compared with singles, fetal and neonatal mortalities are 5-7 times higher in twin pregnancies. 25% of twins require intensive care service. In the long period, physical and mental problems are seen in this group more frequently. For example, cerebral palsy is found in twins 12 times higher and this rate only reduces to 3 times even delivery week is fixed.[5] The main reason of this high perinatal morbidity and mortality are early deliveries and complications such as respiratory distress syndrome developed accordingly, necrotising enterocolitis and intraventricular bleeding.[6] Thus, prematurity is responsible for _ of neonatal mortality and half of the long-term neurological complications.[6] The increase in fetal malformations, intrauterine growth retardation, discordant growth, monochorionicity complications and intrapartum complications are the other reasons of morbidity mortality.[7]

Developments in assisted reproductive techniques during last two decades in our country have been done thanks to technology, knowledge and experience and baby numbers going their home alive have increased. However, development in antenatal and neonatal care services could not keep pace with this speed.[8] Though neonatal mortality reduces across the country, current developments indicate that problems especially in premature and severe premature cases will continue. In this study where we examined the outcomes of multiple pregnancies in some centers in Turkey, perinatal mortality rate was found as approximately 107 per thousand, rate of pregnants who lost any of fetuses during antenatal period or at delivery as 14% and rate of pregnants who lost all fetuses or newborns as 7%. According to clinical results reported in our country, in 1990s perinatal mortality rate of twins was found as 17% for those after week 28 in the retrospective study of Buyru et al.,[9] 7.8% in the study of Karlık et al.,[10] 7.8% in the study Kayıkçıoğlu et al.,[11] 8.9% in the study of Nas et al.[12] while it was

reported in 2000s as 7.7% in the study of Güney et al.[13] where complicated cases were excluded from the series after week 24, 8.9% in the study of Yıldırım et al.[14] where again some complicated cases were excluded. Kamacı et al.[15] reported a high rate in Van which was 18%. The reason why our rate in our study was higher than other studies has been considered as including maternal complication cases and pregnancies over 20th week into the study.

Nassar et al.[16] reported 26 perinatal mortality cases from 750 twin pairs (3.5%) in their study between 1984 and 2000 which included only one center and the smallest gestational week was excluded. In the present study, this rate three times higher. When both studies are compared, we consider that the most of the difference between two studies is caused by cases at too early weeks (20th-27th weeks) and non-existence of neonatal care department in half of our centers.

In our study, neonatal survival is at the lowest level in deliveries before 27th gestational weeks for twins. Mean delivery week (30th week) for mortality-observed twin pregnancies was approximately 2.5-8.2 weeks earlier than those where mortality was not observed (35th week). This rate was similarly given as 30th and 35th weeks in the study of Yıldırım et al.[14]

Dead fetuses died were the lighter ones in approximately _ of twins. While twin pairs born alive were 770g heavier than their dead pairs, it was 325g lesser than the birth weight mean of those who both born alive. This situation can be caused by the continuation of growth of living fetus after one is dead or by immediate born of fetus at normal limits after the loss of other fetus in the previous process.

It was claimed that one of the important factors affecting mortality in twins was the discordant development among twins and it was reported that discordant twins had worse prognosis than concordant twins even there was no twin transfusion syndrome (TTS) or congenital anomaly.[16] It was reported in the study of Nassar et al[16] that 12% discordant development (>25% weight difference) might be seen in those both born alive and that approximately 2/3 of mortality in discordant twins belonged to younger twin pair. When we evaluate same criteria in our study, we observed that discordance rate was similarly just below 16% and 90% of mortality belonged to younger twin pair. It was emphasized in another newborn study of 136 cases in our country that while mortality was not different, hypoglycemia and cesarean rates were found high in discordant twins.[17] We consider that the difference in our study is caused by stillbirths which we excluded from our study.

Chorionicity is very important in terms of complications in twin pregnancies. For example, fetal risks are higher in monochorionic (MC) pregnancies than dichorionic (DC) pregnancies.[14,18] While fetal loss rate is 1.8% in DC twins between 12th and 24th gestational weeks, it is 6 times higher in MC (12.2%). Perinatal loss risk after 24th gestational week is 1.6% in DCs while it is 2.8% in MCs. IUGR and preterm delivery risk is 2 times higher in MCs than DCs. Twin transfusion syndrome which is a serious complication for MC pregnancies affects approximately 15-20% of MC pregnancies and it is very important in terms of fetal morbidity and mortality.[18] With death of one of monochorionic fetuses, there is a 38% chance that other surviving fetus may have mortality and 46% chance that it may have intracranial lesions.[19] This rate explains us why cerebral palsy rate is high after death of a fetus in multi-

ple pregnancies with same genders. Also monoamniotic pregnancies proceed with 32% perinatal mortalities. Cord entanglement found in 71% of monoamniotic pregnancies has a leading role for this rate.[19] In a wide twin series reported in our country, rate of dichorionics was 85% and in these dichorionics, perinatal mortality was 6%, monochorionics was 15% and perinatal mortality was 14%.[14] Erdemoğlu et al.[20] reported dichorionics as 69%, monochorionics as 31% while Üstün et al.[21] reported dichorionics as 64% and monochorionics as 36%. It was not possible in our study to determine the chorionicity distribution due to both characteristics of questionnaire and deficiencies in general records.

Aslan et al.[22] reported antenatal loss rate as 3.3% in their study where they examined single losses in their 972 cases of twin series and also stated that 31% of fetuses were lost after delivery. Zorlu et al.[23] found these rates as 3.8% and 12% respectively. Buyru et al.[9] found death rate of single twin pair as 2.9%. Our single antenatal loss rate was 2.5% similarly. However, due to the characteristics of the study, time of antepartum mortality and its effect on other fetus could not be determined.

Mortality risk is higher in twins with same gender than those with different genders.[19] Gender distribution in single losses was equal in our study. In dual losses, the dominance of losses from same genders (89%) was striking. This can be explained by the existence of monochorionic pregnancy. Besides, losses in girl-girl twins were almost two times more than boy-boy twins. Therefore, general loss rate in girls was also higher than boys. This finding can be explained by male fetuses being heavier than female fetuses and being born at a later gestational week (2243g versus 2089g).

According to the studies performed, 13-17% of twin pregnancies is delivered before 27th week or lighter than 1000g.[9,10,15] Perinatal mortality is higher in them. A large number of twins are delivered in a period between 34th and 37th weeks called “late preterm period”. Although mortality and morbidity are lower in this period compared to the period before 34th week, the low birth weight and risks of prematurity should not be overlooked.[24,25] Moreover, it was shown that after 39th gestational week the perinatal mortality increases 13 times more than the period before.[1]

In our study, while mortality was 100% in those born before 25th week or lighter than 500g, mortality reached to 5% as gestational weeks passed. The limit of relatively relaxive gestational week was determined as 30 while weight limit was determined as 1000g. No neonatal mortality was observed after 38th gestational week despite there was antenatal mortality.

Anomaly incidence in twins was reported between 3.6% and 6.3%.[8-10,20,26,27] Gül et al.[26] reported 6.3% anomaly incidence in twins while they found 76% of them in a single fetus and they expressed that such type of discordant anomalies caused 22% increase in mortality (9% versus 31%). No comparison was performed in our series since anomaly and autopsy data were reported at a low rate.

When twins in our study are evaluated in terms of maternal morbidity, the existence of a significant relationship between EMR and fetus losses can only be explained by the occurrence of delivery after EMR and loss of preterm-premature fetuses. However, no statistical relationship was found in our study showing that systemic diseases were directly effective on losses.

## Conclusion

One or more perinatal loss can be encountered in 15% of twin pregnancies today. In such cases, gestational week is earlier and birth weight is lighter. Gender uniformity, disproportionate growth, spontaneous multiple pregnancies (probably relatively increasing monochorionic pregnancies) appear as indicators intensifying mortality. Perinatal mortality only reduces after the limits of 30th gestational week and 1000g weight.

Though this multicentric study which is first in Turkey is narrow-scoped, it offers an insight into the twin deliveries between 2003 and 2004 and it may play a guiding role for studies to be performed later. To our knowledge, the most important way to decrease morbidity and mortality in multiple pregnancies is to keep early diagnosis records from the very beginning of pregnancy. Conservative approach for using assisted reproductive technique may also slow down the increase rate of multiple pregnancies. Using pregnancy certificate, providing communication between associations and physicians by computerized system, collecting data within a national database to be established and monitoring risky twins in perinatology centers will bring negative rates to an acceptable point.

**References**


1. Yu VYH. Contribution of multiple pregnancies to perinatal mortality and morbidity. *Perinatoloji Dergisi* 2003; 11: 109-12.
2. Allen VM, Wilson RD, Cheung A. Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC); Reproductive Endocrinology Infertility Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC). Pregnancy outcomes after assisted reproductive technology. *J Obstet Gynaecol Can* 2006; 28: 220-50.
3. Sherer DM. Adverse perinatal outcome of twin pregnancies according to chorionicity: review of the literature. *Am J Perinat* 2001; 18; 23- 37.
4. Yayla M, Baytur Y. Multicentric multiple pregnancy study I - Epidemiology. *Perinatal Journal* 2008; 16: 1-8.
5. Newman RB. Multiple gestation. *Clinical Obstet Gynecol* 2004; 47; 1: 116-7.
6. Reddy UM, Wapner RJ, Rebor RW, Tosca RJ. Infertility, assisted reproductive technology and adverse pregnancy outcomes: executive summary of a National Institute of Child Health and Human Development workshop. *Obstet Gynecol* 2007; 109: 967-77.
7. Müngen E, Tütüncü L. İkizden fazla sayıdaki çoğul gebelikler. *Perinatoloji Dergisi* 2001; 9: 149-56.
8. Saygan-Karamürsel B, Tekşam O, Aksu T, Yurdakök M, Onderoğlu L. Perinatal outcomes of spontaneous twins compared with twins conceived through intracytoplasmic sperm injection. *J Perinat Med* 2006; 34: 132-8.
9. Buyru F, Yüksel A, Demirören T, Kovancı E, Mutafoğlu T, Bengisu E. Evaluation of multiple pregnancies who has labored in our clinic. *Perinatal Journal* 1996, 12: 12-6.
10. Karlık İ, Kesim M, Çalışkan K, Koç G, İnan R. Kliniğimizde doğum yapan çoğul gebeliklerin değerlendirilmesi. *Perinatoloji Dergisi* 1996; 4: 83-7.
11. Kayıkçıoğlu F, Koçak M, Pata Ö, Dölen İ, Haberal A. İkiz gebeliklerde perinatal sonuçlar: 268 vakanın değerlendirilmesi. *MN-GORM* 2001; 7: 13-6.
12. Nas T, Noyan V, Öktem M, Maral I, Himmetoğlu Ö. 1988-1999 yılları arasındaki ikiz gebeliklerimiz; doğum şekli ve neonatal sonuçlar. *MN-Klinik Bilimler&Doktor* 2000; 6: 503-6.
13. Güney M, Oral B, Mungan T, Özbaşar D. Antepartum, intrapartum and perinatal outcome of twin pregnancies after in vitro fertilization. *J Turkish-German Gynecol Assoc* 2006; 7: 115-9.
14. Yıldırım G, Gül A, Aslan H, Erol O, Güngördük K, Ceylan Y. İkiz gebeliklerde koryonisitenin neonatal ve maternal sonuçlara etkisi. *Türk Jinekoloji ve Obstetrik Derneği Dergisi* 2007; 4: 178- 83.
15. Kamacı M, Zeteroğlu Ş, Şahin HG, Şengül M, Gülümser S, Bolluk G. Çoğul gebeliklerde doğum yöntemleri: Obstetrik komplikasyonlar ve perinatal mortalite. *Jinekoloji ve Obstetrik Dergisi (Logos)* 2004; 18: 135-9.
16. Nassar AH, Usta IM, Khalil AM, Aswad NA, Seoud AF. Neonatal outcome of discordant twin gestations. *J Perinat Med* 2003; 31: 330-6.
17. Kilic M, Aygun C, Kaynar-Tunçel E, Küçüködük S. Does birth weight discordance in preterm twins affect neonatal outcome? *J Perinatol* 2006; 26: 268-72.
18. Sebire NJ, Snijders RJM, Hughes K, Sepulveda W, Nicolaides KH. The hidden mortality of monochorionic twin pregnancies. *Br J Obstet Gynaecol* 1997; 104: 1203-7.
19. Pasquini L, Wirmalasundera RC, Fisk NM. Management of other complications specific to monochorionic twin pregnancies. In: Arulkumaran S, Keith L, Pena L (Eds).

Best Practice & Research Clinical Obstetrics & Gynaecology. Multiple Pregnancy. London: Elsevier; 2004; 18: 4: 577-99:

20. Erdemoğlu M, Kale A, Akdeniz N, Yalınkaya A, Özcan Y, Yayla M. Çoğul gebeliklerin retrospektif analizi. *Perinatoloji Dergisi* 2005; 13: 213-7.
21. Üstün Y, Engin Y, İltemir C, Cengiz B, Koç A, Cengiz L. Çoğul gebeliklerde obstetrik ve perinatal sonuçlar. *MN-Klinik Bilimler & Doktor* 2002; 8: 506-9 .
22. Aslan H, Gul A, Cebeci A, Polat I, Ceylan Y . The outcome of twin pregnancies complicated by single fetal death after 20 weeks of gestation. *Twin Res* 2004; 7: 1-4.
23. Zorlu CG, Yalcin HR, Caglar T, Gokmen O. Conservative management of twin pregnancies with one dead fetus: is it safe? *Acta Obstet Gynecol Scand* 1997, 76: 128-30.
24. Lee MY, Cleary-Goldman J, D'Alton ME. Multiple gestations and late preterm (near term) deliveries. *Semin Perinatol* 2006; 30: 103-12.
25. Huang CT, Au HK, Chien LW, Chang CW, Chien YY, Tzeng CR. Twin pregnancy outcome among cases of spontaneous conceptions, intrauterin insemination, and invitro fertilization/intracytoplasmic sperm injection. *Fertil Steril* 2006; 86: 1017-9.
26. Gul A, Cebeci A, Aslan H, Polat I, Sozen I, Ceylan Y. Perinatal outcomes of twin pregnancies discordant for major fetal anomalies. *Fetal Diagn Ther* 2005; 20: 244-8.
27. Aköz İ, Benk D, Ayas S, Yakut Y. 2000-2003 yılları arasındaki çoğul gebeliklerde obstetrik ve perinatal sonuçlarımız. *Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi* 2003; 14: 180-3.

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# The Role of Maternal Serum Leptin andMalondialdehyde Levels in Screening andDiagnosis of Gestational Diabetes Mellitus

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**Abstract**

**Objective:** To evaluate the role of maternal serum leptin and malondialdehyde (MDA) levels in screening and diagnosis of gestational diabetes mellitus (GDM).

**Methods:** Two hundred and twelve pregnant patients which were followed-up in our clinic were enrolled. Between the 24th and 28th gestational weeks we performed single step (75 g) OGTT in 96 pregnant patients and two steps (50/100 g) OGTT in 116 pregnant patients. We measured maternal leptin, MDA and HbA1c levels in all patients and compared the results of the GDM group and the control group.

**Results:** In two steps OGTT we detected 31 (26,7%) GDM cases out of 116 patients. In the single step OGTT we detected 23 (24,0%) GDM cases out of 96 patients (p>0.05). GDM was detected in 54 of 212 patients (25,5%). Pregnant women with GDM had significantly higher levels of leptin (46,52±14,99 ng/ml vs. 39,13±17,04 ng/ml, p: 0,005), MDA (3,83±0,91 nmol/L vs. 2,57±0,76 nmol/L, p<0,001) and HbA1c (5,33±0,47 vs. 5.12±0,47, p:0,001) compared to pregnant women without GDM.

**Conclusion:** Leptin, MDA and HbA1c levels are significantly elevated in GDM patients and these are found to improve the specificity of GDM screening tests.

**Keywords:** Gestational diabetes mellitus, leptin, malondialdehyde, oral glucose tolerance test, HbA1c.

## *Gestasyonel diabetes mellitus tanı ve taramasında maternal serum leptin ve malondialdehitin yeri*

**Amaç:** Gestasyonel diabetes mellitus (GDM) tanı ve taramasında maternal serum leptin ve malondialdehit (MDA) seviyesinin öneminin irdelenmesi.

**Yöntem:** Çalışmaya kliniğimizde takipleri yapılan 212 gebe dahil edildi. 24-28 gebelik haftasında 96 gebeye tek aşamalı 75 gr OGTT ve 116 gebeye de iki aşamalı gebelik diyabeti tarama testi uygulandı. Tüm gebelerin aynı zamanda maternal leptin, MDA ve HbA1c düzeylerine bakıldı. Uygulanan testler sonucu GDM tanısı koyulan gebelerle kontrol grubunun verileri karşılaştırıldı.

**Bulgular:** Yüz on altı hastadan oluşan iki aşamalı test grubunun 31'inde (%26,7) GDM tespit edilirken, 96 gebeden oluşan tek aşamalı test grubunun 23'ünde (%24,0) GDM tespit edildi (p>0.05). Toplam 212 hastanın 54'ünde (%25,5) GDM olduğu görüldü. Yapılan testler sonucunda GDM tespit edilen gebelerde, GDM görülmeyen gebelere kıyasla, serum leptin (46,52±14,99 ng/ml'ye karşı 39,13±17,04 ng/ml, p: 0,007), MDA (3,83±0,91 nmol/L'ye karşılık 2,57±0,76 nmol/L, p<0,001) ve HbA1c (5,33±0,47'ye karşılık 5.12±0,47, p:0,001) değerlerinin anlamlı derecede yüksek olduğu tespit edildi.

**Sonuç:** Gestasyonel diyabetli gebelerde Leptin, MDA ve HbA1c düzeyleri anlamlı olarak artmış olup, saptanan bulgular GDM taramasında yapılmakta olan testlerin özgüllüğünü artırıcı nitelikte olacağı bulunmuştur.

**Anahtar Sözcükler:** Gestasyonel diabetes mellitus, leptin, MDA, oral glukoz tolerans testi, HbA1c.

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## Introduction

Gestational diabetes mellitus (GDM) is defined as hyperglycemia seen after the 20th gestational week or a carbohydrate intolerance which either begins or is diagnosed during pregnancy.[1]

Leptin (greek: leptos=thin) is a protein hormone which contains 167 aminoacids and resembles cytokines, is discovered by Zhang et al.[2] in 1994. It has a molecular weight of 16 kDA.[3] It's shown to have many functions in the body. Leptin is coded on the ob/ob gene, in the long arm of the 7th chromosome (7q31) and is mainly secreted from adipose tissue. It's first detected as a mutagenic gene product in ob/ob mutant rats.[4,5] In addition to adipose tissue, it's also shown to be secreted from placenta, gastric epithelium, skeletal muscle, pituitary gland and mammary glands.[6] It's found in free and protein-bound forms in blood. Free form is thought to be responsible from its activity. Free form of leptin is shown to be the major form of leptin in obese patients.[7] Therefore increased concentrations of leptin in obese patients indicate that the main problem in development of obesity is leptin resistance, not leptin deficiency.

Many factors play role in regulation of leptin, however the main regulators of leptin levels are amount of body fat and body mass index (BMI).[8,9] Insulin, glucocorticoids and prolactin stimulate; whereas thyroid hormone, growth hormone, somatostatin, free fatty acids, cold exposure and catecholamines inhibit leptin synthesis.

In pregnant women plasma leptin concentrations are shown to be increased compared to nonpregnant women at the same age group.[10-12] Increased level of plasma leptin is correlated with free plasma leptin concentrations and alterations in leptin binding proteins.[12] Although placenta is the major source of leptin during pregnancy, the reason and function of leptin secretion is not clear yet.[11] Gestational hormones, most of the estrogens and cortisol also stimulate leptin secretion from adipose tissue.[10] Though the accumulation of fats and increased body mass in first two trimesters may be responsible for secretion of leptin, however it can also be secondary to hyperinsulinemia, considering that late pregnacy is characterized by physiologic insulin resistance and compansatory increase in insulin secretion.[10]

Maternal leptin concentrations increase 2-3 folds during pregnancy and peak at the 28th gestational week.[13] It's also shown that leptin correlates with systemic blood pressure, triglycerides and covariants of metabolic syndrome such as postpartum waist-hip ratio. Pregnancy is known to induce gestational diabetes in women with previous latent metabolic syndrome. This may imply that hyperleptinemia may be a marker for latent metabolic syndrome which reversibly proceeds to diabetes during pregnancy.[10]

It's not clear if changes in leptin concentrations are the cause or the result of gestational diabetes.[10,14]

The correlation between increased serum leptin concentrations and glucose intolerance has been shown in women with normal body weight and it's associated with increased risk of development of type II DM.[15] Leptin levels are found to increase due to increased fasting insulin levels in pregnant women with GDM and impaired glucose tolerance compared to healthy pregnant women.[16,17]

Oxidative stress and malondialdehyde is that cell membrane is prone to oxidative damage because of the presence of polyunsaturated fatty acids. Lipid peroxidation is a chemical reaction induced by free radicals and progresses by oxidation of polyunsaturated fatty acids in cell membrane. A strong oxygen derivative free radical which is present in organism separates the hydrogen atom from the α-methylen groups of polyunsaturated fatty acid chains in cell membrane, starting the reaction.[18]

The fatty acid chain gains features of a radical. The lipid radical produced is a labile compound, it undergoes several reactions. "-dien" compounds are formed by intramolecular double-bond transfer, followed by production of lipid peroxide radical which is formed as lipid radical reacts with molecular oxygen.[18] Lipid peroxide radicals react with polyunsaturated fatty acids in the membrane producing new lipid radicals and collect new hydrogen atoms to transform into lipid peroxides. So the reaction continues in an autocatalytic way.

Lipid peroxidation ends when lipid hydroperoxides are transformed into aldeyhde and carbonyl compounds. These compounds include malondialdehyde (MDA), 4-hydroxynoneal (HNA), alcohols, ethan and penthan. MDA and HNA can be used to detect lipid peroxide levels. MDA can lead to cross-binding and polymerization of the membrane components which effects functions of the internal membrane such as flexibility, ion transfer, enzyme activity and it may also react with the DNA bases causing damage. It has mutagenic, carcinogenic and genotoxic effects.[19,20] Thiobarbituric acid (TBA) test is the most important method to detect the hydroxyl radical damage in the cells, which detects the presence of MDA..[21]

Fetal hyperglycemia, maternal hyperlipidemia, hyperinsulinemia, placental endothelial dysfunction and also oxidative stress are responsible in the pathogenesis of maternal and fetal complications seen in GDM.[22] A product of lipid peroxydation, MDA, can be measured as an indicator of oxidative stress.[21,23]

HbA1c, measaurement of glycated hemoglobin is the standard method for assessing long term glycemic control. When plasma glucose is consistently elevated there is an increase in nonenzymatic glycation of hemoglobin; this alteration reflects the glycemic history over the previous 2 to 3 months, since the red blood cells have a life span of 120 days. It's a highly specific and reliable marker HbA1c should be measured in all individuals with DM during their initial evaluation and to predict long term complications of DM.

Screening and diagnosis of gestational diabetes mellitus Either 75 g OGTT or 50/100 g OGTT is used in screening or diagnosis of gestational diabetes mellitus. World Health Organisation (WHO) recommends the use of 75 g OGTT in diagnosis of GDM whereas in many countries including Turkey 50/100 g OGTT is used for screening and diagnosis of GDM.

## Methods

Two hundred and seventy pregnant women who had been followed in pregnancy outpatient clinic and division of perinatology in Cerrahpasa Medical Faculty, Department of Obstetrics and Gynecology, March 2005-February 2006 inclusive, were enrolled to our study. Our study is designed as a descriptive study. Fifty eight patients were excluded due to inadequacy of their data, and remaining 212 women have been investigated.

Gestational ages of the women were calculated according to the last menstral period, and early pregnancy ultrasound measurements if in doubt. 10 cc of venous blood samples from all patients in the study group were collected in dry tubes before performing the diabetes screening tests between 24-28 GWs. Serum parts were separated and preserved in -80°C to be evaluated at once, when target patient population is reached. Leptin and malondialdehyde levels were measured in biochemistry laboratory. GDM screening and diagnosis tests were performed between 24-28 GWs in all 212 patients. Single step 2 hours 75 g OGTT was performed in 125 patients. The test results were interpreted according to the American Diabetes Association (ADA) criteria (≥2 values above treshold, fasting glucose levels: 95 mg/dl, 1 hour: 180 mg/dl, 2 hours 155 mg/dl). Two steps 50 g OGTT was performed in 149 patients. The patients with 1 hour blood glucose levels of ≥140 mg/dl were accepted as screening test positive according to ADA and American College of Obstetricians and Gynecologists (ACOG) criteria. The diagnostic test was performed in screening test positive patients after 3 days standard diet (at least 250 g of daily carbonhydrate). After a fasting period of 12-16 hours, the blood samples were collected at 8 am and the 1st, 2nd and 3rd hours. Carpenter and Coustan's criteria were considered in the interpretation of 100 g OGTT and ?2 levels above treshold (fasting: 95 mg/dl, 1. hour 180 mg/dl, 2. hour 155 mg/dl, 3. hour 155 mg/dl) were accepted to have GDM. HbA1c levels were measured in all patients at the time of screening.

**Serum MDA level measurement:** The absorbance of the complex which is produced by the reaction between MDA and thiobarbituric acid is measured spectrophotometrically. MDA level for the measured absorbance was calculated from the curve.

Serum MDA levels are given in nmol/L. Serum leptin levels were measured by a kit which is based on ELISA (Human Leptin Elisa DSL-10-23100i, Texas, USA).

Leptin levels are expressed in ng/ml. Statistical Package for Social Sciences (SPSS Release 11,5, SPSS inc., Chicago, IL, USA) was used during statistical calculations. Student's t test was used for parametric variables and chi-square test was used for comparing qualitative data. 0.05 was accepted as treshold for statistical significance. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under curve values were calculated ROC (Receiver operating characteristic) curves.

## Results

GDM was detected in 54 (25.4%) of 212 pregnant women enrolled in our study. Two steps OGTT was performed in 116 cases and single step OGTT was performed in 96 women. These two groups were similar in age, gravidity, parity, maternal weight, body mass index and gestational weeks at the time of test. GDM was diagnosed in 31 (26.7%) of 116 pregnant women who underwent 50/100 g OGTT and 23 (24%) of 96 pregnant women who underwent 75 g OGTT.

Serum leptin, MDA and HbA1c levels measured between 24-28 gestational weeks were statistically different in GDM and non-GDM groups. Leptin levels of women with GDM and without GDM were 46.52±14.99 ng/ml and 39.13±17.04 ng/ml, respectively (p:0.007, AUC: 0.623, %95 CI: 0.542-0.703). Malondialdehyde levels of women with GDM and without GDM were 3.83±0.91 nmol/L and 2.57±0.76 nmol/L, respectively (p<0.001, AUC: 0.856, %95 CI: 0.800-0.912). HbA1c levels of women with GDM and

without GDM were 5.33±0.47 and 5.12±0.37, respectively (p: 0,001, AUC: 0.655, %95 CI: 0.565-0.744) (Table 1). Thirty four pregnant women who were 50 g OGTT positive and 100 g OGTT negative, and 178 women without GDM were compared; no significant difference between two groups in terms of mean serum leptin (38.38±17.62 ng/ml vs 39.36±16.94 ng/ml respectively, p >0.05) (Table 2), MDA (2.59±0.77 nmol/L vs 2.57±0.71 nmol/L respectively, p >0.05) (Table 3) and HbA1c (5.24±0.41 vs 5.08±0.36 respectively, p>0.05) levels (Table 4).

**Table 1.** Leptin, MDA and HbA1c levels of GDM and non-GDM groups.

| | Normal | GDM | p |
|---|---|---|---|
| Number of patients (n) | 158 | 54 | |
| Leptin (ng/ml) | 39.13±17.04 | 46.52±14.99 | 0.007 |
| MDA (nmol/L) | 2.57±0.76 | 3.83±0.91 | <0.001 |
| HbA1c (%) | 5.12±0.37 | 5.33±0.47 | 0.001 |

p<0.05: Significant; **MDA:** Malondialdehyde, **GDM:** Gestational diabetes mellitus.

**Table 2.** Sensitivity, specificity, PPV and NPV for various leptin levels of women with GDM..

| Leptin level | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| 23.06 ng/ml | 100 | 22,5 | 30 | 100 |
| 30.21 ng/ml | 83 | 45 | 34 | 88 |
| 40.08 ng/ml | 64 | 54 | 31 | 80 |
| 50.09 ng/ml | 42 | 68 | 30 | 76 |
| 60.00 ng/ml | 20 | 88 | 36 | 76 |
| 70.1 ng/ml | 7 | 97.5 | 42 | 75 |

**GDM:** Gestational diabetes mellitus, **PPV:** positive predictive value, **NPV:** negative predictive value.

**Table 3.** Sensitivity, specificity, PPV and NPV for various MDA levels of women with GDM.

| MDA level | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| 1.79 nmol/L | 100 | 11 | 27 | 100 |
| 2.53 nmol/L | 92 | 66 | 52 | 96 |
| 3.50 nmol/L | 55 | 88 | 61 | 85 |
| 4.50 nmol/L | 31 | 98 | 84 | 80 |
| 5.00 nmol/L | 5 | 99 | 60 | 75 |

**GDM:** Gestational diabetes mellitus, **MDA:** Malondialdehyde, **PPV:** Positive predictive value, **NPV:** negative predictive value.

**Table 4.** Sensitivity, specificity, PPV and NPV for various HbA1c levels of women with GDM.

| HbA1c level | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| % 5.0 | 76 | 47,5 | 34 | 87 |
| % 5.5 | 26 | 87 | 4 | 77 |
| % 5.9 | 7 | 98 | 50 | 75 |
| % 6.3 | 2 | 99 | 50 | 75 |

**GDM:** Gestational diabetes mellitus, **PPV:** Positive predictive value, **NPV:** negative predictive value.

## Discussion

It's not only controversial whether screening for GDM in all patients or only the risk groups, but also the method of choice. Screening for GDM in most population groups may seem unnecessary regarding that its prevalence is below 5%, but if the 4 folds increase in perinatal mortality is considered, it's a reasonable effort.[24]

Although the average incidence of GDM is 3-5%, it may vary between 1-14% depending on the method used. GDM incidence in Turkey is reported as 1.23-6.6%. In our study, GDM incidence was found as 21,1% and this high ratio is attributed to the fact that our clinic is a tertiary (reference) center. Recently it's emphasized that leptin is effective not only in obesity but also in glucose regulation.[28,29] Weight loss and fasting is known to decrease leptin concentration whereas weight gain and hyperinsulinemia increase it.[30,31] Increased leptin concentration in pregnant women is attributed to the changes in maternal fat and glucose metabolism.[13]

Maternal leptin levels increase 2-3 folds during pregnancy and peak at the 28th gestational week.[13] Clinical studies suggest that increased maternal leptin concentrations are associated with insulin resistance and hyperinsulinemia which occurs in the second trimester.[31] Qiu et al.[14] enrolled 823 pregnant women and investigated the effects of increased leptin levels in

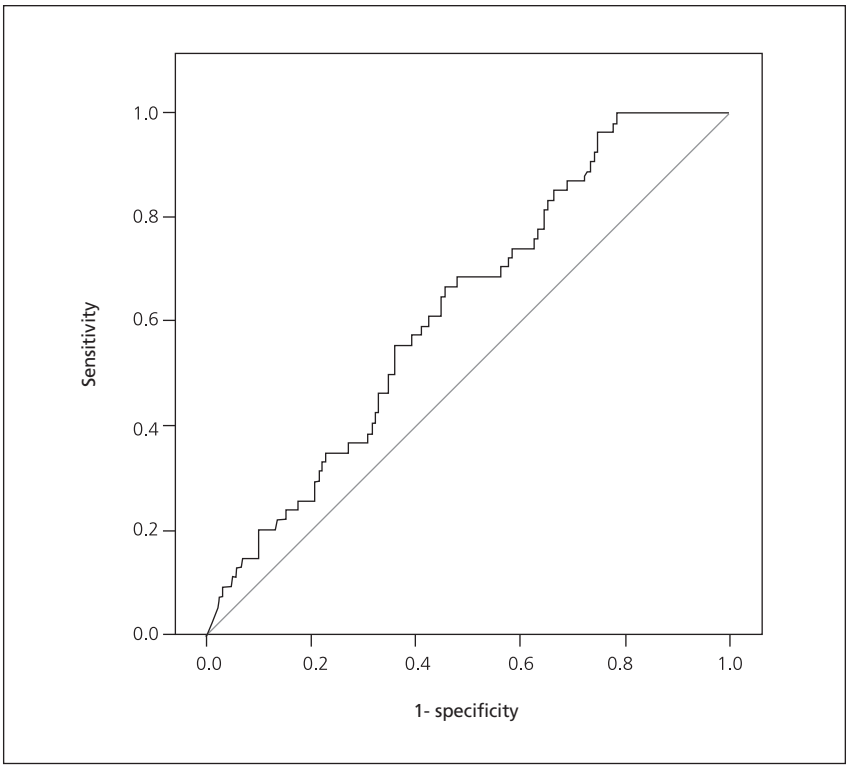


**Figure 1.** ROC curve for serum leptin levels in patients with GDM.

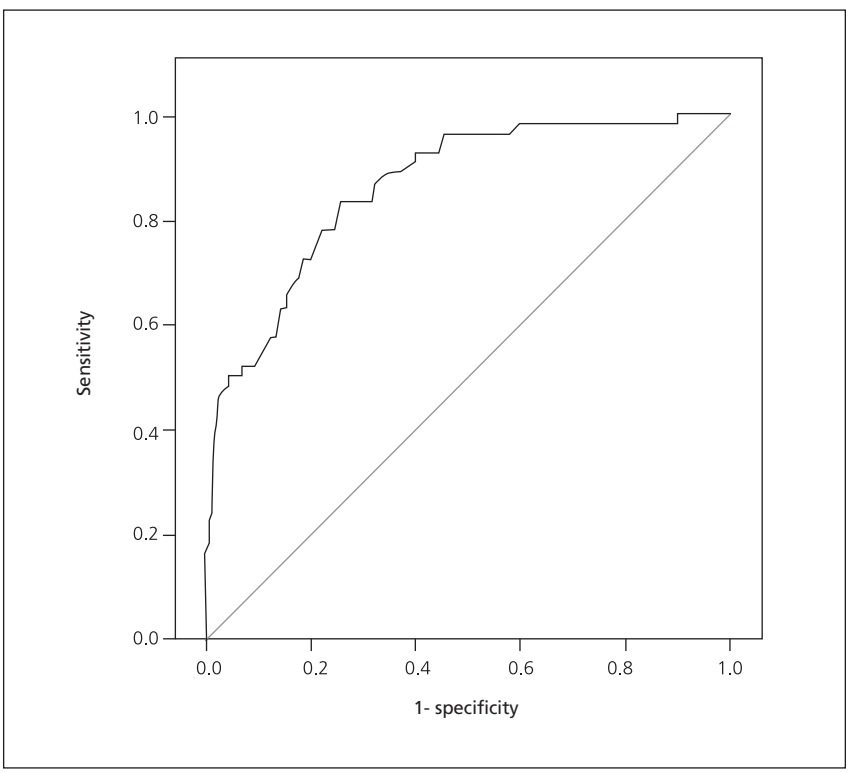


**Figure 2.** ROC curve for serum MDA levels in patients with GDM.

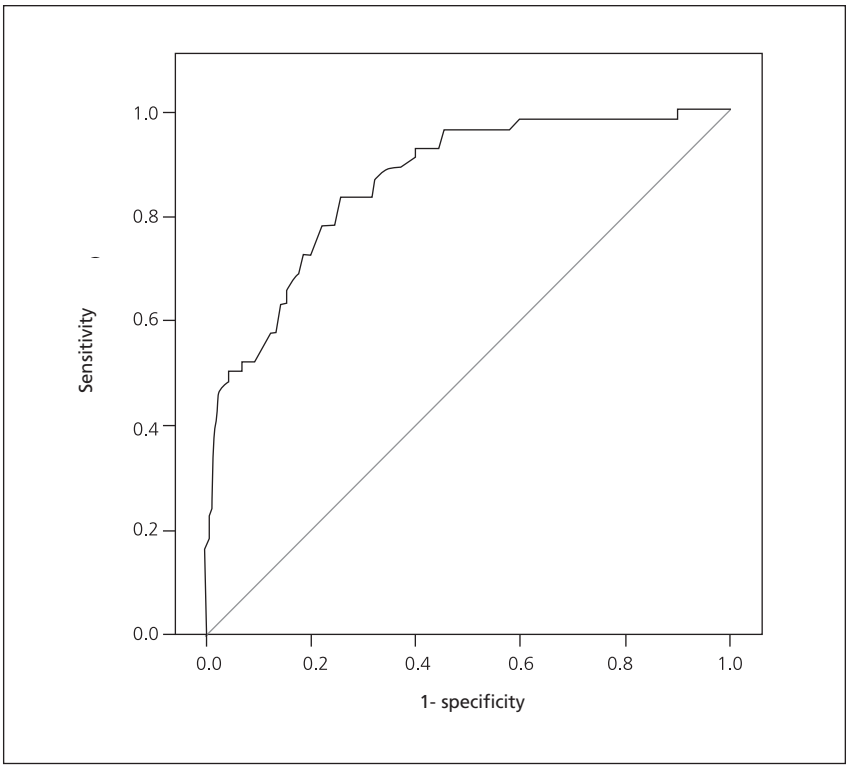


**Figure 3.** ROC curve for serum HbA1c levels in patients with GDM.

early pregnancy. They observed that increased leptin concentrations in early pregnancy are associated with 4.7 folds increase in GDM risk, compared to women with leptin levels below 14.3 ng/ml. It's estimated that every 10 ng/ml increase in leptin concentration leads to 20% increase in GDM risk.[14] Serum leptin levels measured between 24-28 gestational weeks were statistically different in GDM and non-GDM groups. Leptin levels of women with GDM and without GDM were 46.52±14.99 ng/ml and 39.13±17.04 ng/ml, respectively (p:0.007). Kautzky-Willer et al.[10] investigated leptin levels in 25 healthy pregnant women, 55 women with GDM, 10 type I DM and 10 healthy nonpregnant women.

Leptin levels are shown to be increased in all pregnant women compared with nonpregnant women at the same age group. (p<0.0005) Increased level of plasma leptin is correlated with free plasma leptin concentrations and alterations in leptin binding proteins.[12] Although placenta is the major source of leptin during pregnancy, the reason and function of leptin secretion is not clear yet.[11] Gestational hormones, most of the estrogens and cortisol also stimulate leptin secretion from adipose tissue.[10] Though the accumulation of fats and increased body mass in first two trimesters may be responsible for secretion of leptin, however this can also be secondary to hyperinsulinemia. Leptin levels are shown to be significantly high in women with GDM compared to pregnant women with type I DM and pregnant women with normal glucose tolerance (p<0.008).[10] Moriya et al.[32] have shown that hyperglycemia has an inhibitory effect on leptin secretion in patients with non-insulin dependent DM by

showing that HbA1c is negatively correlated with leptin concentrations. Previous studies implied that insulin stimulates leptin secretion from adipocytes. In patients with uncontrolled diabetes it's observed that longstanding hyperglycemia has a suppressive effect on insulin. In these patients decreased insulin levels may be accompanied by decreased leptin.

In contrast leptin levels are expected to rise in hyperinsulinemia which is seen in the 2nd trimester in patients with GDM.[32] Results of our investigation support the hitherto publications, leptin levels are significantly high in women with GDM. Therefore leptin can be used as a marker in screening and diagnosis of GDM. Fetal hyperglycemia, maternal hyperlipidemia, hyperinsulinemia, placental endothelial dysfunction and also oxidative stress is responsible in the pathogenesis of maternal and fetal complications seen in GDM.[22] Oxidative stress in diabetes may be associated with increased reactive oxygen radicals such as O2-, OH- and H2O2 or deficiency in antioxidant defence mechanisms. Increase in oxygen radicals can be attributed to protein glycosylation or autooxidation of glucose in hyperglycemic media.[33-35]

Superoxide dismutase (SOD) activity is shown to decrease in red blood cells in studies on diabetic rats[36] and humans.[37] Glutathione peroxidase and catalase enzyme activities are decreased in chronic diabetes.[38] Vitamin E is one of the major intracellular nonenzymatic antioxidants and it's known to be decreased in patients with diabetic patients.[39] In an experimental study free oxygen radical activity is observed in embryos of diabetic rats and is thought to be the underlying mechanism in teratogenicity in diabetic pregnant women.[40] Besides antioxidant therapy is shown to prevent in vivo and in vitro embryonic dysmorphogenesis associated with diabetes.[41] On the other hand, glucose regulation alone can maintain better perinatal outcomes in these patients.[42] Kharb et al.[43] studied on 25 healthy pregnant women and 25 women with GDM and they have shown that maternal MDA and SOD levels are increased whereas vitamin C and E levels are decreased in women with GDM. Peuchant et al.[22] also observed high plasma and free erythrocyte MDA levels in women with GDM, this may be a proof for oxidative stress. In the same study significant decrease in glutathione peroxidase and low vitamin E and erythrocyte vitamin A levels imply deficiency in antioxidant mechanisms.[22]

In our study, significantly low MDA levels seen in women with GDM indicate that oxidative stress begins to be effective since very early stages of pregnancy in these patients. This finding may imply that oxidative stress may play a role in pathogenesis of maternal and fetal complications. Few studies have been made so far on this issue, but all support our study. A potential bias in our study is that MDA levels were measured indirectly, and our results should be tested by MDA spesific kits.

## Conclusion

In conclusion MDA levels are shown to increase in women with GDM and it may increase the specificity of the other tests used in screening of GDM.

### References

1. Passa P, Vague P. Diabetes and Pregnancy. *Diabet Metab* 1990; 16: 113-85.
2. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. *Nature* 1994; 372: 425-32.

3. Pelleymounter MA, Cullen MJ, Baker MB, ve ark. Effects of the obese gene product on body weight regulation in ob/ob mice. *Science* 1995; 269: 540-3.
4. Friedman JM. Role of leptin and its receptors in the control of body weight. In: Blum WF, Kiess W & Rascher W (Eds). Leptin-the voice of adipose tissue. Heidelberg; Johann Ambrosius Barth Verlag; 1997; p: 3-22.
5. Campfield LA, Smith FJ, Guisez Y, Devos R, Burn P. Recombinant mouse ob protein: evidence for a peripheral signal linking adiposity and central neural networks. *Science* 1995; 269: 546-9.
6. Sinha MK. Human leptin: the hormone of adipose tissue. *Eur J Endocrinol* 1997; 136: 461-4.
7. Brabant G, Horn R, Mayr M, Wurster U, Schnabel D, Heidenreich F. Free and protein bound leptin are distinct and independently controlled factors in energy regulation. *Diabetologia* 2000; 43; 438-42.
8. Frederich RC, Hamann A, Anderson S, Löllmann B, Lowell BB, Flier JS. Leptin levels reflect body lipid content in mice: evidence for diet-induced resistance to leptin action. *Nat Med* 1995; 1: 1311- 4.
9. Ma Z, Gingerich RL, Santiago JV, Klein S, Smith CH, Landt M. Radioimmunoassay of leptin in human plasma. *Clin Chem* 1996; 42: 942- 6.
10. Kautzky-Willer A, Pacini G, Tura A, ve ark. Increased plasma leptin in gestational diabetes. *Diabetologia* 2001; 44: 164-72.
11. Senaris R, Garcia-Caballero T, Casabiell X. Synthesis of leptin in human placenta. *Endocrinology* 1997; 138: 4501-4.
12. Lewandowski K, O'Callaghan CJ, Dunlop D, ve ark. Free leptin, bount leptin, and soluble leptin receptor in normal and diabetic pregnancies. *J Clin Endocrinol Metab* 1999; 84: 300-6.
13. Schubring C, Englaro P, Siebler T, ve ark. Longitudinal analysis of maternal plasma leptin levels during pregnancy, at birth and up to six weeks after birth: relation to body mass index, skin-folds, sex steroids and umbilical cord blood leptin levels. *Hormone Res* 1998; 50: 276–83.
14. Qiu C, Williams MA, Vadachkoria S, Frederick IO, Luthy DA. Increased Maternal Plasma Leptin in Early Pregnancy and Risk of Gestational Diabetes Mellitus. *Obset Gynecol* 2004; 103: 519-25.
15. McNeely MJ, Boyko EJ, Weigle DS, ve ark. Association between baseline plasma leptin levels and subsequent devolepment of diabetes in Japanese Americans. *Diabetes Care* 1999; 22: 65-70.
16. Liu ZJ, Liu PQ, Ding Y, Wang AM, Zhang JJ, Zhao XF. Maternal plasma leptin levels and their relationship to insülin and glucose in pregnant women with gestational diabetes mellitus and gestational impaired glucose tolerance. *Zhonghua Fu Chan Ke Za Zhi* 2003; 38: 261-3.
17. Vitoratos N, Salamalekis E, Kassanos N, Loghis C, Panayotopoulos N, Kouskouni E, Creatsas G. Maternal plasma leptin levels and their relationship to insülin and glucose in gestational-onset diabetes. *Gynecol Obstet Invest* 2001, 51: 17-21.
18. Mitchell RN, Cotran RS. Cell injury, adaptation and death. In: Kumar V, Cotran RS, Robbins SL (Eds). Robbins Basic Pathology. 7. baskı. Philadelphia: W.B. Saunders; 2003; p: 3-25.
19. Halliwell B. Reactive oxygen species in living systems: Source, biochemistry and role in human disease. *Am J Med* 1991; 91: 14-22.
20. Yurdakul Z. Canlılar ve Oksijen. Klinik Biyokimya Seminer Notları, İzmir: 2003.
21. Dalle-Donne I, Rossi R, Giustarini D, Milzani A, Colombo R. Protein carbonyl groups as Biomarkers of oxidative stress. *Clin Chim Acta* 2003: 329: 23-8.
22. Peuchant E, Brun JL, Rigalleau V, ve ark. Oxidative and antioxidative status in pregnant women with either gestational or type 1 diabetes. *Clinical Biochemistry* 2004; 37: 293-8.
23. McCord JM. The evolution of free radicals and oxidative stress. *Am J Med* 2000; 108: 652-9.
24. Uludağ S, Gezer A. Gebelik Diabeti. *Türk Jinekoloji ve Obstetrik Derneği, Uzmanlık Sonrası Güncel Gelişmeler Dergisi* 2005; 1: 5 5-61.
25. Yalcin HR, Zorlu CG. Threshold value of glucose screening tests in pregnancy: could it be standardized for every population? *Am J Perinatol* 1996; 13: 317-20.
26. Erem C, Cihanyurdu N, Deger O, Karahan C, Can G, Telatar M. Screening for gestational diabetes mellitus in northeastern Turkey (Trabzon City). *Eur J Epidemiol* 2003; 18: 39-43.
27. Tanir HM, Sener T, Gurer H, Kaya M. A ten-years gestational diabetes mellitus cohort at a university clinic of the mid-Anatolian region of Turkey. *Clin Exp Obstet Gynecol* 2005; 32: 241-4.
28. Ceddia RB, Koistinen HA, Zierath JR, Sweeney G. Analysis of paradoxical observations on the association between leptin and insulin resistance. *FASEB J* 2002; 16: 1163-76.
29. Al-Dahhri N, Bartlett WA, Jones AF, Kumar S. Role of leptin in glucose metabolism in type 2 diatetes. *Diabetes Obes Metabol* 2002; 4: 147-55.
30. Jequier E. Leptin signaling, adiposity and energy balance. *Ann NY Acad Sci* 2002; 967: 379–88.
31. Laivuori H, Kaaja R, Koistinen H, ve ark. Leptin during and after preeclamptic or normal pregnancy: its relation

to serum insulin and insulin sensitivity. *Metabolism* 2000; 49: 259-63.

32. Moriya M, Okumura T, Takahashi N, Yamagata K, Motomura W, Kohgo Y. An inverse correlation between serum leptin levels and hemoglobin A1c in patients with non-insulin dependent diabetes mellitus. *Diabetes Research and Clinical Practice* 1999; 43: 187–91.
33. Gillery P, Monboise JC, Maquart FX, Borel JP. Glycation of proteins as a source of superoxide. *Diabetes Metab* 1988; 14: 25-30.
34. Baynes JW. Role of oxidative stress in development of complication in diabetes. *Diabetes* 1991; 40: 405-12.
35. Hunt JV, Smith CC, Wolff SP. Autoxidative glycosylation and possible involvement of peroxides and free radicals in LDL modification by glucose. *Diabetes* 1990; 39: 1420-4.
36. Loven D, Schedl H, Wilson H, ve ark. Effect of insulin and oral glutathione on glutathione levels and superoxide dismutase activities in organs of rats with streptozotocin-induced diabetes. *Diabetes* 1986; 35: 503-7.
37. Peuchant E, Delmas-Beauvieux MC, Couchouron A, ve ark. Short-term insulin therapy and normoglycemia: effects on erythrocyte lipid peroxidation in NIDDM patients. *Diabetes Care* 1997; 20: 202–7.
38. Wohaieb SA, Godin DV. Alterations in free radical tissue-defense mechanism in streptozotocin-induced diabetes in rats. Effects of insulin treatment. *Diabetes* 1987; 36: 1014-28.
39. Vandewoude MG, Van Gaal LF, Vandewoude MF, De Leeuw IH. Vitamin E status in normocholesterolemic and hypercholesterolemic diabetic patients. *Acta Diabetol Lat* 1987; 24: 133-9.
40. Yang X, Borg LA, Eriksson UJ. Altered metabolism and superoxide generation in neural tissue of rat embryos exposed to high glucose. *Am J Physiol* 1997; 272: 173–80.
41. Eriksson UJ, Siman CM. Pregnant diabetic rats fed the antioxidant butylated hydroxytoluene show decreased occurrence of malformations in offspring. *Diabetes* 1996; 45: 1497-502.
42. Rosenn B, Miodovnik M, Combs CA, Khoury J, Siddiqi TA. Glycemic thresholds for spontaneous abortion and congenital malformations in insulin-dependent diabetes mellitus. *Obstet Gynecol* 1994; 84: 15-20.
43. Kharb S, Singh V, Singh GP. Lipid peroxidation in Gestational Diabetes. *J Obstet Gynecol Ind* 2001; 51: 51-2.

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# The Etiologic and Demographic Factors Related to Anemia Prevalence in the Pregnant Women Admitting to an Education and Research Hospital in Istanbul

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**Abstract**

**Objective:** To detect the regional prevalence and etiology of anemia in the pregnant women admitting to our hospital and to determine the related demographic factors.

**Methods:** The study was conducted in our outpatient clinic between May 2007 and November 2007. A total of 237 consecutive patients between the ages of 17 – 44, having no systemic disease or obstetric vaginal bleeding and who did not use any iron and/or multivitamin supplements during pregnancy were enrolled to the study. The sociodemographic factors and the hemoglobin, hematocrit, serum iron, total iron binding capacity, ferritin, folic acid, vitamin B12 levels of the subjects were then studied. The pregnant women with hemoglobin levels <33% were defined as anemic. Chi-square test and Fisher's exact test were used for detecting the statistical difference between the normally distributed and unequally distributed variables; respectively.

**Results:** The mean hemoglobin, hematocrit, serum iron, ferritin, folic acid, vitamin B12 levels of the subjects were 12.0±1.24 g/dl, %35±5.31, 81.39±40.31 ugr/dl, 48.13±164.94 ng/dl, 18.33±62.89 ng/ml ve 224.5±92.47 pg/ml, respectively. Anemia was detected in 35 of 237 patients; therefore the prevalence of the anemia in our pregnant women was calculated to be 14.7%. The distribution of the etiologic factors for anemia were found as follows: iron deficiency anemia in 15 patients (42.9%), vitamin B12 deficiency in 16 patients (45.7%), folic acid deficiency in one patient (2.9%) and combination of vitamin B12 and iron deficiency in a total of nine patients.

**Conclusion:** In our study, the prevalence of anemia was found to be 14.7 % in our pregnant women population. Vitamin B12 deficiency was also found to be a major causative factor as well as iron deficiency in the etiology of anemia in pregnancy.

**Keywords:** Anemia, etiology, pregnancy, iron, Vitamin B12, micronutrient.

## *İstanbul'da Bir Eğitim ve Araştırma Hastanesine Başvuran Gebelerde Anemi Prevalansını Etkileyen Etyolojik ve Demografik Faktörler*

**Amaç:** Antenatal bakım amacıyla hastanemize başvuran gebelerde anemi prevalansı ile etyolojisinin saptanması ve anemiyle ilişkili demografik faktörlerin tanımlanması.

**Yöntem:** Mayıs 2007-Kasım 2007 tarihleri arasında hastanemiz gebe polikliniğine ilk kez başvuran, yaş aralığı 17-44 arasında değişen, maternal sistemik bir hastalığı bulunmayan, obstetrik nedenli vajinal kanama geçirmemiş ve gebeliği süresince demir ve/veya multivitamin preparatı kullanmamış, toplam 237 ardışık gebe çalışmaya dahil edildi. Gebelere ait sosyodemografik veriler ile hemoglobin, hematokrit, serum demir, total demir bağlama kapasitesi, ferritin, folik asit, vitamin B12 seviyeleri incelendi. Hemoglobin değeri 11

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g/dl'nin ve hematokrit değeri %33'in altında olan gebeler anemik olarak kabul edildi. Normal dağılıma uyan verilerin karşılaştırılmasında ki-kare testi, normal dağılıma uymayan verilerin karşılaştırılmasında ise Fisher's exact testi uygulandı.

**Bulgular:** Çalışmaya katılan gebelerin ortalama hemoglobin, hematokrit düzeyleri, serum demir, ferritin, folik asid ve Vitamin B12 düzeyleri sırasıyla 12.0±1.24 g/dl, %35±5.31, 81.39±40.31 ugr/dl, 48.13±164.94 ng/dl, 18.33±62.89 ng/ml ve 224.5±92.47 pg/ml olarak bulundu. Çalışmaya dahil edilen toplam 237 gebenin 35'inde, anemi saptanmış olup, kliniğimize çalışma döneminde başvuran gebelerdeki anemi prevalansı %14.7 olarak hesaplandı. Anemik gebelerdeki etyolojik faktörlerin sıklığı incelendiğinde, 15 hastada demir eksikliği (%42.9), 16'sında vitamin B12 eksikliği (%45.7), birinde folik asit eksikliği (%2.9) ve toplam dokuz hastada ise vitamin B12 ve demir eksikliği bir arada bulundu.

**Sonuç:** Yaptığımız bu çalışmada, hastanemize başvuran gebelerde anemi prevalansı %14.7 olarak bulunmuş olup, etyolojide demir eksikliği kadar vitamin B12 eksikliğinin de rol olabileceği saptanmıştır.

**Anahtar Sözcükler:** Anemi, etyoloji, gebelik, demir, Vitamin B12, mikrobesin.

## Introduction

It has been estimated that approximately 30% of the population worldwide and more than half of the pregnant women are anemic according to World Health Organisation (WHO). The prevalence of anemia during pregnancy is reported to be 35-100%.[1] There are different claims about the maternal and perinatal affects of anemia during pregnancy. WHO suggested that anemia may contribute to 20% of the maternal mortality.[1] Additionally, maternal anemia is found to be associated with fetal complications such as intrauterine growth retardation, preterm birth, low gestational weight and maternal complications such as preeclampsia and eclampsia; conversely in other studies it has been found not to be related to adverse perinatal outcomes.[2-5] Therefore, anemia is an important health condition from the point of woman and maternal health. In pregnancy, plasma volume is increased up to 50% to support fetal growth and provide sufficient placental blood flow. However, maternal still declines since the increase in erythrocyte mass lags far behind the the increase in plasma volume. This condition is called as the physiologic anemia of the pregnancy and the hematocrit value reaches its nadir at 30-34 weeks of gestation.[6,7] Some other factors triggering anemia during pregnancy are depletion of the iron stores due to malnutrition and frequent pregnancy intervals.[8,9] There are numerous regional studies about anemia in our country, where it is an important public health problem, studied on subjects from varying age groups. Prevalence of anemia during pregnancy is reported to be highly varying between 29.4% and 95.2% in these studies.[10-15] However, the data is limited about the etiology of anemia in these studies. Furthermore, their results are insufficient to reflect the prevalence of anemia all over the whole country. Accordingly, a national prevalence study is essential to determine the prevalence and etiology of anemia during pregnancy in Turkey. Nevertheless, until such an epidemiologic study is carried out, the regional anemia frequency has to be determined and follow-up and treatment has to be planned accordingly. The aim of the present study was to detect the regional prevalence and etiology of anemia in the pregnant women admitting to our hospital and to determine the related demographic factors.

## Methods

The study was conducted in our outpatient clinic between May 2007 and November 2007.

A total of 237 consecutive patients between the ages of 17 – 44, having no systemic disease or obstetric vaginal bleeding and who did not use any iron and/or multivitamin supplements during pregnancy were enrolled to the study. Local ethics committee approval was obtained. The frequency and etiology of anemia was investigated in a cross-sectional fashion. The pregnant women with hemoglobin levels <11 g/dl and hematocrit levels < 33% were defined as anemic in accordance with the recommendations of Centers for Disease Control (CDC).[16] After receiving informed consent, all of the pregnant women attending to our outpatient clinics were asked to complete a survey questioning the risk factors. The demographic data included patient age, place of birth, healthcare insurance status, obstetric history, area of residence, highest level of education attained, employment status, annual household income. Hemoglobin (Hb), hematocrit (Htc), serum iron (Fe), total iron binding capacity (TIBC), ferritin, folic acid, vitamin B12 (vit B12) levels were then studied. Thirteen patients never gave a blood sample and the samples of 11 patients were not studied due to hemolysis. Hemogram analyses were performed by XT2000İ Sysmex and serum iron, ferritin, folate, vitamin B12 levels were studied by Modularanalytics E170, Cobas® (Roche, Germany). The descriptive and analytic statistical tests were performed by SPSS 13.0. Chi-square test and Fisher's exact test were used for detecting the statistical difference between the normally distributed and unequally distributed variables. Statistical significance was set to $p<0.05$.

## Results

The demographics of the patients and mean values of serum vit B12, folic acid, iron, TIBC are shown in Table 1. Serum iron levels were above 37 ugr/dl in 73.8% of the participitants. Accordingly, the prevalence of iron deficiency in the study population was 12%. In 35 of the 237 women anemia was detected according to the pre-defined criteria (Hb <11 g/dl and/or Htc <33); the anemia prevalence in the pregnant women admitted to our clinic in the study interval was calculated to be 14.7%. In the anemic patients, the distribution of etiologic factors were as follows: iron deficiency anemia in 15 patients (42.9%), vitamin B12 deficiency in 16 patients (45.7%) and folic acid deficiency in one patient (2.9%). In a total of nine patients, a combination of vitamin B12 and iron deficiency were detected. The mean hematocrit and hemoglobin values of the patients are shown in Table 2. In our study, 45.7% of the anemic patients were found to be between ages of 20-25, 45.7% of them were gravida 3-5 and 77.1% were in their second trimester of the pregnancy. No statistically significant differences were detected between the anemic and non-anemic pregnant women when compared in terms of place of birth, area of residence, healthcare insurance status, employment status and annual household income. The mean serum iron level was statistically significantly lower and the mean TIBC was statistically significantly higher in the anemic population when compared to the non-anemic group (Table 3).

## Discussion

It has been estimated that approximately 30% of the population worldwide and more than half of the pregnant women are anemic according to World Health Organisation (WHO).[1] WHO also estimated that the prevalence of iron deficiency anemia was 14% in Europe and 25% in Turkey.[12] In our study, the prevalence and etiologic factors of anemia in the pregnant women attending primarily and

who did not use any iron supplements during pregnancy were investigated; and the mean Hb and Htc levels were found to be 12 g/dl and 35%, respectively. According to the pre-defined criteria, anemia prevalence in the pregnant women attending to our clinic was calculated to be 14.7%. Considering the etiology of anemia, iron deficiency was found to be the responsible factor in half of the patients and combination of iron and vitamin B12 deficiency was detected in one forth of the patients. Consequently, the prevalence of iron deficiency anemia was identified to be 10.1% in our study group. In most of the studies of anemia in pregnancy, factors related to the etiology of anemia, such as serum Fe, TIBC, ferritin, vit B12, folic acid levels were seen not to be investigated, rather hemoglobin and hematocrit levels were studied. One of the few studies which investigated these parameters was conducted by Al Khatib et al.[17] In this study from Lebanon, iron deficiency anemia was detected in 7.7%, folic acid deficiency in 25.9% and vit B12 deficiency in 39.4% of the women of childbearing age. Therefore, the authers underlined the role of folic acid deficiency as well as iron deficiency in the etiology of anemia in women during their reproductive years. In another study from Africa, 23% of the study group demonstrated iron deficiency anemia solely, 32% demonstrated iron deficiency anemia together with deficiencies of different micronutrients (folic acid, vit B12, vit A), whereas 26% of the patients had only micronutrient deficiencies.[18] Our study is one of the few researches investigating the relation between anemia and micronutrients in Turkey and is valuable to underline the importance of vitamin B12 deficiency in the etiology of anemia in pregnancy. When we searched the national studies about the prevalence of anemia in our

**Table 1.** Demographic parameters and average values of Hb, Htc, iron, ferritin folic acid, vitamin B12 of pregnant women (N=213).

| | Number of patients | % |
|---|---|---|
| **Hematocrit** | | |
| Less than %30 | 10 | 4.2 |
| %30-33 | 47 | 19.8 |
| %34-39 | 126 | 53.2 |
| %40 and above | 16 | 6.8 |
| Unkown | 38 | 16.0 |
| **Hemoglobin (gr/dl)** | | |
| 0-11 | 28 | 11.8 |
| 11 and above | 184 | 77.6 |
| Unkown | 25 | 10.5 |
| **Fe (ugr/dl)** | | |
| <37 | 24 | 10.1 |
| >37 | 174 | 73.8 |
| Unkown | 38 | 16.0 |
| **Ferritin (ng/ml)** | | |
| <13 | 55 | 23.2 |
| >13 | 143 | 60.3 |
| Unkown | 39 | 16.5 |
| **Folic acid (ng/dl)** | | |
| <3,1 | 3 | 1.3 |
| >3,1 | 189 | 79.7 |
| Unkown | 45 | 19.0 |
| **B12 vitamin (pg/ml)** | | |
| <197 | 82 | 34.6 |
| >197 | 112 | 47.3 |
| Unkown | 43 | 18.1 |

**Table 2.** Demographic parameters and average values of iron,total iron binding capacity, folic acid, vitamin B12 of pregnant women with and without anemia.

| | With anemia (average ± SD) (N=35) | Without anemia (average ± SD) (N=176) | P value |
|---|---|---|---|
| **Demographic parameters** | | | |
| Gestational age | 22,65±6,62 | 20.80±8,16 | 0,153 |
| Maternal age | 26,05±5,49 | 27,20±5,38 | 0,250 |
| Gravida | 2,28±1,22 | 2,09±1,12 | 0,401 |
| Parity | 0,91±0,68 | 0,23±0,50 | 0,861 |
| Abortus | 0,34±0,68 | 0,23±0,50 | 0,366 |
| **Hematological parameters** | | | |
| Iron | 63,05±47,58 | 85,15±37,90 | 0,015 |
| TIBC | 437,31±106,14 | 394,22±82,88 | 0,014 |
| Folic acid | 25,19±87,47 | 16,80±16,80 | 0,449 |
| Vitamin B12 | 210,11±128,66 | 228,29±83,12 | 0,328 |

country, we could not identify any epidemiologic study with a large sample size sufficient to represent the whole country population. The national studies are usually designed for detection of anemia prevalence in pregnant women attending to the primary care centers, performed with relatively small sample size. The frequency of anemia shows a great variation among different regions of the country ranging between 29.4% and 95.2%.[10-15] Accordingly, the lowest and highest frequencies are in Afyon; and Diyarbakır and Karadeniz Region, respectively. We think that, regional differences in dietary habits and parturition rates may be the causative factors for this high variation. As an example, in a study investigating the dietary habits, anemia was seen 3.5 times more frequently in pregnant women consuming boiled grape juice (pekmez) in comparison to women who do not.[12] However, we did not investigate the nutritional status of the women in our study. On the other hand, we searched for the possible effects of the socioeconomical status parameters which may indirectly reflect the nutritional status (e.g. annual household income, employment status, area of residence, healthcare insurance status, highest level of education attained) but we found no relationship between these and the prevalence of anemia. One other factor assumed to have an effect on the anemia frequency is the total number of pregnancies. In a study from Turkey, a significant association was found between the number of pregnancies and anemia.[15] On the contrary, no significant association between the number of pregnancies and anemia could be demonstrated in the studies conducted by Pirinçci et al, Toksöz et al and Mersin et al.[10-12] Similarly, we also could not detect any statistically significant relationship. However, 67.2% of the patients included in our study were women with a gravida 2 or less. When we investigated the frequency of the the adolescent pregnancy, we found that 82% of our patients were between ages of 20-35 and 5.2% were adolescents (<19 years of age). According to TNSA (Türkiye Nüfus ve Sağlık Araştırması – Turkey Population and Health Investigation) 1998 revision, the prevalence of adolescent pregnancy in Turkey was reported to be 14.6%.[19] According to WHO data, severe anemia causes a five times increase in the maternal mortality rates.[1] When the prevalence of anemia is <40%, WHO suggests an intake of 60 mg iron supplement daily starting after the second trimester, and when the prevalence of anemia is ≥ 40%, WHO suggests an intake of 60 mg iron supplement daily for six months after the second trimester and for three months postpartum, for a total of nine months. In our country, in the light of these suggestions, the Ministry of Health and AÇSAP (Mother's and child's health-family planning center) started an iron supplement program.[20] According to this program, an intake of 50- 60 mg iron supplement daily for six months after the second trimester and for three months postpartum, for a total of 9 months has been advised. On the contrary, National Institute for Clinical Excellence (NICE) from England does not advise the routine iron supplement, because its benefits are not proven for mother and the fetus and this suggestion is reported to based on an evidence level A.[21] Upon literature review, there exists only one study comparing the effects of routine and selective iron supplementation in pregnancy and this study consists of 2912 patients.[22] According to the results of this study, although there was an increase in cesarean sections and postpartum blood transfusions in the selective iron supplementation

group, the perinatal mortality rate was detected to be lower. Additionally, in the studies regarding anemia in pregnancy, high maternal hemoglobin levels were not found to have improved the maternal outcome in cases with obstetric hemorrhage. In a Cochrane review by Mahomed et al, routine iron and folic acid supplementation during pregnancy was found not to improve perinatal morbidity and mortality; it was only found to prevent low hemoglobin levels at birth and six weeks postpartum.[23] In another Cochrane review published in 2006, in a meta-analysis of 40 studies conducted with 12,706 women, routine iron supplementation during pregnancy was detected to increase antenatal and postpartum hemoglobin levels but also cause significant gastrointestinal side effects and hemoconcentration.[24] Hemococentration in pregnancy has been linked to some serious adverse events such as low birth weight, preterm birth and small-for-gestational-age (SGA) neonates and high hemoglobin levels has been advised not to be taken as a reflection of good levels of iron stores (25). Selective iron supplemention during pregnancy seems to be wiser than routine supplemention especially in the areas where iron deficiency anemia is not prevalent. Therefore, we advise that the markers of iron stores and other micronutrients should as well be studied as the levels of hemoglobin and hematocrit during screening for anemia during pregnancy.

## Conclusion

As a conclusion, we found a lower prevalence of anemia than expected among our pregnant women population; and vitamin B12 deficiency also detected as an important etiologic factor together with iron deficiency. The factors that affect anemia in pregnancy and the regional differences in anemia still have to be determined. For this to be achieved, a large database of the patients should be established with the contributions of an important number of the health services among the whole country; such as local health offices, teaching and research hospitals and university hospitals.

**References**


1. World Health Organisation. The prevalance of anemia in women: a tabulation of available information. 2nd ed. Geneva; WHO; 1992.
2. Huisman A, Aarnoudse JG. Early evidence of a reduced plasma volume. *Acta Obstet Gynecol Scand* 1986; 65: 605-8.
3. Murphy JF, O'Riordan J, Newcombe RG, Coles EC, Pearson JF. Relation of haemoglobin levels in first and second trimesters to outcome of pregnancy. *Lancet* 1986; 1: 992-5.
4. Stephansson O, Dickman PW, Johansson A, Cnattingius S. Maternal hemoglobin concentration during pregnancy and risk of stillbirth. *JAMA* 2000; 284: 2611-7.
5. Levy A, Fraser D, Katz M, Mazor M, Sheiner E. Maternal anemia during pregnancy is an independent risk factor for low birthweight and preterm delivery. *Eur J Obstet Gynecol Reprod Biol* 2005; 122: 182-6.
6. Hytten F, Paintin DB. Increase in plasma volume during normal pregnancy. *J Obstet Gynaecol* 1963; 70: 402-27.
7. Steer PJ. Maternal hemoglobin concentration and birth weight. *Am J Clin Nutr* 2000; 71: 1285-7.
8. Fich CA, Cook JD. Iron deficiency. *Am J Clin Nutr* 1984; 39: 471-7.
9. Allen LH.Pregnancy and iron deficiecy: unresolved issues. *Nutr Rev* 1997; 55: 91-101.
10. Pirinççi E, Açık Y, Bostancı M, Eren S, Beritanlı H. Elazığ il merkezinde yaşayan gebelerde anemi prevalansı. *Fırat Üniversitesi Sağlık Bilimleri Dergisi* 2001; 3: 449-54.
11. Toksöz P, Ilçin E, Özcan M. Diyarbakır Bağlar Sağlık Ocağı bölgesinde gebe kadınlarda anemi prevalansı. *Beslenme ve Diyet Dergisi* 1990; 19: 61-9.
12. Mersin S, Kuş C, Yeşildal N, Mayda AS, Şerifi B. Konuralp Kamil Furtun Sağlık Ocağı bölgesi gebelerde anemi araştırması. 8. Ulusal Halk Sağlığı Kongresi, Eylül 2002, Diyarbakır, s257-260.
13. Beştepe G, Bilgin N. Afyon ili 2 ve 4 No'lu sağlık ocaklarındaki gebelerde anemi prevalansı ve anemiyi etk-

ileyen bazı faktörlerin incelenmesi. *Sağlık ve Toplum* 2002; 12: 43-53.

14. Pekcan G, Karaağaoğlu N. State of nutrition in Turkey. *Nutrition and Health* 2000: 14: 41-52.
15. Oruç O, Tuncer A, Apan E. Adana Yenibaraj Sağlık Ocağı bölgesinde gebelerde anemi prevalansı, V. Ulusal Halk Sağlığı Kogresi Bildiri Kitabı, İstanbul, 1996; 374-8.
16 Centers for Disease Control. Anemia during pregnancy in low-income women. *United States MMWR* 1987; 1990; 39: 73.
17. Al Khatib L, Obeid O, Sibai AM, Batal M, Adra N, Hwalla N. Folate deficiency is associated with nutritional anaemia in Lebanese women of childbearing age. *Public Health Nutr* 2006; 9: 921-7.
18. van den Broek NR, Letsky EA.Etiology of anemia in pregnancy in south Malawi. *Am J Clin Nutr* 2000; 72: 247-56.
19. Türkiye Nüfus ve Sağlık Araştırması 1998. Sağlık Bakanlığı, Macro International Inc. BM Nüfus Fonu. HÜNEE Türkiye Nüfus ve Sağlık Araştırması; 1999.
20. Sağlık Bakanlığı Web Portal.Gebelerde demir destek programı bilgi notu. http://www.saglik.gov.tr/TR/BelgeGoster.aspx?F6E10F8892433CFF8FE9074FF19B0005CF18F145EBDBEB5B31 Ocak 2007.
21. NICE Clinical Guidelines.Antenatal care: Routine care for the healthy pregnant woman. http://www.nice.org.uk/guidance/index.jsp?action=download&o=40109 March 2008.
22. Hemminki E, Rimpelä U. A randomized comparison of routine versus selective iron supplementation during pregnancy. *J Am Coll Nutr* 1991; 10: 3-10.
23. Mahomed K.Iron and folate supplementation in pregnancy. *Cochrane Database Syst Rev* 2000;(2):CD001135. Review. Update in: *Cochrane Database Syst Rev* 2006; (3): CD001135.
24. Pena-Rosas JP, Viteri FE. Effects of routine oral iron supplementation with or without folic acid for women during pregnancy. *Cochrane Database Syst Rev* 2006; 3: CD004736.
25. Scanlon KS, Yip R, Schieve LA, Cogswell ME. High and low hemoglobin levels during pregnancy: differential risks for preterm birth and small for gestational age. *Obstet Gynecol* 2000; 96: 741-8.

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# Practical Guideline for Labor

**Abstract**

This guideline was prepared by the Laboring Program Science Board of the General Directorate of Family Planning and Maternal and Infant Department of Health of Turkish Health Ministry in close cooperation with Turkish Gynaecology and Obstetrics Society, Turkish Perinatology Society, Turkish Maternal Fetal Medicine and Perinatology Society to provide the unity in application and to be a guide in clinical practices of physicians. Practical Guideline for Labor is not a series of unchangeable rules and does not constitute the judicial standards of the services offered to patient. It admits that it is a basic principle to evaluate every single patient within his/her own special conditions.

**Keywords:** Labor, practical guideline.

### *Doğum eylemi yönetim rehberi*

Bu rehber, uygulamada birlikteliği sağlamak ve hekimlerin klinik pratiklerinde yol gösterici olması amacı ile, Türk Jinekoloji ve Obstetrik Derneği, Türk Perinatoloji Derneği, Türkiye Maternal Fetal Tıp ve Perinatoloji Derneği işbirliğinde Sağlık Bakanlığı Ana Çocuk Sağlığı ve Aile Planlaması Genel Müdürlüğü Doğum Programı Bilim Kurulu ile tarafından hazırlanmıştır. Doğum Eylemi Yönetim Rehberi değişmez kurallar dizisi değildir ve hastaya sunulan hizmetlerin hukuki standartlarını oluşturmaz. Tıbbın ana prensibi olarak hastalık değil hasta vardır kuralına uygun olarak her hastanın durumunun kendi özel koşulları içerisinde değerlendirilmesini temel prensip olarak kabul eder.

**Anahtar Sözcükler:** Doğum eylemi, yönetim rehberi.

## Introduction

Cesarean is generally applied in cases where it is not possible to complete vaginal delivery safely or when there is a certain increase in maternal and/or fetal morbidity and mortality together with vaginal delivery.

According to the Turkish Population and Health Research (TNSA) in 2003, it is seen that cesarean rate which was 21.2% have reached 40% in recent delivery rates. It is known that the current rate is over the goal (5-15%) set by World Health Organization and the rates of developed countries.

While large-scale retrospective and prospective studies have been planned by the General Directorate of Family Planning and Maternal and Infant Department of Health of Turkish Health Ministry of in order to reveal the reasons, it is considered that the factors such as the increase of discretionary and repeated cesareans and extending the indications are among the reasons increasing this rate. Today, risks such as infection, bleeding, transfusion need, thromboembolic risks, long hospital stayings, late recovery, having more pains continue while anesthesia, drugs and materials used, and developments in surgical and postoperative care have decreased mortality and morbidity due to cesareans.

American Congress of Obstetricians and Gynecologists (ACOG) declared in their statement on May 9th, 2006 that cesareans should be performed not discretionally but due to medical reasons. The studies to follow deliveries and their outcomes in public and private health associations have been initiated by the ministry throughout the country to protect mother health. In this context, it is important to follow

cesarean indications and outcomes. Obeying the medical reasons and indications suggested by modern obstetrics, keeping patient records in a certain form and within an application unity in detail and correctly, keeping statistics accurately and following ethic rules are the most important precautions to reach this goal.

### Application-Oriented Basic Priorities

- Delivery by cesarean is a surgical intervention and it is essential to perform it for medical reasons, and it is an alternative to vaginal delivery. Advantages and risks peculiar to pregnant and pregnancy should be taken into consideration when planning cesarean delivery.
- While the request of mother is not a sufficient reason by itself for cesarean, psychological conditions of individual such as fear, anxiety, panic should be taken into consideration. Adequate and accurate consultancy should be given.
- Cesarean decision should be given by individualizing the diagnoses of each patient.
- As in all medical interventions, informed consent from should be taken from patient in also cesarean cases.

### Reducing the Cesarean Possibility

- In all pregnancies where delivery is followed up, partograph should be used to follow up spontaneous delivery progress.
- Beginning from the 36th gestational week, external cephalic version (ECV) can be suggested to pregnants who have single rectal baby without complication, excluding exceptional cases (pregnants whose deliveries have already begun and who have uterine scar and abnormality, fetal distress, membrane rupture and vaginal bleeding).

The risks of intervention should be explained to mother-to-be by informed consent before the application.

- It is suggested to determine delivery type by individualizing treatment and deciding as to case for pregnants who exceed their 42nd gestational week and have single pregnancy without complication.

It should be kept in mind that there may be increase in cesarean rate and other complications by the induction of delivery. Mother should be informed about this matter.

- In appropriate cases, post-cesarean vaginal delivery can be suggested. The risks of intervention should be explained to mother-to-be by informed consent before the application.

## Cesarean Indications

While delivery by cesarean is generally preferred in cases given below, these indications are not certain and they should be determined according to current conditions by individualizing delivery type as to case characteristics.

1. **Fetal Indications**
   - 1.1. Fetal distress
   - 1.2. Fetal presentation anomalies
     - 1.2.a. Rectal presentation
     - 1.2.b. Other presentation anomalies (transverse, forehead, face presentation etc.)
   - 1.3. Multiple pregnancies
   - 1.4. Fetal anomalies (hydrocephalia, sacrococcygeal teratoma etc.)
2. **Maternal Indicationsr**
   - 2.1. Performed uterus surgery (cesarean, other operations)
   - 2.2. Systemic diseases (DM, HT, pregnancy induced hypertension etc.)
   - 2.3. Vertical transitive maternal infections (HIV, HSV-2, HCV vb.)
3. **Labor or Natal Indications**
   - 3.1. Cephalopelvic disproportion
   - 3.2. Prolonged labor
   - 3.3. Fetal Macrosomia
4. **Indications of Umbilical Cord and Placenta**
   - 4.1. Cord prolapse
   - 4.2. Placenta previa
   - 4.3. Ablatio placentae
   - 4.4. Vasa praevia

## Fetal Anomalies

### Related Messages

- Delivery by cesarean can be suggested in cases such as fetal myelomeningocele, sacrococcygeal teratoma, fetal abdominal anterior wall defects and non-immune hydrops.
- Generally, delivery type in fetal anomalies should be individualized according to case characteristics. This decreases perinatal morbidity and mortality expected in cesarean.

## Fetal Distress

### Related Messages

- Gestational week during delivery, existence of congenital anomaly and development disorders affect perinatal outcome seriously.
- The technology used by newborn experts and advancements in prenatal care (such as determining high-risk patients, increasing use of antenatal steroids by those with ultrasonography and early labor risk etc.) affect perinatal outcome positively.
- Fetal distress is diagnosed by applying one or more methods given below according to risk situation.
  1) Monitoring partogram and fetal heat beat rate by fetoscope
  2) Discontinuous or continuous electronic fetal monitorization
  3) Fetal scalp blood sampling or palse oximeter
- If there is a situation where fetal heart beat does not get normal, cesarean is suggested to prevent perinatal morbidity and mortality.
- It is needed to do cesarean within 30 minutes at the latest when a patient is diagnosed as having fetal distress.

## Protocol

### Reminder: 1 - Fetal Distress Diagnosis

- Abnormal heart rate curve.
- Amnion fluid with dark-dense meconium.
- Determining fetal hypoxia by using fetal pulse oximeter and scalp blood sampling.

Today, these methods can be applied by limited number of hospitals and they are not practical.

### Reminder: 2 - If Fetal Distress Diagnosis Exists

- Pregnant should be laid down on its left side or be kept in sitting position.
- Oxytocin infusion (if given) or another induction should be stopped.

### Reminder: 3 - Heart Rate

- Normal heart rate can slow down during contraction but it returns to normal as soon as uterus loosens up.
- Very slow heart rate when there is no contraction or slow heart rate after contraction may indicate fetal distress.
- Fast heart rate may develop as a response to high fever, drugs accelerating heart rate of mother (i.e. tocolytic drugs), chorioamnionitis, hyperthyroidism or high tension. In the light of this information, to research the maternal-oriented reasons is the first thing to do when fast heart rate is found.
- The existence of fast heart rate of fetus despite the normal heart rate of mother should be considered as a diagnosis of fetal distress.

### Reminder: 4 - Meconium

- As fetus maturates, amnion fluid stained with meconium is seen frequently and it may not be an indication of fetal distress on its own. It must be paid attention in the existence of amnion fluid stained with meconium without any abnormality in heart rate.
- Dense-dark meconium presence shows the meconium transiton into decreased amnion fluid and it is required to hasten the delivery.

If this diagnosis occurs on the early phase of delivery and if it is predicted that the delivery will take long (primigravida), then cesarean may be considered. Mouth-nose aspiration required during delivery should be performed rapidly in order to prevent meconium aspiration.

- Meconium transition occurs due to pressure on fetus abdomen during delivery through rectal presentation. It is not a diagnosis of fetal distress providing that the situation is not on the early phase of delivery.

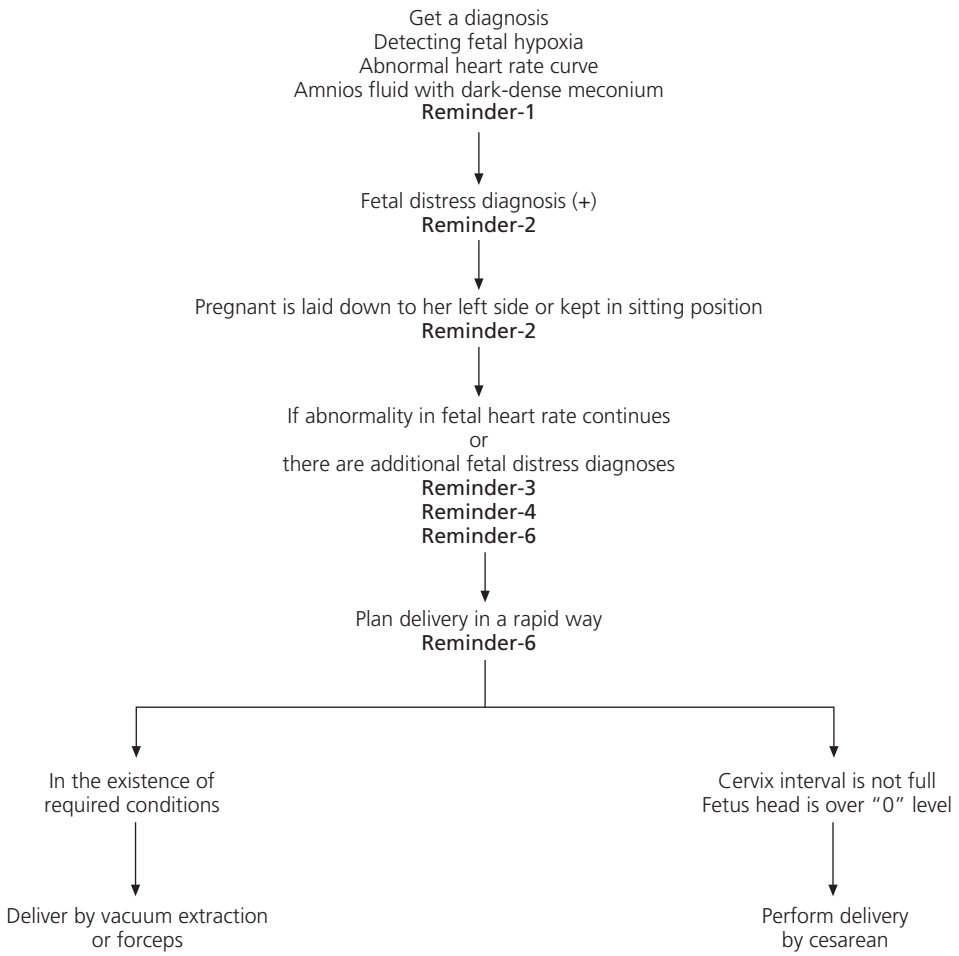
### Reminder: 5 - Additional Clinical Diagnosis (Chart-1)

- If there are infection diagnoses (fever, fetid vaginal discharge), antibiotics should be given as in chorioamnionitis.
- If the cord is below the incoming part or in vagina, it should be managed as cord prolapse.

### Reminder: 6 - Delivery

- If abnormality in fetus heart rate continues or there are additional diagnoses for distress

**Fetal Distress Flow Chart**




**Reminder-5** Evaluate if there are infection diagnoses and initiate antibiotic treatment if necessary. Manage it as if it is cord prolapse if there is any cord prolapse.

(amnion fluid with thick-dense meconium), delivery should be planned:

- In the presence of required conditions, vacuum extraction or forceps can be tried. Otherwise, delivery is performed by cesarean.
- If cervix is not fully open or fetus head is over 0 level, delivery should be performed by cesarean.

## Rectal Presentation

### Related Messages

- Approximately 4% of single pregnancies are rectal presentation. Prevalance decreases as gestational weeks increase (3% in term pregnancies).
- Delivery of all rectal presentations should be done in hospitals which are capable of performing operation.
- Plannned vaginal delivery can be suggested to multipara pregnants who have pure and full rectal presentation between 2500 gr and 3500 gr estimated fetal weight.
- It is important to specialize on vaginal rectal deliveries and it is not suggested to try delivery without having the experience of this practice.
- ECV performed on 36th gestational week and over can turn the position in pregnants with noncomplicated (full and pure rectal presentation) rectal presentation from rectal presentation to cephalic presentation. However, ECV is not a method used frequently by obstetrics in Turkey. It can be offered as an alternative if physician is experienced on the subject matter.
- If ECV succeeds, normal action follow-up is performed. If ECV fails, vaginal rectal delivery is followed or delivery is performed by cesarean.
- Pregnant should be examined regularly and delivery progress should be marked on delivery monitorization graph.
- Elongated action in rectal presentation is a cesarean indication.
- Membranes should not be opened; when they are opened, pregnant should be examined immediately in terms of cord prolapse.
- If the cord prolapsed and the delivery is not soon, then the delivery should be performed by cesarean.
- If gestational week of fetus is less than 34th gestational week in early rectal delivery, then the cesarean appropriate.
- In rectal presentation, delivery by cesarean is frequently suggested in cases given below;
  1. Big fetus,
  2. Inappropriate pelvis,
  3. Cord entanglement on neck,
  4. Hyperextension of head,
  5. Being unable to initiate spontaneous labor in presence of membrane rupture developed 12 hours or long ago,
  6. Uterus dysfunction,
  7. Foot presentation,
  8. In pregnancies at 34th gestational week or below, being on active delivery action of mother when preterm fetus is apparently healthy,
  9. Serious fetal growth retardation,
  10. Perinatal death undergone or childhood background with birth trauma,
  11. Sterilization request

## Protocol

### Reminder: 1 - Evaluation in Antenatal Period

Consultation of pregnant with an obstetrician before 36th week:

The definition of noncomplicated single rectal presentation:

- Pregnancy of 37th-42nd week,
- Full (with flexion) or pure (with extension) rectum,
- No feto-pelvic disproportion,

- Fetal head is at full flexion or does not have hyperextension (Leopold 3, 4),
- No fetal anomaly,
- No mechanical obstacle,
- Clinically calculating fetus under 3500 gr,

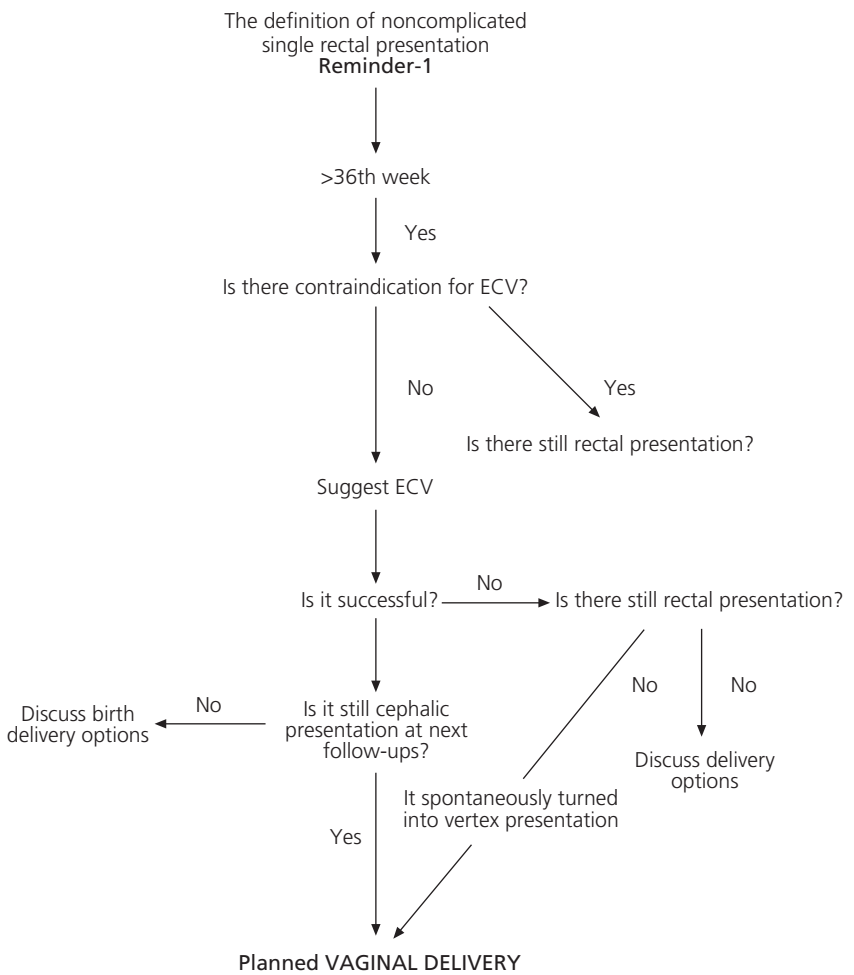
Reminder: 2 - Progress of Delivery

- **Cervical dilatation**:
  - Proceeding by opening at least 0.5 cm per hour after 3 cm for multiparas.
  - Proceeding by opening at least 0.5 cm within 1.5 hour after 3 cm for nulliparas.
  - Rectum going down to perineum within 2 hours after full dilatation.

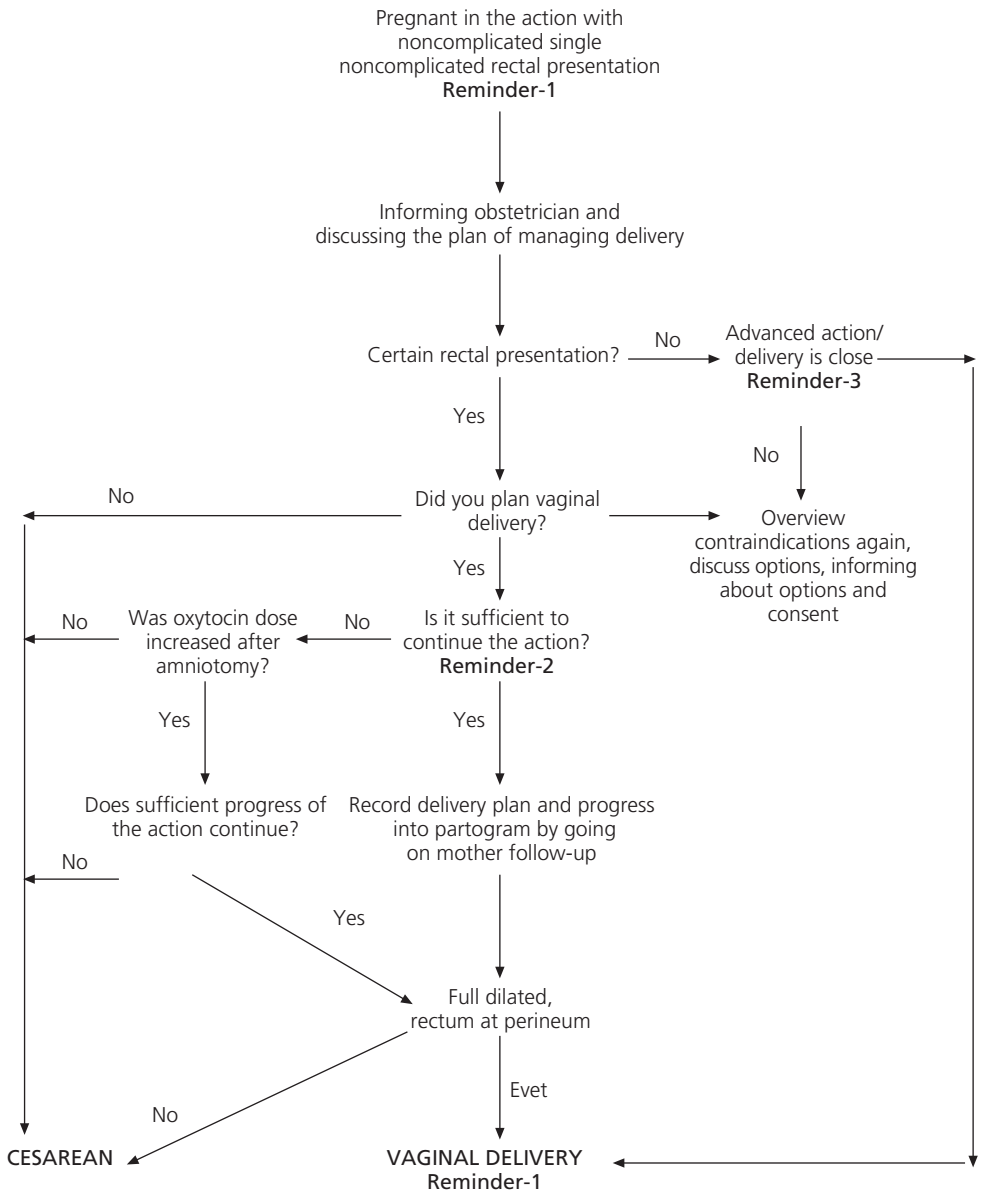
Reminder: 3 - Suggestions for the Action (Chart-2 and Chart-3)

- Pregnant should not be made to do active pushing move until rectum goes down to perineum.
- Delivery is close after one hour of active pushing.
- Pregnant is given active delivery position.
- If delivery of thorax gets slow, "Lovsett" maneuver should be done. Then, head

**Prenatal Care Flow Chart of a Pregnant with Rectal Presentation**



**Action and Delivery Flow Chart in Rectal Presentation**




should be delivered in a controlled and gentle way.

- When needed, forceps can be applied to head coming from back by obstetrician who is sufficiently qualified and experienced for such cases. Obstetrician should be informed beginning from first moments of active delivery action. Hospital conditions required for a planned vaginal rectal delivery are: Experienced midwife, expert pediatrician, obstetrician who is qualified to follow delivery, operating room for emergency cesarean and existence of emergency conditions.

## Transverse Presentation

### Related Messages

It can be tried to rotate fetus from outside (external version) if it is early period of the action and membranes are not open. It should be discussed with mother scientifically that this procedure may cause early labor and ablatio placentae and cesarean should be arranged under elective conditions by the consent of mother to be if needed. After 36th gestational week, pregnant should reside in a place close to hospital where she will deliver at. If the attempt of rotating from outside becomes successful, normal action follow-up is performed. If this attempt is fails or it is not safe to do, cesarean should be applied. Obstetrician should be aware of cord prolapse and perform the follow-up carefully. If cord prolapse happens when delivery is not soon, cesarean should be applied. Transverse presentation is the most dangerous one among malpresentations and elective cesarean can be arranged without considering the exceptional examples (ECV etc.) since it has a risk of high morbidity. If case is neglected, uterus rupture may develop. Obstetrician should discuss with mother to be about the risk of maternal-fetal mortality and suggest cesarean.

## Forehead Presentation

### Related Messages

- If fetus is alive, then it is delivered by cesarean. If it is dead, vaginal delivery should be considered as the first option.

## Facial Presentation

### Related Messages

It is delivered by mento-posterior cesarean. If fetus is dead, vaginal delivery should be considered as the first option. For mentum anterior, vaginal delivery can be provided by close follow-up.

## Multiple Pregnancies

### Related Messages

- Multiple pregnancies are observed among pregnancies with a frequency of 15/1000, which are mostly twin pregnancies (twin pregnancies: 14.4/1000; triplet pregnancies: 4/1000). Since perinatal morbidity and mortality (cerebral palsy, stillbirth, neonatal death etc.) rates increase significantly in multiple pregnancies, it is an important process to determine the delivery type.

**MULTİPLE PREGNANCIES SHOULD BE PLANNED FOR DELIVERING IN CENTERS WHICH HAVE SUFFICIENT EXPERIENCE AND EQUIPMENT.**

- **If first baby is vertex, second baby is vertex presentation;**
  - Vaginal delivery is preferred.
  - Though second fetus has always high risk in terms of mortality and morbidity, most of this risk is caused by inappropriate growth in favor of first fetus.
- **If second baby is vertex, second baby is not vertex presentation;**
  - In cases where where second fetus is not vertex, vaginal delivery can be provided after deliver of first one if presentation is rectal. In transverse position, second fetus can be delivered through vaginal way by means of internal podalic version (IPV). In both cases, cesarean can be preferred if sufficient experience and favorable conditions do not exist.
- **First baby is not vertex presentation;**
  - Delivery by cesarean is a preferred method.
  - In non-complicated twin pregnancies, the most ideal week for planned cesarean seems as 38th gestational week. However, most of twin pregnancies are delivered between 35th and 38th gestational weeks. The risk of respiratory problems increase in babies delivered before 35th gestational week.

**Twins with Low Birth Weight**

- If the presentation is vertex-vertex and it is considered that birth weights of fetus are under 1500 gram, literature supports vaginal delivery. Besides, it should not be overlooked that low birth weight can be a result of chronic hypoxy such as intrauterine growth retardation (IUGR) and fetal distress may be seen. In multiple pregnancies, it should be remembered that there may be an unbalance among twins according to chorionicity determination and thus Dopper USG may be needed for evaluating placental reserve. If any or both of fetuses have chronic hypoxy diagnoses, it is suitable to end pregnancy by cesarean.
- The case of second twin which does not have vertex presentation without low birth weight (under 1500 gram) is very controversial and it is hard to evaluate the profit-loss rate between mother and baby. Physician should plan delivery by taking conditions and his/her training into consideration in this case.

**Monoamniotic twins;**

- These twin pregnancies are related with the characteristics increasing perinatal mortality such as twins being locked up during delivery, cord entanglement and transfusion between twins. Diagnosis is possible by USG use. In such case, delivery preference should be cesarean.

**Triplet and above pregnancies;**

- Cesarean is applied since it decreases possibility of low Apgar score at delivery and perinatal death incidence.

## Protocol

### Delivery at Multiple Pregnancies

Reminder: 1- Diagnosis

- Fetus count is determined by USG and abdominal examination.

Reminder: 2 - First Baby

- If it is vertex presentation, the action is allowed to proceed as vertex presentation and the progress of action is followed up by using partogram; vaginal delivery is applied if there is no extraordinary situation.

Reminder: 3 - First Baby

- If it is rectal presentation, cesarean is a performed method.
- If it is a transverse presentation, then delivery is done by cesarean.

Reminder: 4 - Monoamniotic Twins

- These twin pregnancies are related with the characteristics which increase perinatal mortality such as twins being locked up during delivery, cord entanglement and transfusion between twins. Diagnosis is possible by USG use. In such case, delivery preference should be cesarean.

Reminder: 5 - Second Baby
Vertex Presentation

- Vaginal delivery is performed.
- Fetal distress diagnoses are examined after delivery of first baby.

Reminder: 6 - Second Baby
Rectal Presentation

- Vaginal delivery is planned.
- Fetus heart rate is checked between contractions.
- If there is any extraordinary situation and vaginal delivery is not possible, then delivery is doen by cesarean.

Reminder: 7 - Second Baby
Transverse Presentation

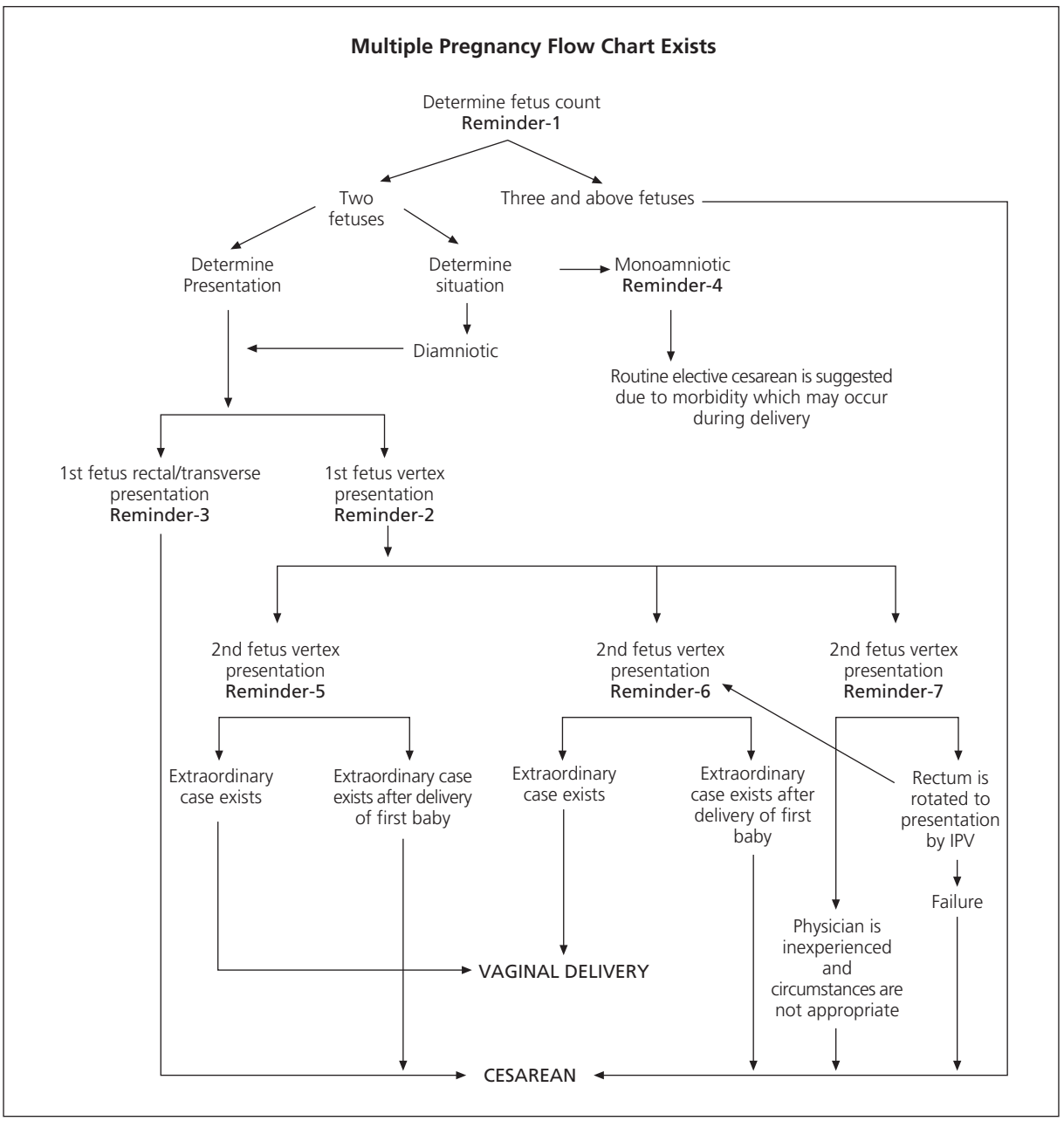
- Vaginal delivery is planned by internal podolic version (IPV) (if physician has sufficient experience and technical conditions exist). IPV processes may progress together with high morbidity and mortality. Therefore, cesarean may be planned if malpresentations or malpositions of fetuses can be predicted beforehand (Chart-4)

**Note:** If there is scar in uterus, membranes are opened, amnion has run out of fluid and operator has no training, IPV initiative is not performed. It is not insisted if baby is not rotated easily.

**Extraordinary Situations**

- Abnormal bleeding,
- Cord prolapse,
- Second baby much bigger than first baby,
- Contraction of cervix and getting thicker after delivery of first baby, not being dilated of itself,
- Fetal heart beats decreasing under 100/min, increasing above 180/min,

In such cases, cesarean should be planned as an emergency delivery.



## Vaginal Delivery After Cesarean

### Related Messages

- In order to make a proper preference between vaginal delivery after cesarean and cesarean after cesarean, required briefing for both cases should be performed fully.
- Vaginal delivery after cesarean (VDAC) should only be performed in appropriate centers. In such centers, blood bank providing service for 24 hours, teams performing fetal monitorization and surgery for 24 hours are required. Therefore, this practice should not be performed when emergency consultancy physician and anesthetists are not in hospital.
- Follow-up should be carried out in a place where cesarean and delivery will be performed immediately and immediate blood transfer is possible.
- If there is no proven contraindication, after a proper discussion about maternal and perinatal risks and benefits, VDAC in centers with appropriate conditions can be suggested to pregnants who had delivered by cesarean with transverse sub-segment incision. However, if there is any possibility that scar tissue in uterus may exist anywhere but sub-segment localization, then vaginal delivery should not be attempted.
  - If pregnant prefers VDAC, she should express it clearly. If she is not aware of the location of previous uterine incision, she should be informed certainly that perinatal mortality risk increases. This information should be within prenatal records clearly.
  - Pregnants who delivered by cesarean before should be examined by an obstetrician preferably before 36th week during antenatal care.
  - Preferences and priorities of mother, general risks and benefits (indefinite specific risks and benefits) and also uterine rupture and perinatal mortality and morbidity should be taken into consideration when deciding delivery type.
  - After risks and benefits (mentioned above) are expressed, planned vaginal delivery can be suggested to pregnants who had delivery before by cesarean twice and did not have any additional risk factor.
  - Limited number of data suggests pregnants who delivered by cesarean before that assisting delivery by oxytocin should be handled carefully.
  - Epidural anesthesia can be suggested to pregnants who delivered by cesarean before though there is no evidence that it increases the chance of performing a successful vaginal delivery.
  - Regular electronic fetal follow-up should be carried out on pregnants who had delivery by cesarean before.
  - No matter which follow-up method is chosen, fetal heart rate should be recorded. Disorders in fetal heart beat require urgent consultation of obstetricians.
- It should be suggested to pregnants who delivered by cesarean before that they should take regular midwife care during pregnancy and delivery.
  - It should be remembered that pregnants who had both cesarean and vaginal deliveries before are more prone to vaginal delivery.
  - Each hospital should have a written policy about how to get to its consultation physician responsible for a possible emergency cesarean.

## Conditions of Vaginal Delivery After Cesarean (VDAC)

- Performing cesarean by sub-segment transverse incision,
- Non-existence of scar or abnormality in uterus except cesarean,

- Non-existence of pelvic stenosis,
- Fetus below 4000 gram,
- Follow-up of a patient by a physician during whole action and existence of conditions to do emergency cesarean when required,
- Existence of conditions for 24-hour fetal monitorization,
- Existence of conditions for anesthesia and operating room required for an emergency case,
- Existence of conditions allowing blood transfer required for an emergency case.

**Vaginal Birth Contarindications**

**After Ceserean Operation**

- Those with classical or reverse T incision before,
- Hysterotomy and myomectomy operations undergone before,
- Uterus rupture undergone before,
- Cases where the action is contraindicated like in some placenta previa and presentation disorders,
- If pregnant who had cesarean operation before in an unknown way (sub-segment, T, classical incision) requests vaginal delivery, it should be explained to pregnant that risks of uterus rupture and perinatal mortality are higher than cases where previous uterine incision is not sub-segment incision.

## Protocol

### Reminder: 1 - Evaluating Antenatal Process

**Factors to be considered**:

- Previous uterus incision type,
- Pregnancy age,
- Other medical conditions.

### Reminder: 2 - Evaluating Risks and Benefits

**Benefits**:

- Decreased infection risk,
- Decreased blood loss and blood transfusion, decreased coagulation disorders,
- Early mobilization,
- Decreased medical intervention necessity,
- Success rates of vagial delivery of pregnants who had cesarean before and currently have suitable delivery conditions are 60-80%.

**Risks**:

- Uterus rupture [0.2-1.5% (if it is sub-transverse incision in previous cesarean)]
- Urgent cesarean requirements (30%),
- Fetal distress and requirement of newborn unit for baby.

### Reminder: 3 - Specialist Evaluation

- Elective cesarean should be suggested to pregnants who have rectal presentation, multiple pregnancy or placenta previa and macrosomic fetus.

### Reminder: 4 - At Delivery

- Conditions that hospital should have for a planned vaginal delivery:
  1. Sufficiently qualified midwife, obstetrician and newborn specialist,
  2. Existence of fetal monitorization facility,
  3. Operating room and anesthesia facilities for emergency cesarean cases,
  4. Decreasing pain at delivery (personal preference),
  5. Follow-up by electronic methods or monitoring,
  6. Opening of vascular access,
  7. Blood transfusion facility,
  8. Assisting the action by oxytocin (not contraindicated)

### Reminder: 5 - Oxytocin

- There is no effective oxytocin dose to be suggested based on evidence,
- Oxytocin exposure time is limited to 6 hours,
- As mentioned in Reminder 4, follow up should be carried on for uterus rupture (Chart-5).

## Maternal Infections that may Contaminate to Fetus from Mother

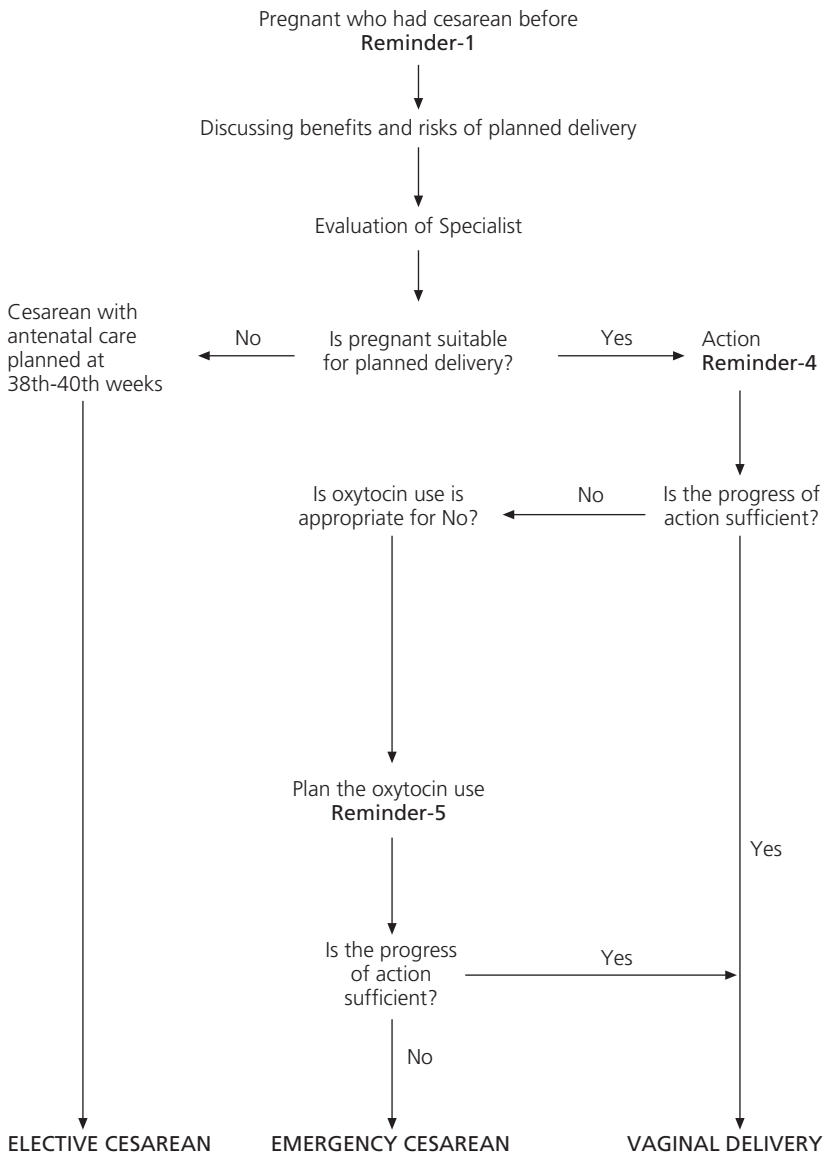
### Related Messages

- HIV (Human Immunodeficiency Virus), hepatitis B virus, hepatitis C virus and genital herpex simplex virus (HSV-2) are discussed under this topic.

HIV

- Contamination from mother to baby is seen approximately 25.5% of deliveries which are not intervened.
- This rate decreases to 1% by antiretroviral treatment, delivery by cesarean and not nourishing by breastfeeding.

**Multiple Pregnancy Flow Chart**



- Delivery by cesarean significantly reduces contamination to baby (0.05 vs 0.55).
- Planned cesarean should be suggested to HIV positive pregnants.

**Hepatitis B virus**

- Contamination is observed during delivery and postnatal period.
- Contamination significantly decreases by applying hepatitis B immunoglobulin and hepatitis B vaccines at delivery and later (at 1st and 6th months).
- Although it is considered that contamination will decrease by cesarean, there is no sufficient study supporting the idea.
- Since there is no sufficient evidence, planned cesarean is not suggested to pregnants with hepatitis B positive.

**Hepatitis C virus**

- Contamination risk is low (3-5%).
- According to the data we have, contamination risk of virus does not change as to delivery type.
- Since contamination risk does not change, planned cesarean is not suggested to pregnants with hepatitis C positive.
- However, planned cesarean is suggested to pregnants who are hepatitis C positive and co-infected by HIV virus.

**Genital Herpex Simplex Virus (HSV-2)**

- It is a sexually infecting ulcerative infection.
- Neonatal HSV is a systemic disease with high mortality and it is considered that it contaminates through delivery canal of infected mother (1.65/100,000 alive delivery).
- Even though there is no sufficient evidence, delivery by cesarean is suggested in primary HSV-2 infectin since nonatal herpex progresses with high mortality.
- It is not certain that planned cesarean in pregnants with recurrent HSV-2 infection decreases neonatal HSV risk. Delivery by cesarean can be suggested.

## Hypertensive Diseases of Pregnancy

### Related Messages

**Preeclampsia-Eclampsia**

- If there is serious growth retardation or distress diagnosis of fetus in pregnant with hypertension, pregnant should be hospitalized for advanced evaluation and accelarting possible delivery. On the other hand, even only high tension may require hospitalization for follow-up.
- Pregnant and her family should be informed about the hazard diagnoses of preeclampsia and eclampsia.
- Mild preeclampsia cases should be evaluated according to gestational week and fetus maturation and their treatments should be arranged accordingly.
- Middle Preeclampsia under 32nd gestational week should be followed unly under hospital conditions and its possibility of suddenly turning into a heavy preeclampsia should not be overlooked.
- Regardless of gestational week in heavy preeclampsia and eclampsia, maternal clinical condition should be stabilized and delivery should be provided.
- In heavy preeclampsia and eclampsia, delivery action should be inducted under MgSO4 perfusion. When induction fails, delivery by cesarean can be considered. If delivery is predicted before 34th gestational week, maternal steroid application can be done to provide fetal lung maturation. Additionally, postnatal newborn conditions should also be supplied.
- Eclamptic pregnants should be made to deliver in the shortest possible time. After necessary vital diagnoses of pregnant are fixed, it is tried to do delivery by induction; delivery by cesarean should be planned if induction fails or other obstetric inducations appear.

- Cervix should be evaluated.
  1. If cervix is mature (soft, thin, partially open), membranes are opened and delivery action is inducted by using oxytocin.
  2. If there is abnormality in fetal heart rate, delivery by cesarean is performed.
  3. If cervix is not mature (hard, thick, closed), cervix can be matured by using prostaglandins or delivery is performed by cesarean.
- If fetus is dead or very premature to survive;
  1. Vaginal delivery is planned.
  2. If cervix is not mature (hard, thick, closed), cervix is matured by prostaglandins.
  3. If vaginal delivery can not be performed despite all, delivery by cesarean can be planned.

### Chronic Hypertension

- If complication is not developed in a patient with chronic hypertension, plan the delivery at term. However, it should be taken into consideration that there will be an increase in fetal morbidity and mortality due to chronic hypertension. Also it is a fact that preeclampsia risk increases in such patients, therefore it is required to follow cases closely.
- If there is abnormality in fetal heart rate curve, fetal distress should be suspected.
- If there is a serious growth retardation and gestational age is reliable, delivery should be considered after cervix is evaluated.

**Note:** Evaluating pregnancy by ultrasonography at late pregnancy is not safe in terms of gestational age.

- If cervix is mature (soft, thin, partially open), delivery action should be inducted by using oxytocin after opening membranes.
- If cervix is not mature (hard, thick, closed), cervix should be matured by using prostaglandins.
- If any extraordinary situation occurs in the follow-up of delivery action, delivery is done by cesarean.

## Prolonged Labor (Dystocia)

### Related Messages

- Dystocia is formed of the appearance of four anomalies either one by one or as a combination;
  1. Abnormality in driving forces; uterine contractions (uterine dysfunctinos) at a rate not enough to dilate or wipe cervix or deliberate muscle effort at second phase of delivery.
  2. Maternal bone pelvis abnormalities; Pelvic contraction.
  3. Fetus development, position or presentation abnormalities.
  4. Urogenital system soft tissue abnormalities preventing fetus to progress.

### Abnormal Action Due to Cephalopelvic Disproportion

- The statement of cephalopelvic disproportion is used in cases where fetal head and maternal pelvis shapes (three dimensional) do not allow vaginal delivery and thus delivery action is blocked. Most of these disproportions are caused by malposition of fetal head (asynclitism, hyperextension etc.).
- In a case where the action is stopped despite the augmentation by oxytocin, cephalopelvic disproportion or a possible macrosomic fetus should be suspected. In such cases;
  1. Carrying on vaginal delivery increases the risks of bleeding and uterine rupture.
  2. Due to prolonged membrane rupture, it increases the infection risk for mother and fetus.
  3. Mother and fetus with shoulder dystocia increases trauma risk. On the other hand, shoulder dystocia may occur even in

babies which are not macrosomic. It is not possible to predict shoulder dystocia before and during delivery.

- Pelvimetry is not useful for predicting "non-progress" in the action, therefore it should not be used for deciding delivery type.
- In intrapartum care, those given below are seen that they affect cesarean possibility for "the progress of action" and thus they are not suggested unless required:
  - o Active management of delivery action (induction)
  - o Early amniotomy.
- In order to decrease unnecessary cesareans due to dystocia, it is required to avoid delivery inductions without indication and to benefit prostaglandin preparations maturing cervix in patients with inappropriate cervix.

## Protocol

### 1st Phase

- Early diagnosis and management of prolonged labor should be performed by using partogram.
- The first intervention after diagnosing prolonged labor is to increase uterus activity by doing amniotomy and applying oxytocin.
- Early amniotomy, early oxytocin application and regular professional support will make the action to progress and normal delivery will be done in this way.
- If uterus activity is provided and still the action hardly progresses, mechanical prevention should be considered. This case may occur because of cephalopelvic disproportion or relative cephalopelvic disproportion due to misplacement of head.

### 2nd Phase

- Pregnants with fetuses who are in the position of forehead and face presentations may be suitable for vaginal delivery with intervention at operating room; however, cesarean should be preferred in such cases.
- It should be remembered that delivery actions of pregnants who are in occipito-lateral or -posterior position may take longer. Also vaginal delivery with intervention can be tried in operating room for such preg-

**Diagnosis of non-progressive action**

| Finding | Diagnosis |
|---|---|
| Cervix is not open<br>No/less contraction | False Labor |
| Cervix opening is not more than 4 cm despite regular contractions more than 8 hours | Prolonged Latent Phase |
| Cervical opening is on the right side of warning line on delivery action | Prolonged Active Phase |
| Despite sufficient contrations, discontinuation of cervical opening and descend of incoming part | Cephalopelvic Disproportion |
| Big head, 3rd level of edema (moulding) on scalp, inconsistency of cervix with incoming part, edema on cervix, aneurysm on inferior part of uterus, formation of retraction ring, discontinuation of cervical opening and descend of incoming part by reasons such as distress in mother and fetus, distractions less than 3 within 10 minutes which are shorter then 40 seconds | Obstructed Labor (Obstruction) |
| Incomings except occiput anterior vertex | Insufficient Uterus Activity, Bad Presentation or Position |
| Cervix is fully open but there is no descend despite powerful pushes of women | Prolonged Push (Expulsive) Phase |

**Abnormal delivery patterns, diagnosis criteria and treatment methods**

| | Diagnosis Criteria | | | |
|---|---|---|---|---|
| Delivery Pattern | Nullipara | Multipara | Preferred Treatment | Exceptional Treatment |
| Prolonged latent phase | >20 hours | >14 hours | Bed rest, nourishment | Oxytocin or cesarean delivery for emergency problems |
| Extension Disorders | | | | |
| Extension of active phase dilatation | <1.2 cm/h | <1.5 cm/h | Wait-support treatment | For cephalopelvic disproportion |
| Extension of descend | <1.0 cm/h | <2.0 cm/h | | |
| Discontinuation disorders | | | | |
| Extension of deceleration phase | >3 hours | >1 hour | No cephalopelvic disproportion – oxytocin | Bed rest if there is fatigue |
| Secondary discontinuation in dilatation | >2 hours | >2 hours | cephalopelvic disproportion – cesarean | Cesarean delivery |
| Descending discontinuation | >1 hour | >1 hour | Decide according to patient | |
| Insufficiency of descending | There is no descending at second or third deceleration phase of delivery | | | |

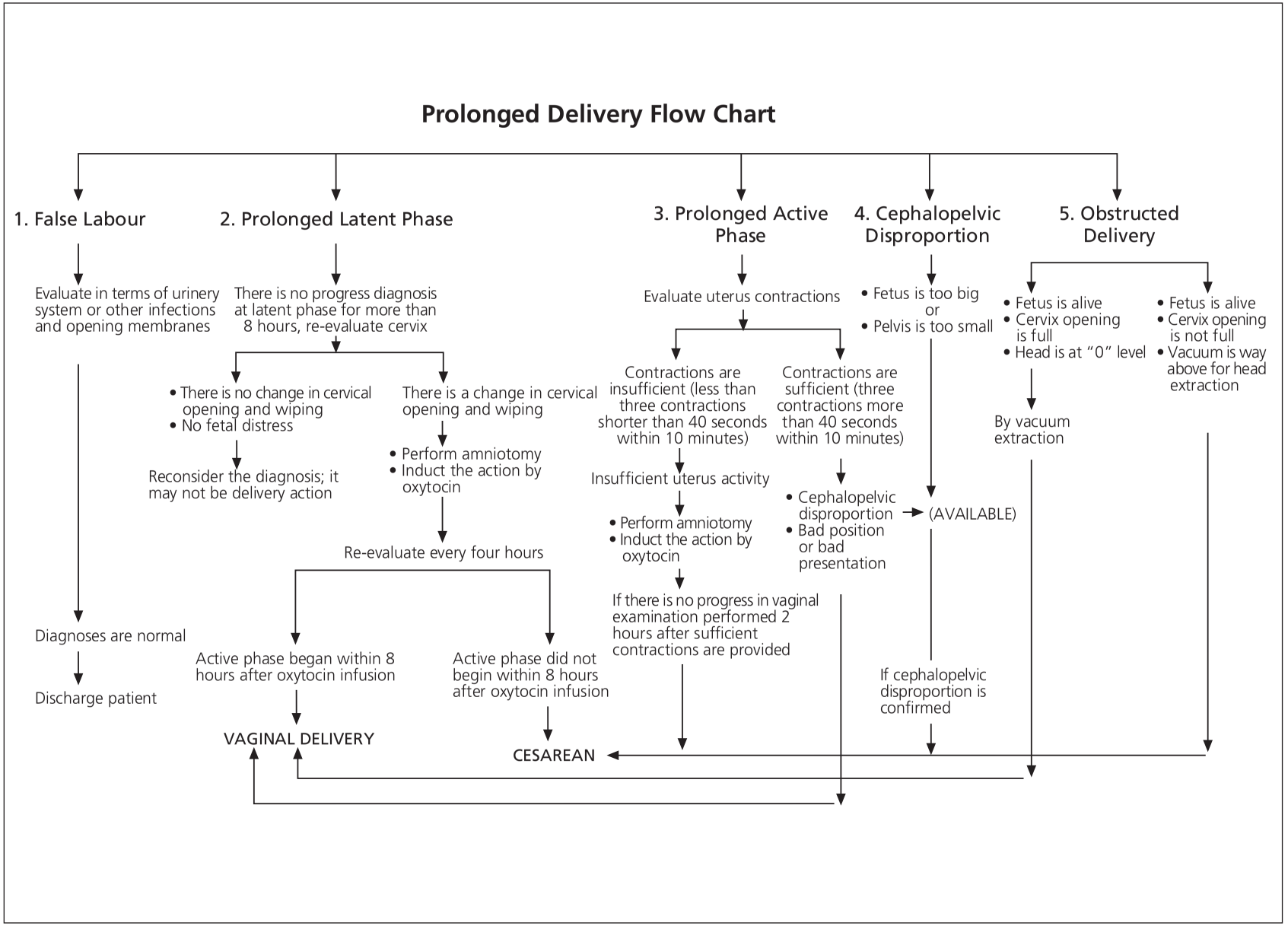
nancies. If delivery can not be done despite all these efforts, cesarean should be preferred.

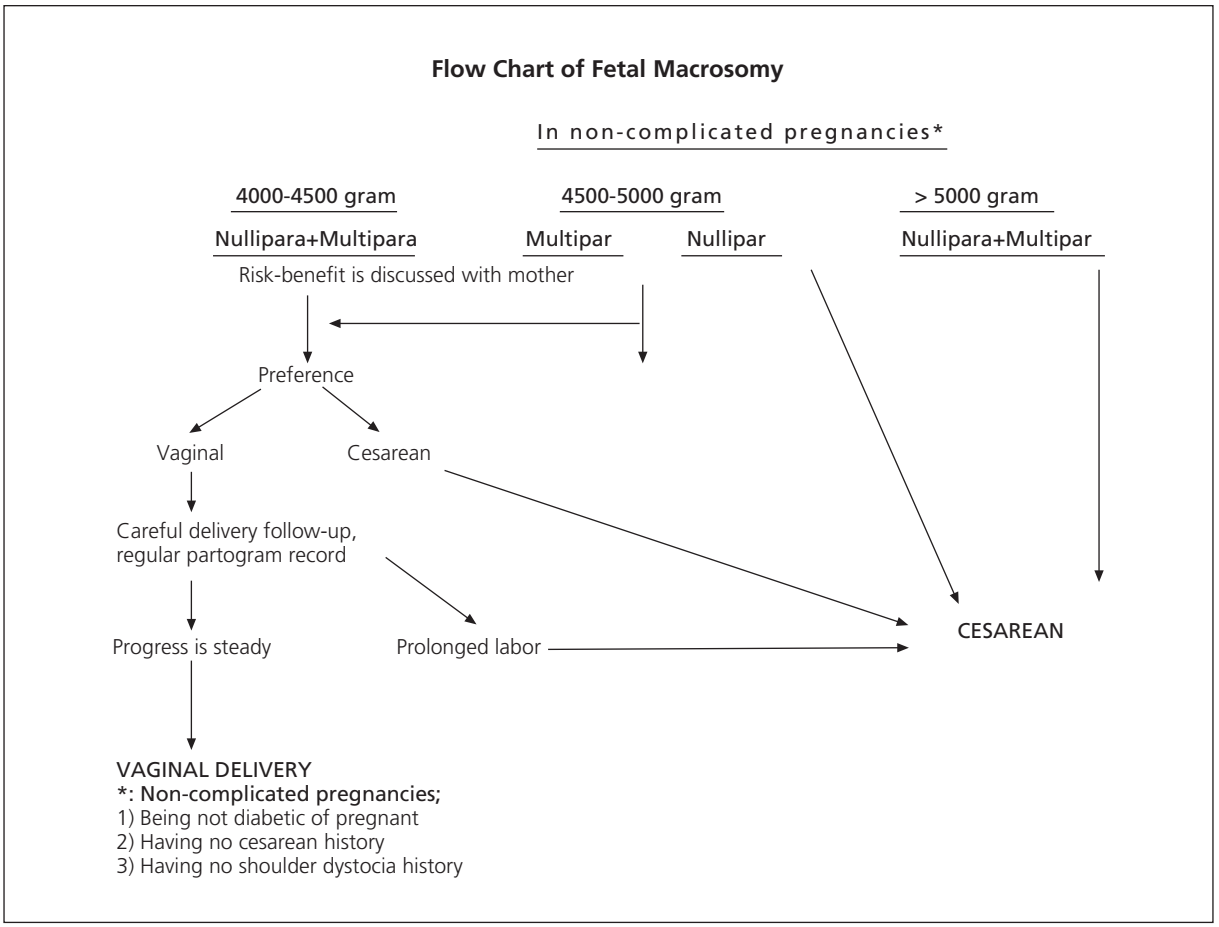
- Prolonged labor can only be considered;
  - ❖ If pregnant has not proceeded to active period 8 hours after initiating oxytocin infusion,
    - If cervical opening is on the right side of warning line on delivery action graph (partogram),
    - If delivery is not carried out despite delivery pains of pregnant which continue for 12 hours or more.

## Fetal Macrosomy

### Related Messages

- It is the state that birth weight of fetus is 4000 gr and above (incidence: 9%).
- Fetal macrosomy increases the rates of maternal (postpartum haemorrhage, anal sphincter laceration, postpartum infection) and fetal (prolonged labor, delivery possibility with increased intervention, shoulder dystocia, brachial plexus injury, meconium aspiration, fetal mortality) morbidities.
- Approximate fetal weight should be determined in pregnancy follow-up both clinically (fundal length-Leopold maneuver) and ultrasonographically (if applicable).
- It is required to be awake in pregnants with obese, diabetic and macrosomic infant delivery history in terms of fetal macrosomy.
- Pregnant should be evaluated carefully in terms of approximate fetal weight in postterm pregnancies.
- Normal vaginal delivery can be performed in non-diabetic pregnants with 4000-4500 gr


Prolonged Delivery Flow Chart
1. False Labour
2. Prolonged Latent Phase
3. Prolonged Active Phase
4. Cephalopelvic Disproportion
5. Obstructed Delivery
Evaluate in terms of urinery system or other infections and opening membranes
There is no progress diagnosis at latent phase for more than 8 hours, re-evaluate cervix
Evaluate uterus contractions
• Fetus is too big or
• Pelvis is too small
• Fetus is alive
• Cervix opening is full
• Head is at "0" level
• Fetus is alive
• Cervix opening is not full
• Vacuum is way above for head extraction
• There is no change in cervical opening and wiping
• No fetal distress
There is a change in cervical opening and wiping
Contractions are insufficient (less than three contractions shorter than 40 seconds within 10 minutes)
Contractions are sufficient (three contractions more than 40 seconds within 10 minutes)
By vacuum extraction
Reconsider the diagnosis; it may not be delivery action
• Perform amniotomy
• Induct the action by oxytocin
Insufficient uterus activity
• Cephalopelvic disproportion
• Bad position or bad presentation
(AVAILABLE)
Re-evaluate every four hours
• Perform amniotomy
• Induct the action by oxytocin
Diagnoses are normal
If there is no progress in vaginal examination performed 2 hours after sufficient contractions are provided
Active phase began within 8 hours after oxytocin infusion
Active phase did not begin within 8 hours after oxytocin infusion
If cephalopelvic disproportion is confirmed
Discharge patient
VAGINAL DELIVERY
CESAREAN




approximate fetal weight (AFW) (after all risks and benefits are discussed with mother). Follow-up of delivery action should be carried out carefully and progress should be recorded regularly by using partogram. Induction assisting delivery can be used (it should be remembered that it increases cesarean rates). Delivery is done by cesarean if prolonged action is considered.

- Cesarean is suggested for nullipara pregnancies with >4500 gr AFW and diabetic mother candidates with >4000 gr AFW.
- Delivery of pregnants who have >4000 gr AFW with cesarean history should be performed by cesarean.
- Delivery of pregnants who have >4000gr AFW with shoulder dystocia history should be performed by cesarean.

## Cord Prolapse

### Related Messages

- Fetal mortality rate due to cord prolapse regardless of delivery type has recently been increased to 0.55% from 0.43%.
- In 20-30% of cord prolapse, cervix is fully open and head is on or under the level of spinae. In this case, while delivery can be performed by emergency forceps and vacuum, cesarean can be applied since morbidity rates are high (intracranial hematoma, fascial or cranial damages etc.) despite proper vacuum and forceps conditions.

## Protocol

### Reminder: 1 - Diagnosis

- Umbilical cord lies under incoming part of fetus within delivery canal.

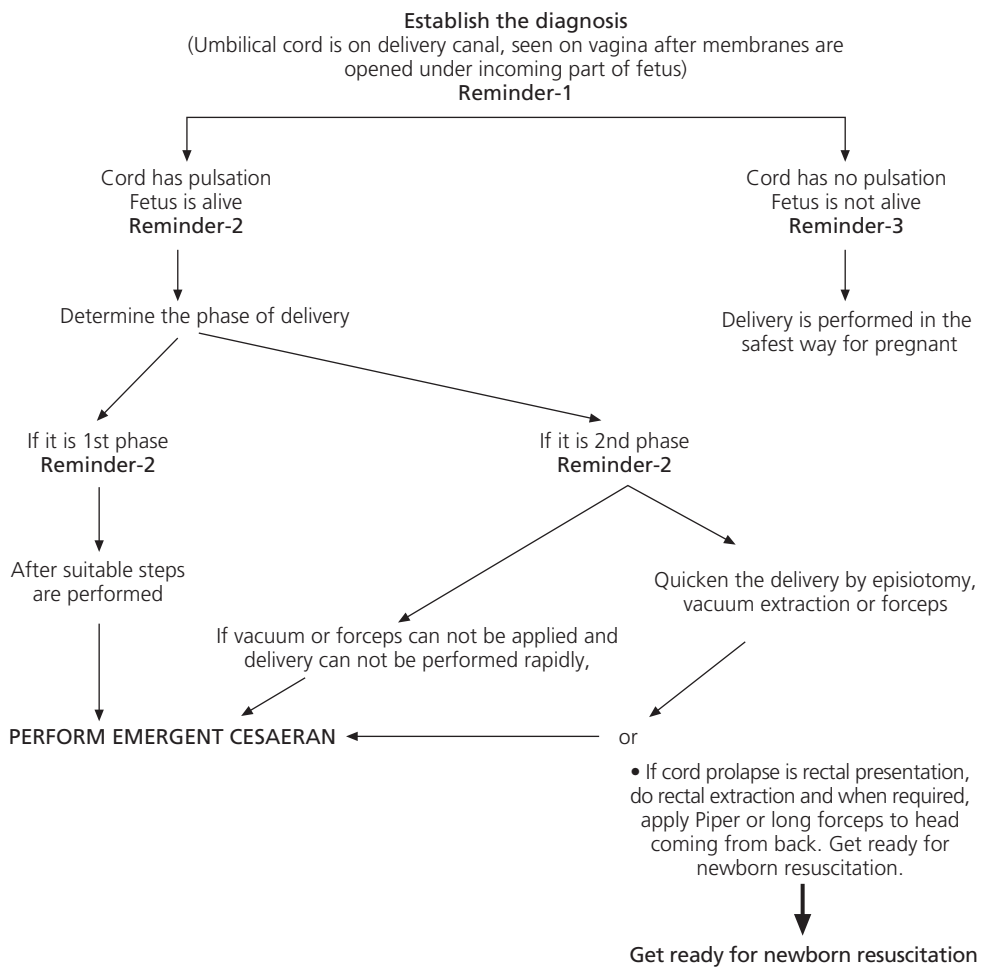
- Umbilical cord is seen in vagina after membranes are opened.

Reminder: 2 - If Cord Has Pulsation

- Fetus is alive.
- The phase of delivery should be determined by doing a vaginal examination immediately.
- If pregnant is in the first phase of delivery, in all cases;

1. Hand should be placed into vagina by wearing a sterile glove and incoming part should be pushed upwards and drawn away from pelvis to decrease the pressure on cord.
2. Other hand should be placed on pubis from abdomen and incoming part should be kept out of pelvis.
3. While incoming part is held on pelvis entrance tightly, hand in vagina should be withdrawn. Hand on abdomen should be kept on its position until cesarean is done.
4. If possible, tocolytic agents should be applied to reduce contractions.
5. Then, emergency cesarean should be performed.

**Cord Prolapse Flow Chart**



If Pregnant is in the Second Phase of Delivery;

1. Delivery should be quickened by episiotomy and (if possible) vacuum extraction or forceps.
2. In case of cord prolapse, if presentation is rectal or foot presentation, rectal extraction is done and Piper or long forceps can be applied to head coming from back. On the other hand, this method requires significant training in terms of its applicability. Additionally, morbidity will increase depending on the procedure. Cesarean can be applied as soon as rectal or foot presentation is detected.
3. Newborn should be prepared with his/her physician for newborn resuscitation.

Reminder: 3 - If Cord Has no Pulsation

- Fetus is dead.
- Delivery should be performed in the safest way for pregnant.

## Placenta Previa

### Related Messages

- Placenta previa (Pp) is seen in 0.3-0.5% of pregnancies.
- Cesarean and uterine surgeries undergone, smoke habits, advanced maternal age, multiparity, multiple pregnancies and cocaine use aer risk factors.
- Pp is the first indication in approximately 3% of all cesareans (2.2% non-active, 0.9% active vaginal bleeding is observed).
- Pp may have painless bleeding. Pregnant is evaluated together with fetus in Pp grade 3 and 4 (with closed placenta internal os) and cesarean possibility of pregnant can be discussed after 36th week. Elective cesarean can be applied at 36th-37th gestational weeks after (if possible) fetal lung maturation is documented.
- Pregnants who had cesarean due to Pp have more blood loss risk compared to other cesarean indications. Therefore, blood transfusion unit and experience obstetrician are required.
- Pregnants whose placenta covers internal cervical os partially or completely (grade 3 or 4 placenta previa) should have cesarean.
- Placenta previa and placenta accrete association should always be kept in mind (and the risk should be eliminated by ultrasonography if applicable).
- If distance between placenta and internal os can be calculated by ultrasonography, vaginal delivery can be tried in cases where this distance is 2 cm and above.
- If there is association between placenta previa and anterior wall placement, incision in cesarean should be performed by taking serious hemorrhage risk into consideration.

## Protocol

### Reminder: 1 - Diagnosis

- Placenta previa is to implant placenta on or near cervix.
- Placenta previa should be determined after 20th week. If placenta covers cervical os, USG should be repeated monthly.
- If there is vaginal bleeding and Pp is diagnosed, at least 4 units of erythrocyte suspension and coagulation factors should be prepared urgently.
- If gestational week is between 24 and 34, steroid should be applied for fetal lung maturation.
- If gestational week is lower than 34, patient diagnosed Pp with active uterine contractions should be dispatched to centers (by stabilizing the condition of mother) which are capable of doing neonatalogical care.

### Reminder 2 - Delivery

1. Vaginal delivery can be tried if Pp grade 1 or 2 and head are settled. On the other hand,

risks during delivery and procedure can be expressed to mother-to-be and cesarean can be considered by cesarean consent. If vaginal delivery is considered, amniotomy should be done in operating room and emergency cesarean measures should be taken.

2. Delivery is performed by cesarean at Pp grade 3 and 4.

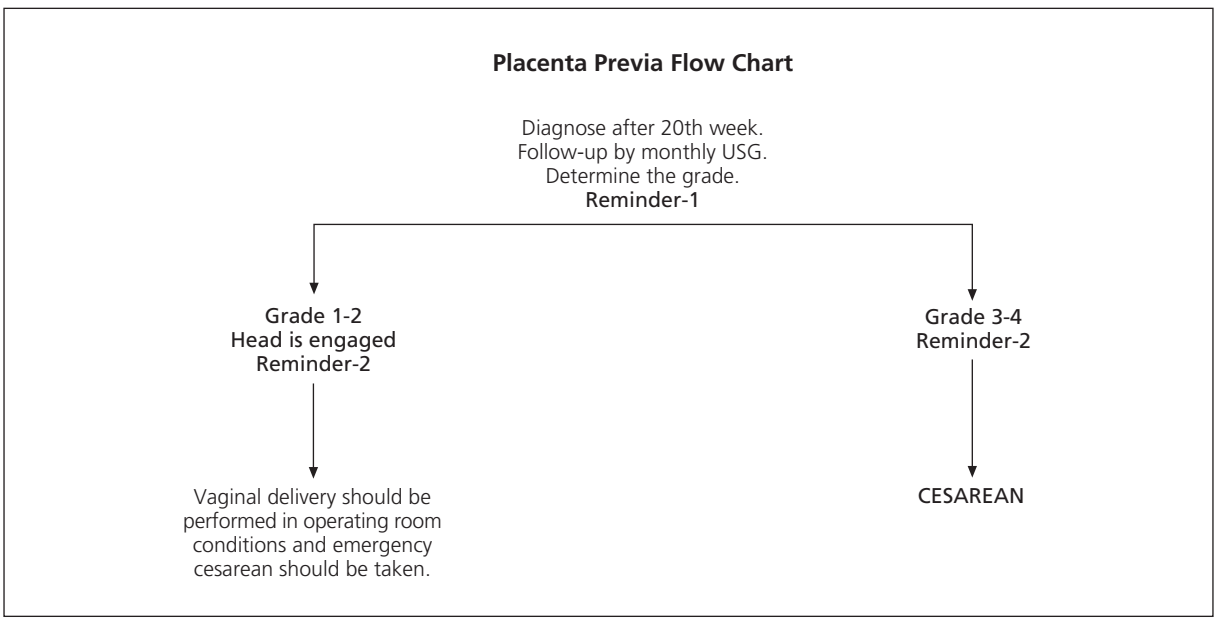
**Warning**: Vaginal examination should not be performed without doing emergency cesarean preparation.

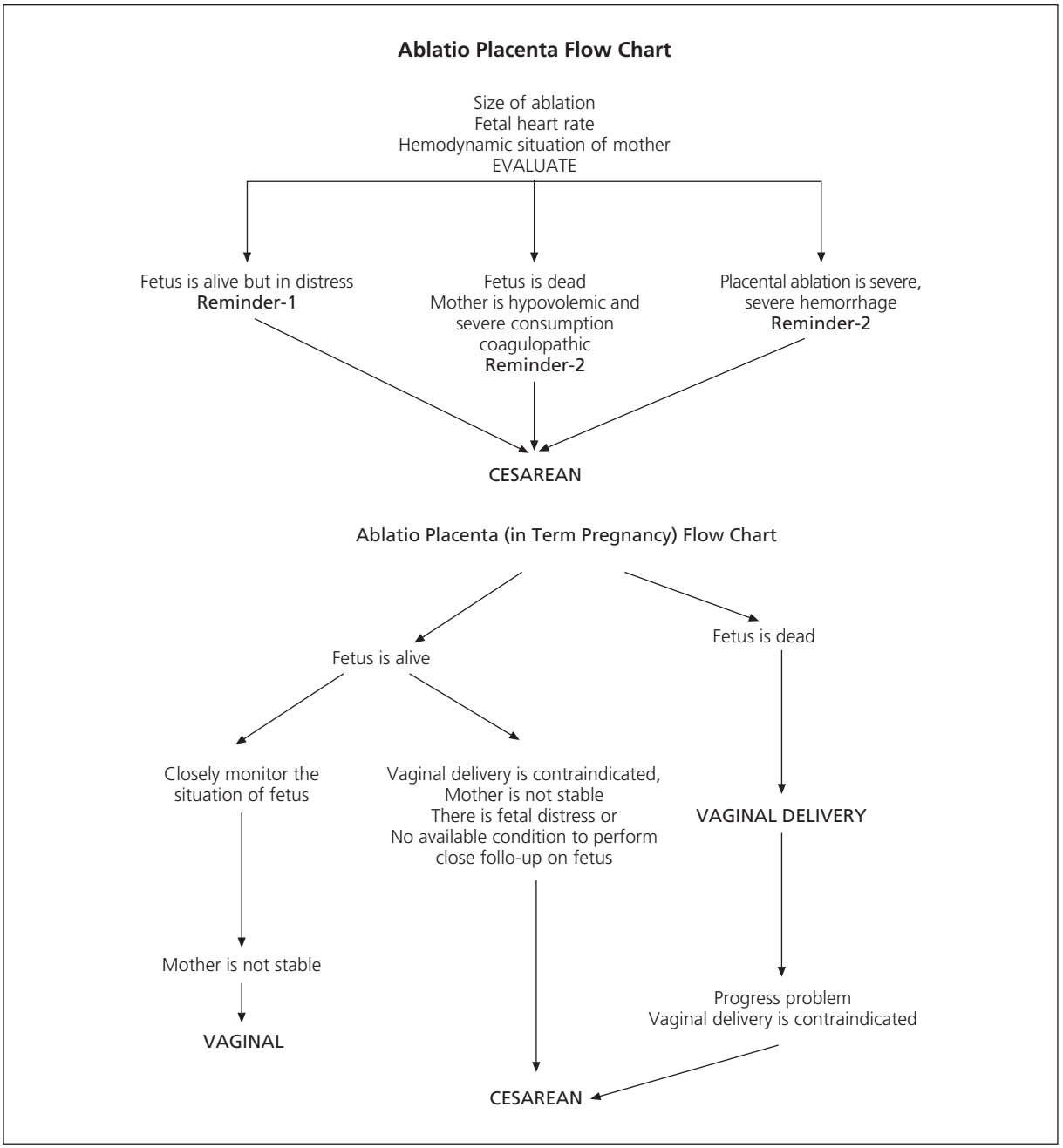
- If bleeding repeates, by comparing wait-and-see treatment with delivery, their benefits and risks in terms of mother and fetus should be considered and treatment should be decided.

## Ablatio Placenta

### Related Messages

- Ablatio placenta is seen approximately in 1% of deliveries.
- Trauma, smoking, multiple pregnancies, hypertension, preeclampsia, thrombophilia, advanced maternal age, intrauterine infections, polyhydramniosis, premature membrane rupture, ablation history in previous pregnancies, male fetus and cocaine use are the risk factors for ablation placenta.
- Diagnosis is basically established clinically, ultrasonography and Kleihauer-Betke test has a limited value in diagnosis.
- Management should be individualized in ablation placenta. Decision should be taken according to patient (according to severity of ablation, gestational week and presentation of fetus).
- In major ablato placenta (>50%), outcomes are fatal in terms of fetus even if fetus is alive.
- In ablation placenta, it should be careful in terms of coagulopathy and hypovolemic and measures should be taken according to these conditions.
- If vaginal delivery is planend, regular fetal follow-up is required to reduce perinatal mortality. Mother-to-be should be informed about the process and emergency cesarean should be applied if mother requests cesarean after information exchange.






- Conservative management policy can be accepted until fetal lung maturation is provided in less serious cases among preterm pregnancies.
- If mother is stable and fetus is lost, vaginal delivery should be preferred.
- Ablatio placenta and severe preeclampsia association should not be forgotten.

## Protocol

### Reminder-1

- Delivery of fetus which is alive but in distress should be performed by cesarean.
- While serious coagulation disorders increase bleeding risk that may develop during cesarean, the possibility of losing fetus during vaginal delivery is also quite high in

case of a severe ablatio placenta. Therefore, pregnant should be informed about possible risks when ablation placenta is detected. When ablation placenta is detected, delivery can be performed by cesarean before the case gets worse.

Reminder: 2

- The cases where cesarean delivery is preferred in ablation placenta;
  - If ablatio placenta is severe, cesarean should be arranged in the shortest possible time by also considering possible coagulation problems (by preparing fresh frozen plasma, fibrinogen, erythrocyte suspension).
  - If mother has hypovolemia and severe consumption coagulopathy and if the reason of the case is ablatio placenta, certain treatment of dissiminated intravascular coagulation (DIC) would be by the immediate practice of delivery.
  - After normal vaginal delivery decision is taken, delivery should be performed by cesarean if delivery act does not progress rapidly.
  - In case of feto-pelvic disproportion, malpresentation, undergone uterus surgery, delivery by cesarean should be preferred since there is a risk of coagulopthy development.

Reminder-3

- Mother should be monitored closely after delivery. Monitorization to follow vital findings and follow-up of incoming-outgoing fluid should be performed. Close monitorization of mother should be provided in terms of coagulopathy.
- Uterine tonus and dimension after delivery should be followed up carefully (hysterectomy may be required if bleeding continues and uterus is hypotonic).

## Vasa Previa

Related Messages

- It is a rare condition which progresses with high fetal mortality.
- Transvaginal ultrasonography and color Doppler ultrasonographic examination can be useful for antenatal examination.
- Elective cesarean should be performed.

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