PRETERM LABOR CONDITIONS OF WOMEN WITH HIGH-RISK PREGNANCY AND RELATED FACTORS: A RETROSPECTIVE COHORT STUDY

YÜKSEK RİSKLİ HAMİLELERDE ERKEN DOĞUM VE İLGİLİ FAKTÖRLER: RETROSPEKTİF KOHORT ÇALIŞMASI

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ABSTRACT

Objective: High-risk pregnancy is a situation associated with pregnancy involving a real or potential risk for the health and well-being of the mother and the fetus. Our study aimed to examine the preterm labor conditions of pregnant women followed up at a high-risk pregnancy outpatient clinic and related factors.

Material and Methods: Designed as a retrospective cohort study, the study was carried out with the participation of 293 pregnant women who presented to a high-risk pregnancy outpatient clinic in the Batman province of Turkey and were followed up between March 2017 and January 2019.

Results: The top three high-risk conditions determined in the pregnant women were pregnancy over the age of 35 (n=83, 28.3%), pregnancy in a shorter interval than two years (n=71, 24.2%) and consanguineous marriage (n=60, 20.5%), respectively. Twenty-point-one percent (n=59) of the pregnant women had preterm labor. It was determined that the rates of cesarean section births and births at a private hospital among the pregnant women who had preterm labor were significantly higher in comparison to the pregnant women who gave birth at term (p=0.001, p=0.037, respectively). It was determined that the risk of preterm labor increased OR=5.6 (1.2-25.6) times in the pregnant women with anemia, OR=12.5 (1.3-122.7) times in those with intrauterine fertilization and OR=32.6 (3.2-332.5) times in those with multiple pregnancies.

Conclusion: Anemia, multiple pregnancy and intrauterine fertilization increase the risk of preterm labor. Quality prenatal care services are important in terms of protecting the health of the mother and the newborn.

Keywords: Preterm birth, risk factors, anemia, multiple pregnancy, intrauterine fertilization

ÖZET

Amaç: Riskli gebelik annenin ve fetüsün sağlığı veya iyiliği için gerçek veya potansiyel bir tehlikeye sahip hamilelikli ilişkili bir durumdur. Çalışmamızda riskli gebelik polikliniğinde takibilen beşerlerin preterm eylem durumu ve ilişkili faktörlerin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Retrospектив kohort olarak tasarlanan bu çalışma Batman ilinde (Türkiye) riskli gebelik polikliniğine başvuran Mart 2017- Ocak 2019 tarihleri arasında takibi yapılan 293 gebel ile gerçekleştirtilmiştir.

Bulgular: Gebelerde tespit edilen ilk üç risk durumu sırasıyla 35 yaş üzeri gebelik (n=83, %28,3), iki yılda kısa aralıklı gebelik (n=71, %24,2), akraba evliliği (n=60, %20,5) şeklindedir. Riskli gebelerin %20,1’inde (n=59) preterm eylem gerçekleşmiştir. Preterm eylem gerçekleşen gebelerin içinde doğum yapan gebelerde görülen sezar bir doğum ve özel hastanede doğum yapma durumunun istatistiksel olarak fazla olduğu tespit edilmiştir (srasıyla p=0,001, p=0,037). Preterm eylem riski değerlendirildiğinde, anemisi olan gebelerde OR=5,6 (1,2-25,6) kattedir. Intrauterin fertilizasyon olan gebelerde OR=12,5 (1,3-122,7) katedilir. Çoğul gebelerde OR=32,6 (3,2-332,5) katedilir.

Sonuç: Anemi, multiparite ve intrauterin fertilizasyon preterm eylem riskini artırılmıştır. Kaliteli doğum sonrası bakım hizmetleri gebecin ve bebeğin sağlığı korumada önemlidir.

Anahtar Kelimeler: Preterm doğum, risk faktörleri, anemi, çoklu gebelik, intrauterin fertilizasyon
INTRODUCTION

Pregnancy is a process in which women experience changes brought about by new biological, physiological and sociological conditions (1). The World Health Organization (WHO) reported that in 2017, 295,000 women (approximately 810 women per day) lost their lives due to preventable causes associated with pregnancy and birth, and 94% of these deaths occurred in countries with lower and lower-middle income levels (2). In the High-Risk Pregnancy Management Guide prepared by the Turkish Ministry of Health, risk assessment is made under the headings of medical history (e.g., cardiovascular diseases, gynecological diseases, endocrine diseases), obstetric history (e.g., previous uterine surgery, pelvic mass, recurrent miscarriage, eclampsia-preeclampsia) and evaluation of current pregnancy (e.g., younger than 18 years old, older than 35 years old, Rh/rh incompatibility, multiple pregnancy, pregnancy in a period of shorter than two years after previous pregnancy). In the case of the presence of these conditions determined in this context in the pregnant woman, she is regarded as carrying a high risk and is referred to a hospital where an obstetrician is available (3). An important condition that may occur in high-risk pregnancies and affect the fetus is preterm labor. Approximately 11% of the births (around 15 million babies) in the world per year are early-term births (4). Many countries have reported an increase in the rate of early term births in the last 20 years, and this general trend has been verified by global research conducted by the WHO (5, 6). The prevalence of preterm births in Turkey was determined to be around 12% (7). Compared to the ones born at term, premature babies are at a higher risk during their lifetime in terms of various disorders, including neurodevelopmental disorders, gastrointestinal complications, cerebral palsy, sensory deficiencies, learning difficulties, and respiratory diseases (8).

In this study, it was aimed to determine the causes of preterm labor in high-risk pregnant women. This study had two main hypotheses. The first hypothesis was that the presence of anemia in pregnant women increases the risk of preterm labor. The second was that the risk of preterm labor is higher in pregnancies induced by assistive reproductive techniques.

MATERIALS AND METHODS

This is a retrospective cohort study. The Turkish Ministry of Health has determined risk factors for pregnant women and created a high-risk pregnancy identification form. The population of this study consisted of pregnant women who presented to a high-risk pregnancy outpatient clinic located in the Batman province in Turkey between March 2017 and January 2019. It was determined that 298 pregnant women presented to the clinic between the specified dates. The inclusion criterion was determined as meeting at least one of the three criteria determined by the Turkish Ministry of Health (medical history, obstetric history, and evaluation of current pregnancy) (Table 1). Pregnant women who were not followed-up (moving to another city, failure to attend clinic follow-up) and those whose pregnancy resulted in a miscarriage were excluded from the study. To elaborate, three of the pregnant women who presented to the high-risk pregnancy outpatient clinic were out of the scope of the study due to moving, one was not attending her follow-up, and one had a miscarriage on the 81st day of her gestation. The study protocol was approved by the Batman State Hospital Ethics Committee (Date: 06.10.2019, No: 200).

The minimum required sample size for this study, which was planned to assess the risk of preterm labor in high-risk pregnant women, was calculated using the G*Power program. A logistic regression analysis, which is a method in the Z-test family, was conducted for the calculation. Based on the result of the study by Rahman et al., with an alpha (α) error margin or 0.05 and an estimated power of 80%, the minimum required sample size was found as 148 participants (9).

Variables

All data for the study were obtained from the records of the high-risk pregnancy outpatient clinic. The risk assessment of the pregnant women was made under three categories determined by the Ministry of Health (medical history, obstetric history, and evaluation of current pregnancy). Seventy-two risk factors in total were inquired about, 19 of which were in the medical history, 17 in the obstetric history and 36 in the evaluation of the current pregnancy. Additionally, information regarding the age of the pregnant women, their parity, gravidity and miscarriage status, vitamin D and iron supplementation status, Td vaccination status and the place and method of birth (vaginal, C/S) was collected. The number of pregnancy follow-ups were calculated over the individuals’ visits to the outpatient clinic. The period of pregnancy at labor was calculated according to the time difference between the pregnant woman’s last date of menstruation and the date of labor. The pregnant women whose calculated period was <37 weeks were evaluated as preterm labor.

Statistical analysis

The statistical analyses of the study were performed with the Statistical Package for the Social Sciences software, version 25.0 (SPSS). Frequencies and percentages were used for descriptive information on the categorical variables, and means and standard deviations were used for the numerical data that displayed a normal distribution, while the numerical data that did not display a normal distribution is represented by medians (25th percentile-75th percentile). The normality of the distribution
of the continuous variables were tested by using visual (histogram and probability charts) and analytical (Kolmogorov-Smirnov Test) methods. In the comparison of the categorical variables in independent groups, Pearson’s chi-squared test or Fisher’s exact test was used. In the comparison of two independent groups, Student’s t-test was employed for the variables with normal distribution, while Mann-Whitney U Test was used for those without normal distribution. The variables that were found to be statistically significant (p<0.05) or p<0.200) were included in the logistic regression model. In the logistic regression model, the Enter and Backward methods were used. In the model, the correction was made according to age. The results were evaluated in a 95% confidence interval by accepting an alpha error of 0.05.

RESULTS

The mean age of the 293 pregnant women who were included in the study was 29.6±6.4 years, and their ages ranged between 16 and 52 years. The descriptive characteristics of the pregnant women are presented in Table 2. Seven (2.4%) out of the 293 pregnancies resulting in live births were twin pregnancies. Ninety-seven-point-six percent (n=286) of the pregnant women were taking iron supplements, and 79.5% (n=233) were taking vitamin D
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supplements. It was observed that 9.9% (n=29) of the pregnant women had never been vaccinated against tetanus. According to the results of the analysis on the medical histories of the pregnant women, 8.9% (n=26) had endocrine diseases, 2.0% (n=6) had chronic respiratory diseases, 1.7% (n=5) had diabetes, 1.4% (n=4) had cardiovascular diseases, 1.4% (n=4) had rheumatic diseases, 1.0% (n=5) had hypertension, and 0.3% (n=1) had epilepsy. Twenty-point-five percent (n=60) of the pregnant women reported that they had a consanguineous marriage. It was also determined that 4.4% (n=13) of the pregnant women had a low socioeconomic level.

According to the results of the analysis on the obstetric histories of the pregnant women, none of them had a history of uterine surgery, low birth weight, fetal macrosomia, post-term birth, antepartum and postpartum birth, venous thromboembolism, difficult and interventional birth, placenta previa, or abruptio placenta. It was observed that 0.3% (n=1) had a pelvic mass, myoma, uterine malformation, 0.3% (n=1) had a baby with a history of anomaly, 0.7% (n=2) had a history of gestational diabetes, 0.7% (n=2) had eclampsia-preeclampsia, 1% (n=3) had a history of preterm labor, 4.8% (n=14) had a history of stillbirth or newborn morbidity, 6.8% (n=20) had a history of recurrent miscarriage, and 13.7% (n=40) had a history of ectopic pregnancy.

In the analysis on the current pregnancies of the participants, it was determined that there was no case of fetal anomaly, gestational diabetes, cervical failure, eclampsia or preeclampsia, surgical intervention during pregnancy, severe infection, early membrane rupture, abnormal pap smear, intrauterine growth restriction (IUGR), phenylketonuria, intrauterine device (IUD) pregnancy, pregnancy following tube ligation, height less than 150 cm, pelvic mass, myoma, or uterine malformation. Zero-point-three percent (n=1) of the pregnant women had a body mass index of <18 kg/m², 0.3% (n=1) had experienced a trauma during pregnancy, 0.7% (n=2) had polyhydramnios-oligohydramnios, 0.7% (n=2) had vaginal hemorrhage, 0.7% (n=2) had hyperemesis gravidarum that required hospitalization, and 0.7% (n=2) had a risk of miscarriage. Moreover, 1.7% (n=5) had placenta previa, 1.7% (n=5) had post-infertility pregnancy, 2.0% (n=6) had preterm labor, 2.4% (n=7) had pregnancy before 18 years of age, 2.4% (n=7) had a multiple pregnancy, 2.7% (n=8) had anemia, 5.5% (n=16) had varicose veins, 9.6% (n=28) had the habit of smoking, 19.8% (n=58) had grand multiparity, 24.2% (n=71) had a pregnancy interval of shorter than two years, and 28.3% (n=83) had pregnancy over the age of 35 years.

It was determined that the frequency of use of the C/S birth method was significantly higher in the pregnant women who had preterm labor in comparison to those who gave birth at term (p=0.001). Besides, it was found that the rates of giving birth at a private hospital in the pregnant women who had preterm labor were significantly higher in comparison to the pregnant women who gave birth at term (p=0.037) (Table 3).

| Table 2: Distribution of the characteristics of the pregnant women |
|---------------------------------------------------------------|
| **Number (%)** |
| **Birth** |
| At term | 234 (79.9) |
| Preterm | 59 (20.1) |
| **Birth method** |
| Vaginal Birth | 259 (88.4) |
| C/S | 34 (11.6) |
| **Sex of the baby born (n=303)** |
| Girl | 145 (47.9) |
| Boy | 158 (52.1) |
| **Place of birth** |
| State hospital | 174 (59.4) |
| Private hospital | 119 (40.6) |
| **Total number of pregnancies** |
| Mean±SD | 4.0±2.5 |
| Median (Min-Max) | 4.0 (1-15) |
| **Live birth** |
| Mean±SD | 3.2±2.1 |
| Median (Min-Max) | 3.0 (0-13) |
| **Miscarriage history** |
| Yes | 126 (43) |
| No | 167 (57) |
| **Pregnancy follow-up number** |
| <4 follow-ups | 56 (19.1) |
| ≥4 follow-ups | 237 (80.9) |

Table 3: The relationship of preterm labor condition with the birth method of the pregnant women and the place of birth

| Birth method | At term (n=234) | Preterm (n=59) | P |
|----------------|----------------|----------------|---|
| Vaginal | 214 (82.6) | 45 (17.4) | 0.001 |
| C/S | 20 (58.8) | 14 (41.2) | |

| Place of birth | At term (n=234) | Preterm (n=59) | P |
|----------------|----------------|----------------|---|
| State hospital | 146 (83.9) | 28 (16.1) | 0.037 |
| Private hospital | 88 (73.9) | 31 (26.1) | |

It was determined that the risk of preterm labor was 5.6 times (1.2-25.6) higher in the pregnant women with anemia, 12.5 times (1.3-122.7) higher in those with intrauterine fertilization and 32.6 times (3.2-332.5) higher in those with multiple pregnancy (Table 4).
DISCUSSION

In this study, the prevalence of preterm labor among the pregnant women who were in the risky category determined by the Turkish Ministry of Health was found to be as high as 20.1%. In studies conducted at various centers across Turkey, it has been reported that the incidence of preterm birth ranged between 10% and 19.1% (10-12). The incidence of preterm birth across Turkey bears similarity to the incidence of preterm birth in the entire world (11.1%). This incidence ranges from 5% to 11% in European countries (6.7% in Spain, 5.9% in Sweden, 6.6% in France, 5.5% in Finland), while it is around 18% in some African countries (18.3% in Kenya, 14.2% in Tanzania, 12.2% in Nigeria). Among some Asian countries, this rate is 13.0% in India, 7.1% in China and 14.0% in Bangladesh. More than 60% of preterm babies were born in South Asia and Sub-Saharan Africa (6, 7, 13). Preterm birth is also a problem for high-income countries such as the United States (US). According to the Centers for Disease Control and Prevention, one out of every 10 births occurred as preterm birth in 2019 (14). The reason why the prevalence of preterm birth was found to be high in our study may have stemmed from the fact that all pregnant women included in the study were in the risky category, while in the studies mentioned above, pregnant women were included without considering their risk categories. In another study conducted in California, it was determined that women with risk scores ≥3.0 in pre-pregnancy and first trimester training and testing samples had a preterm
Despite the success of mother and child health programs, anemia is still the leading cause of maternal deaths and adverse pregnancy outcomes (e.g., preterm birth, low birth weight) in developing countries. In our study, it was determined that the pregnant women with anemia had a higher risk of preterm labor. Haider et al. determined that the risk of preterm labor increased in pregnant women with anemia by 1.21 times (1.13 to 1.30). Likewise, in another study conducted by Rahman et al., this risk was found to increase by 1.63 times (95% CI: 1.33, 2.01), while Rahmati et al. reported an increase in this risk by 1.56 times (95% CI: 1.25-1.95) (9, 28, 29). A retrospective cohort study in California observed that the children of pregnant women with anemia were born preterm at higher rates (8.9% versus 6.5% adjusted for maternal characteristics and obstetric complications) RR 1.3, 95% CI: 1.3–1.4) (30). A study in Taiwan revealed that the preterm labor rates of pregnant women with anemia (Hemoglobin level<10.8 g/dl) increased (adjusted OR: 2.16, 95% CI: 1.54-3.03) (31). A randomized-controlled study carried out in South India reported that the preterm labor risk of women with iron deficiency anemia was more than 3 times higher than other pregnant women (RR: 3.46 (1.81–6.61); p=0.0002) (32).

In a study conducted in Turkey in 2020, the preterm labor rates were found to be significantly higher in pregnant women with anemia compared to pregnant women without anemia (p<0.05) (33). Another study in Turkey (provinces of Rize and Istanbul) found higher rates of preterm labor in pregnant women with lower hemoglobin levels (OR, 2.42; 95% CI: 1.07–5.49) (34).

In our study, another factor that increased the risk of preterm labor was identified as multiparity. Muniro et al. determined that grand multiparity increased preterm birth risk (AOR 1.28; CI: 1.05-1.56). Similarly, Koulliali et al. reported that preterm birth risk increased in pregnant women who were having their fifth pregnancy (OR 1.26; 95% CI: 1.13-1.41) compared to pregnant women having their second pregnancy (35, 36). However, it has not yet been fully understood how parity affects the incidence of preterm births in terms of its biological mechanism, and studies carried out on the relationship between high parity and adverse pregnancy outcomes have pointed to conflicting results (37). A systematic review performed in 2010 demonstrated that grand multiparity and great grand multiparity were not associated with increased preterm birth risk (OR 0.96, 95% CI 0.77, 1.19 and OR 1.32, 95% CI: 0.61-2.83) (38). A study in China determined that multiparity reduced the risk of preterm labor in comparison to nulliparity (ARR 0.91, 95% CI: 0.89-0.93) (39). Chen et al. showed that nulliparity increased the risk of all stages of preterm labor 1.55 times in comparison to multiparity, whereas Dahman similarly stated that it increased this risk 2.08 (respectively, OR 1.55, 95% CI: 1.52-1.59 and OR 2.08, p<0.002) (40, 41).
Limitations
There were some limitations in our study. As our study was record-based and relied on recorded data, there may have been errors in data entry related to the pregnant women. In our retrospective study, we could not obtain data on social factors that might have affected preterm labor such as education and employment status. We also did not have data on exposure duration and severity of some risk factors that were determined (anemia, smoking), so, this may have prevented us from obtaining definitive results regarding the causes of preterm labor.

CONCLUSION
The prevalence of preterm labor, which is a risk factor, in the pregnant women who were included in this study was found to be higher than the prevalence of preterm birth determined across Turkey. In our study, in compliance with our hypotheses, it was observed that the risk of preterm labor increased in cases of anemia in pregnant women and pregnancies induced by assistive reproductive techniques. In future studies, investigating the prevalence of preterm labor based on different types of anemia and different types of assistive reproductive techniques will help us understand the etiology of preterm labor in more detail and prevent it.

Ethics Committee Approval: This study was approved by the Ethics Committee of Batman Regional State Hospital (Date: 10.06.2019, No: 200).

Peer Review: Externally peer-reviewed.

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