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Predictors of adverse perinatal outcomes in women at 40 weeks or more of pregnancy

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ABSTRACT

Introduction and aim. To evaluate the clinical features of women at ≥40 weeks of pregnancy and the utility of obstetric Doppler indices in predicting adverse perinatal outcomes in these pregnancies.

Material and methods. This prospective study was conducted at a single academic medical center between 2020 and 2022. Women aged 18 years and older with no risk factors who were at ≥40 weeks of pregnancy and delivered their babies in our hospital were included in the study. The fetal biometry, placental maturity grading, and doppler velocytometry indices of the pregnant women were evaluated. The cases were divided into two groups according to the development of adverse perinatal outcomes. The relationship between clinical features and adverse perinatal outcomes was evaluated.

Result. Adverse perinatal outcomes developed in 19.6% (42) of the 214 cases. The multiple logistic regression analysis was performed to identify factors affecting perinatal outcomes. Accordingly, a maternal age of ≥35 years (odds ratio [OR]: 1.74, 95% confidence interval [CI]: 1.29–3.96, p=0.038), nulliparity (OR: 1.42, 95% CI: 1.13–4.63, p=0.040), and grade 3 placental calcification (OR: 1.98, 95% CI: 1.11–4.53, p=0.029) were independent predictors of adverse perinatal outcomes.

Conclusion. Care should be taken in terms of adverse perinatal outcomes in the presence of nulliparity, a maternal age of ≥35 years, and grade 3 placental calcification in ≥40 week pregnancies.

Keywords. adverse perinatal outcomes, doppler velocytometry, placental maturity grading, prolonged pregnancy

Introduction

Prolonged pregnancy causes a significant increase in maternal and perinatal mortality and morbidity and has an incidence of 3-14%.[1] The majority of prolonged pregnancy cases have no known cause, but many risk factors, such as nulliparity, advanced maternal age, post-term pregnancy history, male fetus, and maternal obesity, have been implicated in their etiology.[2] One of the most important determinants of perinatal outcomes is the gestational week. It has been found that perinatal adverse outcomes during prolonged pregnancies are especially associated with changes in the placenta (e.g., fatty degeneration of the placenta, placental infarction, and multiple placental calcifications).[3] Prolonged pregnancy has been found to be related to conditions such as stillbirth, oligohydramnios, macrosomia, uteroplacental insufficiency, dysmaturity, meconium aspiration, and a low APGAR score.[4]

Although it is known that the continuation of pregnancy after the expected delivery time increases perinatal mortality, the time to start fetal monitoring and the gestational week to intervene remain controversial issues.[5] Doppler velocimetry is a non-invasive method for evaluating uteroplacental circulation. Many uterine artery Doppler studies have shown a relationship between increased wave resistance in uterine artery flow and preeclampsia and/or fetal growth retardation in the second trimester of pregnancy.[6,7] However, there are only limited data concerning whether Doppler flow changes can predict adverse outcomes in ≥40-week pregnancies.

Aim

Therefore, this study aimed to evaluate the clinical features of women at ≥40 weeks of pregnancy and the utility of obstetric Doppler indices in predicting adverse perinatal outcomes in these pregnancies.

Material and methods

Study design and participants

This prospective observational study was conducted between March 1, 2021, and March 1, 2023 at a tertiary university hospital. The study population consisted of women aged over 18 years with no risk factors who were at a gestational age of ≥40 weeks and delivered their babies in our hospital. All patients were evaluated in terms of gestational age, last menstrual period, and previous ultrasounds. Approval for the study was obtained from the Clinical Research Ethical Committee of Ahi Evran University Faculty of Medicine with a protocol number of 2021-02/23. All women were informed about the study, and their written consent was obtained before participating in the study.

Pregnant women aged under 18, those who delivered their babies before the 40 gestational week, cases in which there was no heartbeat on ultrasound, high-risk pregnant women (those with diabetes mellitus, hypertension, multiple pregnancy, or intrauterine growth retardation), pregnant women with fetal anomalies, macrosomic fetuses, oligohydramnios, or polyhydramnios, and those who withdrew their consent or wanted to withdraw from the study were excluded.

Data collection and process

Age, gravida, parity, body mass index, and mode of delivery were recorded, and fetal biometry, the amniotic fluid index, and placental location and presentation were evaluated in each woman. The Grannum classification (grades 0, 1, 2, and 3) was used for the grading of placental maturity: grade 0, a smooth chorionic plate and homogeneous tissue; grade 1: placental tissue with undulations and scattered echoic areas in the chorionic plate; grade 2, linear hyperechoic plates (calcifications) in the basal plate; grade 3: calcifications along the contour of the cotyledons.[8] The blood flow patterns of the umbilical artery (UA), uterine artery (UtA), ductus venosus (DV), and middle cerebral artery (MCA) were evaluated using Doppler ultrasound. Ultrasonographic examinations were performed using the Samsung RS85 Prestige, ultrasonography device equipped with a CA1-7A convex probe, with the patients placed in the supine position, slightly turned to the left side. The UA pulsatility index (UA-PI), UA resistive index (UA-RI), MCA-PI, MCA-RI, DV-RI, the average UtA-PI (of the right and left UtA-PI values), and UtA-RI were recorded. The cerebroplacental ratio (CPR) was calculated by dividing MCA-PI by UA-PI.

Outcome measures

The primary outcomes of the study were adverse perinatal outcomes, including cesarean section due to fetal distress, a fifth-minute Apgar score of <7, meconium-stained amniotic liquor or meconium aspiration, neonatal intensive care unit (NICU) admission, and perinatal mortality. The secondary outcome was the relationship between clinical features and adverse perinatal outcomes.

Statistical analysis

Statistical analysis was obtained using the Statistical Package for the Social Sciences (SPSS) version 21 (Chicago, IL). In the statistical evaluation of the data obtained from the study, categorical data were expressed as frequencies (n) and percentages (%), and continuous data were expressed as mean ± standard deviation and median (25^{th}-75^{th} percentile) values. The conformity of the data to the normal distribution was analyzed with the Kolmogorov-Smirnov test. Student's t-test was used to compare normally distributed parametric data, and the Mann-Whitney U test to compare non-normally distributed data. Pearson's chi-square or Fisher's test was used to compare categorical variables. Univariate and multivariate logistic regression analyses were conducted to determine the relationship between adverse perinatal outcomes and

clinical variables. Variables that were found significant in the univariate logistic regression analysis were included in multivariate logistic regression analysis. Odds ratios (ORs) and their 95% confidence intervals (CIs) were also calculated. $p<0.05$ was considered statistically significant in all tests.

Results

The study included 214 pregnant women. The rate of adverse perinatal outcomes in women at ≥40 weeks of pregnancy was 19.6% (42/214). The mean age of the pregnant women was 25.9±6.2 years in the group with adverse perinatal outcomes and 27.5±6.2 years in the group without adverse perinatal outcomes. The mean gestational age of the patients at the time of delivery was 284 (281–286) days in the group with adverse perinatal outcomes and 284 (282–286) days in the group without adverse perinatal outcomes. The demographic and clinical features of the cases are shown in Table 1.

Table 1. Demographic and obstetric characteristics of the sample*

Variables	**Adverse perinatal outcomes**		**p**
	Present (n=42)	Absent (n=172)	
Age, years	25.9±6.2	27.5±6.2	0.097
Age ≥ 35 years	9 (21.4%)	14 (8.1%)	0.013
Parity			
Nulliparity	34 (81%)	107 (62.2%)	0.022
Multiparity	8 (19%)	65 (37.8%)	
Gravidity	1.38±0.85	1.50±0.76	0.113
Body mass index (kg/cm^2)	26.9±3.6	25.5±3.4	0.062
GA at delivery, days	284 (281–286)	284 (282–286)	0.221
Placental grading			
Grade 0	11 (26.2%)	66 (38.4%)	0.14
Grade 1	8 (19.0%)	48 (27.9%)	0.242
Grade 2	10 (23.8%)	34 (19.8%)	0.561

Grade 3	13 (31.0%)	21 (9.8%)	0.003
Doppler test			
UA-PI	0.92 (0.83–0.98)	0.88 (0.72–1.12)	0.838
UA-RI	0.59 (0.45–0.78)	0.59 (0.51–0.65)	0.624
MCA-PI	1.61±0.51	1.29±0.57	0.122
MCA-RI	0.73 (0.65–0.89)	0.70 (0.63–0.82)	0.285
CPR	1.61±0.75	1.37±0.5	0.318
UtA-PI	0.94±0.28	0.93±0.23	0.845
UtA-RI	0.99 (0.65–1.03)	0.73 (0.59–0.91)	0.041
DV-RI	0.82±0.23	0.89±0.26	0.492

* Data are presented as mean ± standard deviation, median and 25th–75th percentiles, or n (%). GA – gestational age; UA – umbilical artery; MCA – middle cerebral artery; UtA – uterine artery; DV – ductus venosus; CPR – cerebroplacental ratio (MCA-PI/UA-PI); PI – pulsatility index; RI – resistive index

Nulliparity (81%) and a maternal age of ≥35 years (21.4%) were found at a higher rate in the group with adverse perinatal outcomes. Grade 3 placental calcification and MCA-RI were statistically significantly higher in the group with adverse perinatal outcomes compared to the group without adverse perinatal outcomes. Table 2 shows the distribution of the adverse perinatal outcomes in pregnancies over 40 weeks.

Table 2. Type and rate of adverse perinatal outcomes in the sample*

Adverse perinatal outcome	**Number of cases[a] (%)**
Cesarean delivery due to fetal distress	13 (6.1%)
Presence of meconium stained liquor or meconium aspiration	15 (7%)
Fifth-minute Apgar score < 7	8 (3.7%)
NICU admission	11 (5.1%)

Perinatal mortality	0

* NICU – neonatal intensive care unit; [a] – some women experienced more than one adverse outcome; therefore, the total of all adverse outcomes exceeds the number of women who experienced adverse outcomes (n=42)

The most common adverse perinatal outcomes were the presence of meconium-stained liquor or meconium aspiration (7%) and cesarean delivery due to fetal distress (6.1%). Statistically significant parameters were included in a regression model (Table 3).

Table 3. Univariate and multivariate analyses of predictive factors for adverse perinatal outcomes*

Variables	**Univariate logistic regression**			**Multivariate logistic regression**		
	OR	95% CI	p	OR	95% CI	p
Age ≥ 35 years	2.81	1.63–4.24	0.013	1.74	1.29–3.96	0.038
Nulliparity	2.04	1.49–5.12	0.022	1.42	1.13–4.63	0.04
UtA–RI	2.32	1.17–4.61	0.041	1.23	0.57–2.89	0.582
Placental grading (grade 3)	2.66	1.20–5.96	0.003	1.98	1.11–4.53	0.029

* UtA-RI – uterine artery resistive index; CI – confidence interval; OR – odds ratio

According to univariate logistic regression analysis, a maternal age of ≥35 years, grade 3 placental calcification, UtA-RI, and nulliparity were important predictors of adverse perinatal outcomes. Multiple logistic regression analysis was performed to determine factors affecting adverse perinatal outcomes, and a maternal age of ≥35 years (OR: 1.74, 95% CI: 1.29–3.96, p=0.038), grade 3 placental calcification (OR: 1.98, 95% CI: 1.11–4.53, p=0.029), and nulliparity (OR: 1.42, 95% CI: 1.13–4.63, p=0.040) were found to be independent predictors of adverse perinatal outcomes.

Discussion

In this study, adverse perinatal outcomes developed at a rate of 19.6% in women at ≥40 weeks of pregnancy. When the pregnant women were compared according to the development of adverse perinatal outcomes, nulliparity, a maternal age of ≥35 years, and the presence of grade 3 placental calcification were determined to be associated with adverse perinatal outcomes.

Perinatal morbidities, such as growth retardation, hypoglycemia, polycythemia, meconium aspiration, and pulmonary hypertension, have a higher incidence in postmature babies and present with a higher rate of neurodevelopmental complications.[9] There are many options in fetal monitoring, including the non-stress test (NST), contraction stress test, biophysical profile, and modified biophysical profile (NST and amniotic fluid evaluation). Doppler velocytometry evaluation provides additional information concerning fetal status. Although antepartum fetal monitoring is required at ≥41 0/7 weeks of gestation, there are not sufficient data to define the most appropriate test type and frequency. In addition, only a few studies have investigated Doppler flow changes in post-term pregnancies and reported conflicting Doppler data concerning the increase in placental insufficiency findings. In a prospective study including women at a gestational age of 40 to 42 weeks, Maged et al. showed that women with adverse perinatal outcomes had higher UA-PI and lower MCA-PI values and a lower CPR compared to those with normal perinatal outcomes.[10] In addition, the authors reported that women with adverse perinatal outcomes had a higher rate of cesarean section due to fetal distress and a higher rate of induced vaginal delivery due to oligohydramnios. In contrast, recent studies indicate that the Doppler indices UA, UtA, MCA, and DV are not useful in the follow-up of post-term pregnancies or in predicting and preventing adverse fetal and perinatal outcomes.[5,11] Consistent with these studies, we found that Doppler indices were not predictors of adverse outcomes in women at ≥40 weeks of pregnancy.

It is known that post-term pregnancy is associated with increased fetal and perinatal risks, with most complications developing as a result of excessive fetal growth and placental insufficiency.[12] Placental calcification, characterized by calcium deposits in the placenta, is a very common condition in prolonged pregnancy. Placental calcification is a physiological process associated with a decrease in placental function during prolonged pregnancy.[13] Studies have found that preterm placental calcification is associated with maternal and perinatal adverse outcomes (e.g., preeclampsia, at least one abnormal Doppler index, obstetric cholestasis, placental abruption, intrauterine growth retardation, maternal intensive care unit admission, low-birth-weight infants, and low perinatal APGAR scores) oligohydramnios, perinatal mortality, hypoxia due to placental insufficiency, asphyxia, and cesarean section are also seen at increased rates in post-term pregnancies compared to term pregnancies.[1,14-16] Although the etiology of post-term pregnancies is not yet fully known, it has been reported in the literature that there are many risk factors for the development of a post-term pregnancy, such as obesity, primiparity, advanced maternal age, and low education level.[17,18] In our study, the presence of grade 3 placental calcification seemed to negatively affect perinatal outcomes in women at ≥40 weeks of pregnancy.

A study examining the relationship between advanced maternal age (≥40 years) and pregnancy outcomes in late and post-term pregnancies found that advanced maternal age was associated with adverse pregnancy outcomes (stillbirth, perinatal death, meconium aspiration syndrome, fifth-minute Apgar score<7, NICU admission, and sepsis).[19] In a retrospective study conducted in late and post-term pregnancies, the authors

reported that maternal and perinatal adverse risks increased in primiparous women compared to multiparous women.[19] Our study showed a significant relationship between adverse perinatal outcomes and nulliparity and a maternal age of ≥35 years in women at ≥40 weeks of pregnancy.

Our study has certain limitations, with the first and most important being the single-center design. Another limitation concerns the low number of cases. Multicenter studies with a larger patient population will further contribute to the results obtained from the current study.

Conclusion

Every pregnant woman at advanced gestational age is at a potential risk for adverse perinatal outcomes. We consider that care should be taken in terms of adverse perinatal outcomes in the presence of nulliparity, a maternal age of ≥35 years, and grade 3 placental calcification in ≥40-week pregnancies.

Declarations

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Author contributions

Conceptualization, Z.S.S. and E.T.S.; Methodology, A.E.D. and Z.S.S., Software, Z.S.S. and E.A.; Validation, A.E.D., E.A. and Z.S.S.; Formal Analysis, E.T.S.; Investigation, Z.S.S.; Resources, Z.S.S.; Data Curation, Z.S.S.; Writing – Original Draft Preparation, Z.S.S.; Writing – Review & Editing, Z.S.S.; Visualization, Z.S.S.; Supervision, Z.S.S.; Project Administration, Z.S.S.; Funding Acquisition, Z.S.S.

Conflicts of interest

No conflict of interest was declared by the authors.

Data availability

Data will be provided if necessary.

Ethics approval

This study protocol was approved by Clinical Research Ethical Committee of Ahi Evran University Faculty of Medicine with a protocol number of 2021-02/23 and conducted in accordance with the Declaration of Helsinki and Good Clinical Practices.

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