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Original Article

The Relationship between Preterm Placental Calcification and Adverse Maternal and Foetal Outcome

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Abstract *- Placental calcification identified before 36 weeks of gestation is known as preterm placental calcification (PPC). PPC can be a sign of a poor fetal outcome. However, their association with adverse perinatal outcomes has not yet been confirmed. Objective: The primary objective was to identify and compare the outcomes of pregnancies with and without documented preterm placental calcification of prematurity from 2022 to 2023.Materials and Methods: We successively enrolled 260 prenatal women who came to the antenatal outpatient clinic and obstetrics department after obtaining our consent to participate in the study. Transabdominal ultrasonography was performed monthly between 28 and 36 weeks of pregnancy to document PPC. We compared maternal and fetal outcomes between those identified with grade III PPC (n=80) and those without grade III PPC (n=180). Results: The frequency of PPC was higher in pregnant women who smoked (p-value = 0.03) and those who took high doses of calcium (p-value = 0.001). Each of the following was significantly higher in the PPC group: incidence of prematurity (p-value=0.0001), low birth weight (p-value=0.03), abnormal CTG (p-value=0.001), increased UA RI(p-value=0.03), Absence end-diastolic velocity / Reversal end diastolic velocity (REDV/AEDV) (p-value=0.03). Conclusion: pregnant with PPC Grade III should be advised to have close prenatal follow-up and regular and frequent fetal health check-ups to prevent fetal complications.*

Keywords *- Premature placental calcification, Grade III placenta, Perinatal outcome, Foetal Outcome, Grannum.*

1. Introduction

Placenta acts as a basic endocrine organ while providing nutrient transfer between mother and fetus during pregnancy. Placental Calcification (PC) is a condition frequently detected in ultrasonographic examination during pregnancy. The echogenic focus image in the placenta occurs as a result of calcium accumulation in the placental tissue and is generally seen in the maternal aspect and perivillous areas. Possible causes of tissue calcification can be physiological, dystrophic and metastatic[19]. The calcium/phosphate (Ca/P) weight ratio of the mineral varies according to the mechanism of calcification. For example, the Ca/P weight ratio is greater in mature bone than in the organized apatites associated with metastatic calcification. Thus, the chemical composition of the mineral may distinguish a physiological mechanism (e.g. bone formation) from a metastatic process. Physiological and non-physiological calcification may also be. Placental calcification is a physiologic phenomenon associated with increasing gestational [1,11,15,22].

When calcium accumulates in the basement membrane and lobules, a linear or lobulated echogenic image is formed. Systemic classification of ultrasonographic morphology of the placenta initially proposed by Grannum et al. (1979)[13] has scored the placental changes based on calcium deposition on a semi-quantitative sc11ale (0–III). Grade 0 indicates a smooth chorionic plate and homogenous texture of the placenta, grade I shows occasional calcification in the basal plate, grade II has occasional calcification in placental texture, and grade III indicates a circular appearance of calcifications up to the basal plate and divides the placenta into discrete parts [6]. By term pregnancies, 20% of placentas present as grade III [14]. Normally, a grade III placenta is not frequently found until 36 weeks of gestation, when it is called a preterm placental calcification.

The population-based preterm placental calcification prevalence ranges from 3.8% to 23.7% [9]. Current studies on the clinical significance of preterm placental calcification and pregnancy outcomes are inconsistent. A number of studies show that preterm placental calcification is the pathologic result of smoking [7] and medical problems [16]. It may predict poor foetal and maternal outcomes [16,14]. However, other studies have not reported such associations [20]. The current study evaluated the role of premature calcification in adverse pregnancy outcomes in an attempt to identify potential predisposing parameters of early calcium deposition in the placenta 3.

2. Materials and Methods

This prospective cohort study consecutively enrolled 260 women who presented to the Obstetric department in Tishreen University Hospital from May 2022 to May 2023. this study was conducted according to the principles of the Declaration of Helsinki. Participants gave informed consent prior to the recruitment.

We consecutively invited pregnant women who were referred for obstetric ultrasounds to the Obstetric department to participate in this study. Volunteers completed the consent form and were screened for placental calcification by ultrasound. Participants underwent monthly ultrasound scans between 26 and 36 weeks of their pregnancies, which were repeated at 36 weeks of gestational age to assess the presence of preterm placental calcification.

We performed the transabdominal sonography using a 3.5 MHZ transducer (Siemens). We divided the participants into two groups based on when the placental calcification was detected. Group A consisted of 80 patients with detectable placental calcification prior to 36 weeks of gestation. Group B consisted of 180 patients whose placental calcification was not confirmed between 28 and 36 weeks of gestation.

Maternal outcome measures included placental abruption postpartum haemorrhage (blood loss greater than 500 mL after birth). Foetal outcome measures were foetal anomaly, oligohydramnios, preterm births before 37 weeks of gestation, low birth weight (LBW; under 2500 g), and low Apgar score (less than 7 after 5 min). In addition, we compared the Doppler parameters and delivery route in the two groups. We made CTG and determined the Amniotic Fluid Index (AFI).

If the foetus was diagnosed with abnormal CTG or oligohydramnios, the same perinatologist obtained recordings of the Umbilical Artery (UA) colour Doppler assessment. An abnormal Doppler was recorded if any of the following were present. If the UA flow showed increasing resistance, decreased diastolic velocity that eventually became absent was recorded as Absent End Diastolic Velocity (AEDV), and resistance that increased with progressive worsening as a reversal of diastolic flow was defined as Reverse End Diastolic Velocity (REDV).

Grade III placental calcification was determined by the deep chorionic plate indentation that extended to the basal layer and divided the placenta into discrete parts [13]. Sociodemographic data, including maternal age, smoking habits, and taking calcium supplements with or without foods rich in calcium, were recorded. Gestational age was assessed from the first day of the last menstrual period (LMP) and confirmed by early pregnancy ultrasound measurement. Mothers and newborn babies were followed by an investigation of any medical problems that arose before discharge.

2.1. Ethical Consideration

All patients were provided complete and clear informed consent after discussing the study. This study was performed in accordance with the Declaration of Helsinki.

2.2. Statistical Analysis Data

Statistical analysis was performed by using the IBM SPSS version20. Basic Descriptive statistics included means, standard deviations(SD), median, frequency and percentages. To examine the relationships and comparisons between the two groups, the chi-square test was used. Independent t student tests were used to compare 2 independent groups. All the tests were considered significant at $\alpha = 0.05$.

3. Results

Preterm placental calcification was detected in 80 of 260 (30,7%) pregnancies.

Table 1. Comparison of maternal characteristics and habits between the two groups

Characteristics and Habits	Group A n=80	Group B n=180	P-value
Age	27.52±3.8	28.33±4.1	0.6
Smoking	32(40%)	35(19.4%)	0.03
Taking high doses of calcium	34(42.5%)	39(21.7%)	0.001

As shown in Table 1, both groups were approximately similar in terms of maternal age, as the mean age in group A was 27.52±3.8 years versus 28.33±4.1 in group B and no significant difference was found between the two groups (p=0.6). There were significant differences between the two groups regarding the following variables (group A versus group B): Smoking(40% vs. 19.4%, p= 0.03) and taking a high dosage of calcium(42.5% vs. 21.7%, p= 0.001).

As shown in Table (2), the presence of abnormal CTG was more frequent in the PPC group and statistically significant (12.5% in group A vs. 2.8% in group B, p=0.3). Oligohydramnios were more frequent in the PPC group but without significance (6.3% in group A vs. 3.9% in group B p=0.3). Also, there were significant differences between the two groups regarding the following variables (group A versus group B): Abnormal Doppler findings (17.5% vs 5%, p=0.002) and UA RI (12.5% vs 4.4%, p =0.03), and AEDV/REDV (12.5% vs 2.8%, p= 0.03). In terms of the effects of calcification on the foetus:

Table 2. Comparison of maternal/foetal and neonatal characteristics between the two group

Characteristics	Group A n=80 With PPC	Group B n=180 Without PPC	P-value
Oligohydramnios	5(6.3%)	7(3.9%)	0.3
Abnormal CTG	10(12.5%)	5(2.8%)	0.001
Abnormal Doppler	14(17.5%)	9(5%)	0.002
UA RI	10(12.5%)	8(4.4%)	0.03
AEDV/REDV	10(12.5%)	5(2.8%)	0.03
Lower gestational age	36.92±2.1	39.75±2.4	0 .002
Lower birth weight	29(36.2%)	39(21.7%)	0 .03
Preterm before 37 weeks	37(46.3%)	44(24.4%)	0 .0001
(C/S)	74(92.5%)	161(89.4%)	0.8
Apgar score <7 at 5 min	6(7.5%)	8(4.4%)	0.09
Postpartum hemorrhage	3(3.8%)	9(5%)	0.2
Placental Abruption	2(2.5%)	0(0%)	0.9

The early placental calcification group also had significantly lower gestational age at delivery (36.92±2.1 in group A vs. 39.75±2.4 in group B,p = 0.002). The risk of delivery before 37 weeks of gestation and the risk of LBW was 1.5 times higher in group A compared to group B (Preterm before 37 weeks; 46.3% in group A vs. 24.4% in group B, p = 0.0001. LBW; 36.2% in group A vs. 21.7%, p=0.03). A non-significantly greater for caesarean section(C/S) existed in the early placental calcification group (92.5% in group A vs. 89.4% in group B, p =0.8). As far as neonatal outcome is concerned, there is not a significantly increased incidence of low APGAR score (7.5% in group A vs. 4.4% in group B, p =0.09).

A non-significantly greater for placental abruption(2.5% in group B vs. 0% in group B, p =0.9) and postpartum hemorrhage (3.8% in group A vs. 5% in group B, p =0.2).

4. Discussion

In the present study, mothers had a mean age of 29 years in group A and 27 years in group B, so we did not observe any relationship between maternal age and preterm placental calcification; other researchers have reported that low maternal age influenced the detection of premature placental calcification [16,9]. Our study described a large series of young mothers, which might be why there is no association.

In the current study, smoking predicts early placental calcification. Other investigators reported that maternal cigarette smokers have an increased risk for premature placental calcification [7,4,16]. Smoking is a risk factor for atherosclerosis that can accelerate the narrowing of placental arterioles and is a predisposing factor for calcification.

Also, taking a rich dosage of calcium predicts early placental calcification; maybe Metastatic calcification is the responsible mechanism for this result [2].

Abnormal Doppler patterns of a considerably increased UA resistance index (RI) and significant AEDV/REDV of the UA occurred more frequently in women with early placental calcification. Preterm placental calcification could be a warning sign for uteroplacental insufficiency [4,9, 23]. This might be explained by decreased UA resistance during pregnancy to provide a suitable flow for the foetus. However, the resistance does not decrease in high-risk pregnancies, and umbilical flow might be absent (AEDV). In severe cases, the flow would become reversed (REDV) [24]. These patterns could be observed in pregnancies with placental dysfunction [3,17]. Hence, poor outcomes of pregnancies could be predicted [9].

The risk of delivery before 37 weeks and LBW were higher in the preterm calcification group. This finding approximated the estimates of other researchers [4,9,16,21,23,25]. Logically, the lower the age at placental calcification diagnosis, the lower the age at delivery, birth weight and APGAR score of the first 5 min were observed compared to those patients without early placental calcification due to prematurity and its problems. Our results and those of other researchers [25,4] showed a higher rate of C/S in the preterm calcification group. In line with these results, our study suggested that preterm placental calcification could be a cause of preterm labour in relation to oligohydramnios, fetal distress and, subsequently, an increase in the rate of C/S. Conversely, Hill et al. (1983) [14] studied these parameters and concluded that preterm calcification could not be responsible for poor foetal and maternal outcomes.

Regarding the results of PPC on the mother, there is no significant statistical evidence between the two groups with regard to postpartum hemorrhage and placental abruption, in contrast to Chen 2012 [9], who showed that postpartum hemorrhage increased with early calcification. He also showed that placental calcification is associated with placental abruption, as some unknown pathways in the placenta involved mediate this process.

5. Conclusion

Although the occurrence of placental calcification after 36 weeks of gestation is a placental aging process, preterm calcification can be a landmark for the probability of a high-risk pregnancy and an alarm sign for placental dysfunction. We have observed that smoking and taking rich calcium dosage were predictors of early placental calcification. We observed increased UA RI and AEDV/REDV more often in these pregnancies. Close antepartum follow-up should be advised for these mothers. Regular, frequent foetal well-being tests should be performed to prevent foetal and maternal complications. Larger, more extensive studies could provide more valid results.

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