Journal of Biology and Today's World
ISSN 2322-3308
http://www.journalbio.com

Received: 05 October 2014 • Accepted: 12 November 2014

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doi:10.15412/J.JBTW.01031102

Correlation Between Pathology of Placenta and Preterm Labor: A Case-Control Study

Maryam Azizi[1], Minoo Rejaei[1], Zohreh Pezeshkpour[2*], Mohammad Reza Alipour[3], Elham Kazemi[1], Shahram Zare[4], Seyedhossein Hekmatimoghaddam[5], Mohammadtaghi Sarebanhassanabadi[3]

[1] Obstetrics and Gynecology Department, Hormozgan Fertility and Infertility Research Center, Hormozgan University of medical sciences, Bandar Abbas, Iran

[2] Gynecology Assistance student, Student Research Committee, University of Medical sciences, Bandar Abbas, Iran

[3] Yazd Cardiovascular Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[4] Department of Social Medicine, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

[5] Department of Laboratory Sciences, School of Paramedicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

*correspondence should be addressed to Zohreh Pezeshkpour, Gynecology Assistance student, Student Research Committee, University of Medical sciences, Bandar Abbas, Iran; Tell: +987613337104; Fax: +987613330612; Email: Z.Pezeshkpour@yahoo.com.

ABSTRACT

Preterm labor is caused by several factors including placental infection and thrombosis. To define the changes in placenta of women with preterm labor, pathological examination of placenta is needed. This case control study aims to find correlation between pathological findings of preterm placentas and chance of preterm labor.Placentas of 100 preterm (either early or late) labors and 100 term deliveries were examined both macroscopically and microscopically. Any evidence of inflammatory lesion, calcification, hematoma and neoplastic mass was evaluated and compared. Early preterm deliveries frequently showed placental calcification, significantly more than in term deliveries (p=0.0001). Inflammatory lesions were present in 20% of placentas of full term newborns, in 60% of early preterm labors, and in 46% of late preterm newborns. Placental calcification and placental inflammatory lesions both may be considered as having a positive correlation with preterm labor (p=0.000).several changes are seen in placentas of women with preterm labor, reflecting potential etiologic roles. Each placenta in preterm labor should be pathologically examined for the presence of inflammatory lesions, abnormality of vessels, calcifications, hematomas, tumoral masses, etc. Ultrasound examination of placenta during pregnancy may reveal some of these lesions.

Key words: Preterm labor, Placenta, Pathology, Calcifications, Inflammation

1. INTRODUCTION

Pathologists try to find the causes of preterm birth by evaluation of preterm placentas in many cases (1). The incidence of preterm labor is 12% of all labors in the United States and 5-9% in European countries, while in Iran it is estimated to be 8-10%.(2, 3) Studies show that the incidence of preterm labor is increasing in developing countries. In 1981 the incidence of preterm labor was 9.5% which has increased to 12.7% in 2005 (4). Our knowledge about mechanisms of delivery, preterm labor, and risk factors of preterm labor has improved, but unfortunately preterm labor has also increased, and efforts toward decreasing preterm labor are not effective enough (5). Very few countries gave a reliable number of preterm labors. The overall incidence of preterm labor in African countries was approximately 18%, of which about 85% occurred between 32 to 34 weeks of gestational age, 10% in 28-32 weeks, and 5% before 24 weeks. In contrast, its incidence was 11.99% in the US during 2011, of which 8.49% were at 34-36 weeks, 1.53% happens between 32-33 weeks, and 1.97% was seen before 32 weeks of gestational age (6). Many risk factors have been described for preterm labor including absence of spouse, low socioeconomic status, anxiety, depression, divorce, death of close family members, abdominal surgery during pregnancy, high parity, polyhydramnios, uterine abnormalities, uterine leiomyoma, diethylstilbestrol usage, history of second trimester miscarriage, history of cervical surgery, cervical shortening, sexually transmitted diseases, pyelonephritis, appendicitis, pneumonia, systemic infection, bacteriuria, placenta previa, abrasion, vaginal bleeding for longer than one trimester, history of preterm labor, substance abuse,

smoking, maternal age under 18 years or over 40 years, African race, low weight, anemia (Hb<10 mg/dL), uterine contractions, low educational level, fetal anomalies, intrauterine growth retardation, and environmental factors such as heat or air pollution (7). It is quite difficult to prove correlation between preterm labor and its risk factors, because many preterm labors were seen in persons with no known risk factors. On the other hand, most of the mothers suffering from the risk factors do not face with preterm labor. However, we need more researches to be conducted on this topic on humans and animals (8). In the United States, most preterm labors were seen in young (aged less than 18 years) or old (over 35 years), black- or red-skin races, Hispanics, non-Hispanic minorities, and Asians' mothers (6).

Placental calcification is a factor for inducing preterm labor. Calcium may deposit on all over the placenta, but usually this phenomenon is more frequent on the maternal surface of basal plate. Calcification is correlated with nulliparity, high socioeconomic status, and higher serum calcium levels (9). Most of the specialists believe that routine placenta examination by a pathologist is not necessary; it is controversial which placentas should be evaluated. The college of American pathologists has recommended histopathological evaluation of placenta in a long list of indications. Inflammatory lesions, thrombosis and other risk factors are among them (10). This study aims to compare and find a correlation between pathological findings of preterm and term placentas.

2. MATERIALS AND METHODS

This case control study was conducted in Shariati Women's Hospital in Bandar Abbas, Iran. The control group consisted of 100 women aged 18-45 years with gestational age of 37-40 weeks and 6 days who had full term delivery. The cases included 100 patients of the same age with preterm labor, who were divided into two subgroups, 50 women with gestational age of 20-33 weeks and 6 days as early preterm labor, and another 50 patients with gestational age of 34-36 weeks and 6 days as late preterm labor. Inclusion criteria for all patients were the number of deliveries less than 3, blood pressure (BP) <140/90 mmHg, and hemoglobin ≥10 mg/dL(11). Exclusion criteria for these subjects were preeclampsia, chorioamnionitis, twin or multiple pregnancies, fetal anomalies, intrauterine fetal death (IUFD), and positive history of maternal hypertension or diabetes, chronic or systemic disease. All of the placentas were measured and weighed after delivery, and evaluated macroscopically for possible gross pathologic changes including calcification, vascular thrombus and other abnormalities such as vascular disorders and tumoral masses. In case of any observed abnormality, a biopsy was taken and examined microscopically after fixation in 10% neutral buffered formalin and staining with the hematoxylin and eosin stain, the routine procedure in histopathology. In all cases and controls, even in those without any visible lesion, a full thickness sample was taken from the disc portion of placenta, and sent to the hospital pathology laboratory to be fixed, stained and examined by an experienced pathologist for microscopical investigations (calcification, infarcts, thrombosis, other vascular diseases, possible tumor, and inflammatory lesions). Data from the standard reports were gathered in a table along with data from the labor. For analyzing of the variables the SPSS software (version 15) was used. For quantitative parameters, Chi-square test and Fischer's exact test were used. To find a statistically significant differences between variables, $p<0.05$ was considered as the level of significance.

3. RESULTS AND DISCUSSION

In this study 100 preterm placentas (group A) and 100 full term placentas (group B) were studied. Group A were divided into two subgroups of early (gestational age of more than 20 weeks and less than 34 weeks) and late (gestational age between complete 34 weeks till 36 weeks and 6 days) preterm placentas, each containing 50 placentas. Full term infants were defined as those with gestational age between 37 weeks and 40 weeks & 6 days. Data analysis showed placental calcification in 15% of full term placentas, 90% of early preterm and 14% of late preterm placentas, indicating significant difference between early preterm and term placentas (p=0.000), but there was no significant correlation between late preterm labors and term labors (p=0.54). There was significantly difference (p=0.000) between preterm labors (early & late) and full term placenta in calcification. Therefore, placental calcification can be considered as a risk factor for preterm labor. Inflammatory lesions were present in 20% of placentas of full term newborns, in 60% of early preterm newborns and 46% of late preterm newborns. Statistical analysis revealed that inflammatory lesions of placenta in pre-term labors, either in early preterm labor (p=0.000) or in late preterm labor (p=0.01) were significantly higher than that in term placentas, showed a positive correlation. So, we concluded that, inflammatory lesions of placenta may also be considered as a risk factor for preterm labor. Placental thrombosis was seen in 14% of full term placentas, in 88% of early preterm and in 66% of late preterm placentas, which showed significant difference between term labors and any of the preterm labors (P=0.000), and on the whole increased the likelihood of preterm labor (p=0.000). Chorangiosis (an increase in villous vascular channels) was found in 11% of full term newborns, in 66% of early preterm newborns and 62% of late preterm newborns, which was correlated with preterm labor in early preterm newborns (p=0.000) and also late preterm newborns (p=0.000), and can be a risk factor for preterm labor (p=0.000). None of the placenta had tumoral masses except one placenta (2%) of an early preterm newborn, which showed no significant correlation between placental tumoral masses and preterm labor (p=0.33). The weight of placenta was directly proportional to gestational age. The smallest placenta had a weight of 21 g, and

belonged to a 22 week newborn. The largest placenta weighing 1100 g was found in one full term labor at 40 week gestational age; The results are shown in Table 1.

Table 1. Pathological abnormalities of placenta in preterm labors compared to full term labors

Placental pathology	Preterm labor				Term labor		P value
	Early Preterm		Late Preterm		Positive	Negative	
	Positive	Negative	Positive	Negative			
Calcification	45(90%) (P=0.000)	5(10%) (P=0.000)	7(14%) (P=0.054)	43(86%) (P=0.054)	15(15%)	85(85%)	0.000
Inflammatory lesions	30(60%) (P=0.000)	20(40%) (P=0.000)			20(20%)	80(80%)	0.000
Inflammatory lesions			23(46%)	27(54%)	20(20%)	80(80%)	0.01
Thrombosis	44(88%) (P=0.000)	6(12%) (P=0.000)			14(14%)	86(86%)	0.000
Thrombosis			33(66%)	17(34%)	14(14%)	86(86%)	0.000

In this study, 200 placentas (100 from full term and 100 from preterm deliveries) were studied pathologically. The occurrences of calcification in placentas of early and late preterm deliveries were 90% and 14%, respectively, but 15% in full term labors. A study published in 1983 reported grade 3 calcification in 25% of placentas in full term infant (11). Lee and Chen reported in 2010 that calcification was seen in 9% of preterm placentas (gestational age before 28 weeks), while it was 15% in placentas of fetuses with gestational ages 34-36 weeks, and in full term deliveries it was 23.7% (12). According to our study, placental calcification was correlated with early preterm labor, but in late preterm newborns no association was found between placental calcification and preterm labor. A study in June 2012 found out that grade 3 calcification in placentas of 28-36 weeks was accompanied by every adverse fetal outcomes such as preterm labor, low birth weight, low Apgar score, and fetal death (13). In this study inflammatory lesions were seen more in placentas of early and late preterm infants than placentas of full term infants (60%, 40% and 20%, respectively). In Altunca's study in 2007 the frequency of inflammatory lesions in placentas of preterm infants was 20%, but 23% of preterm placentas had unknown pathology (14). It is already known that inflammatory lesions of the placenta are a risk factor for preterm labor. In a similar study, the frequency of inflammatory lesions in placentas of preterm born babies was 37.3%, and inflammatory lesions of the placenta had a significant correlation with recurrent preterm labor (15). Another study by Ghidini et al. showed a positive history of one or more preterm labors before 32 weeks, since they had findings in favor of acute or chronic inflammation (16). In a study was done by Goldenberg et al., it was shown that recurrence of preterm labor is closely correlated with acute inflammatory placental lesions (17). In this study, placental thrombosis in early preterm and late preterm fetuses was found in 88% and 66% of cases, respectively, but only 14% in placenta of full term babies, which denoted a statistically significant correlation. Kraus and Acheen showed that placentas of 19% of stillborn babies had thrombotic vasculopathies (18). Germain found that placentas of 28.3% of preterm babies had ischemic lesions, reflecting a significant correlation with preterm labor (19). Kelly et al. considered vascular lesions of placenta as a risk factor for preterm labor(20). Overall, this study showed that presence of pathology in placenta could increase the probability of preterm labor which was associated with maternal and infantile complications, and highlighted the importance of pathological examination of placenta in preterm labors.

4. CONCLUSION

According the results of this attempt, this can be stated that, there is a significant correlation between placental pathology and preterm labor. Placental abnormalities including placental calcification, inflammatory lesions, thrombosis and chorangiosis should be evaluated prenatally by imaging studies or laboratory modalities, because they may lead to many instances of maternal and neonatal complications. It was suggested that pregnant mothers should be screened for uterine and thrombotic disorders, and in case of any of these disorders appropriate treatment should be initiated to reduce placental pathology for the final goal of preventing preterm or recurrent preterm labor.

ACKNOWLEDGMENT

No mentioned any acknowledgment by authors.

AUTHORS CONTRIBUTION

This work was carried out in collaboration between all authors.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

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