

Histologic Evidence of Placental Inflammation and Risk of Placental Abruption in Term and Preterm Gestations

By

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Abstract:

Objective: To determine whether placental abruption is associated with an increased incidence of histologic chorioamnionitis among singleton gestations in both term and preterm births and whether this association is dependent on the severity of histologic chorioamnionitis. **Pateints and patients :** A prospective case- control study was conducted at Al-Yarmouk Teaching Hospital, Department of Obstetrics and Gynecology from 2018 to 2020. this Study included 72 singleton pregnant women with clinical and / or sonographic diagnosis of placental abruption, 44 cases were preterm gestations and 28 were term gestations and their matched controls, who all attended the labor ward in Al-Yarmouk Teaching Hospital, Department of Obstetrics and Gynecology during the study period. After delivery, all study population were submitted for histologic examination of their placentae. Each placenta was reviewed for gross findings and histologic evidence of chorioamnionitis. The degree of chorioamnionitis is then sub classified into mild, moderate or severe. The association between histologic chorioamnionitis and placental abruption were analyzed in all groups. **Results:** Histological chorioamnionitis were more common in abruption cases than controls in both preterm and term groups, among preterm abruption cases chorioamnionitis was present in 70.4% versus 25% of controls. At term gestations the corresponding rates were 64.3% and 35.7% respectively. Severe histological chorioamnionitis was 7.62 times more common in preterm abruption cases than controls but it did not reach statistical significance, while mild, and moderate chorioamnionitis were statistically significant, OR 6.35, 95% CI (1.79-23.95), OR 8.25, 95% CI (1.99-39.81) respectively. **Conclusion:** Histologic chorioamnionitis is associated with placental abruption. The association is strongest in the presence of severe chorioamnionitis at preterm and, to a lesser extent, at term gestations.

Keywords: Histologic chorioamnionitis; Placental Inflammation; Risk of Placental Abruption and Preterm Gestations

Introduction

Placental separation from its implantation site before delivery has been variously called (placental abruption, abruptio-placentae, or accidental haemorrhage). The Latin term abruptio-placentae means (rending asunder of the placenta) and denotes a sudden accident, which is a clinical characteristic of most cases⁽¹⁾. Placental abruption is defined as premature separation of the normally implanted placenta, it is the most descriptive. The condition is associated with a high perinatal mortality and severe maternal morbidity⁽¹⁾.

The bleeding of placental abruption typically insinuates itself between the membranes and the uterus, ultimately escaping through the cervix (external or revealed haemorrhage), less often the blood does not escape externally but retained between the detached placenta and the uterus, leading to (concealed haemorrhage)⁽²⁾ which carries much greater maternal and fetal hazards. It can also be total or partial⁽¹⁾

The reported incidence varies from 0.49%-1.8%⁽²⁾, its occurrence is significantly higher in preterm pregnancies complicating as much as 5.1% of preterm deliveries⁽³⁾. The incidence varies depending on criteria used for diagnosis. When the diagnosis is based on histologic examination of the placenta it is reported as high as 4%. This suggests that small episodes of placental abruption are more common than those diagnosed clinically⁽⁴⁾ The haemorrhage of placental abruption is concealed in 20%-35% of cases which is less often than the revealed haemorrhage which occurs in 65%-80% of cases⁽²⁾. Approximately 30% of cases of third trimester bleeding are due to placental separation with the initial haemorrhage usually encountered after 26th weeks gestation⁽⁵⁾. It is the leading cause of perinatal mortality accounting for 10%-15% of perinatal deaths⁽⁶⁾.

Aim of the study: The aim of the study was to determine whether placental abruption is associated with an increased incidence of histologic chorioamnionitis among

singleton pregnancies in both preterm and term gestations and whether this association is dependent on its severity.

Patients and Methods

This study was a prospective case-control study which was conducted at Al-Yarmouk Teaching Hospital, Department of Obstetrics and Gynecology from 2018 to 2020.

The study population consisted of a total of 72 women with placental abruption diagnosed clinically and / or sonographically, 28 cases term gestations (completed 37 weeks and longer), 44 cases preterm gestations (completed 20-36 weeks), all attending the labour ward and their matched controls. Exclusion criteria include, placenta previa in present pregnancy and previous history of abruption, multiple pregnancy. After an informed consent was obtained from each patients involved in this study, a full history was taken from each woman including age, parity, education status, smoking, history of watery vaginal discharge, and gestational age.

Examination was done including general examination including height , weight, and body mass index (BMI) was calculated and obstetrical examination. Placental abruption cases were identified by clinical and /or sonographic criteria. The clinical criteria for diagnosis of abruption include, the classical signs and symptoms of painful vaginal bleeding which was either revealed or concealed, uterine pain or tenderness, and uterine hypertonicity, non reassuring fetal status, some patients presented with a shock state. The sonographic criteria include retroplacental clot or hematoma on the placental surface diagnosed sonographically. The ultrasonic device named SIMENS-SONOLINE (SL1)-Elegra. Control patients were a healthy pregnant women that delivered at gestation of 20 weeks or longer and had no evidence of abruption . After delivery the placetae from each group were taken and sent for histological examination.

Histological examination

Placenta from each included patient were examined fresh. At least two section of the placental disks were taken by a non toothed forceps and scalpel for microscopic examination, each of which measuring 1.5 cm in length, 0.5 cm in depth and 1 cm in breadth including the centre of a placental lobule, chorionic plate, and decidual floor. One of the disc sections was taken close to the site of umbilical cord insertion. The other was taken midway between cord insertion and placental margin. At least one section of the umbilical cord 2 cm from the disc insertion site and rolled strip of extraplacental membranes were also examined histologically.

Once it was taken, each histological specimen was immediately placed on a piece of filter paper and was allowed to adhere for few seconds. The excess filter paper was then cut away and the portion carrying the biopsy was inverted and placed in 4% buffered neutral formaldehyde-saline solution. After 24 hours of primary fixation, the biopsy specimen is cut into strips of about 3mm breadth, each strip being properly oriented in the ultimate wax block to yield perpendicular sections of the placental layers. The sections were first assessed by hematoxylin and eosin stain. Slides of the placentas were then reviewed for the presence or absence of histologic chorioamnionitis and its degree.

A pathologist, who was blinded to abruption status, performed the histologic evaluation of the placentas, and each placenta was reviewed for gross findings and histologic lesions.

Histologic chorioamnionitis was defined by the presence of inflammatory infiltrate of neutrophils at two or more sites on the chorionic plate and extraplacental membranes. The degree of chorioamnionitis was then subclassified into the following categories:

1-*None*; There is no neutrophils per high power field.

2-*Mild chorioamnionitis*; It was defined by the presence of a few scattered (5-10 per HPF) neutrophils in the subchorionic space and adjacent chorion.

3-*Moderate chorioamnionitis*; Defined by the presence of many (11-30 per HPF) neutrophils in the lower half of the chorionic plate.

4-*Severe chorioamnionitis*; Defined by the presence of a dense infiltrate of neutrophils (more than 30 per HPF) throughout the chorionic plate into the amnion.

Statistical analysis: Analysis of data was carried out using the available statistical package of SPSS-18 (Statistical Packages for Social Sciences- version 18 "PASW" Statistics). Data were expressed in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). Odd ratio (OR) and its 95% confidence interval (95% C.I.) was also calculated. The significance of difference of different percentages (qualitative data from patients group and control group) were tested using Pearson Chi-square test (χ^2 -test) for proportions, students-t-test for difference between two independent means, ANOVA test for more than two independent means. Statistical significance was considered whenever the P value was less than 0.05, P value less than 0.01 was considered to be highly significant.

Results:

Sociodemographic characteristic of placental abruption cases and controls delivered at preterm and term gestations (see table -1)

Maternal characteristics	Preterm births (20-36 weeks)				Term births (37 weeks or longer)			
	Cases (n=44)		Controls (n=44)		Cases (n=28)		Controls (n=28)	
	No	%	No	%	No	%	No	%
Age (years) <20	6	13.6	6	13.6	6	21.4	7	25.0
20—24	7	15.9	9	20.5	9	32.1	9	32.1
25—29	25	56.8	24	54.5	9	32.1	9	32.1
=>30 years	6	13.6	5	11.4	4	14.3	3	10.7
P value	0.948				0.974			
Parity Para 0	7	15.9	10	22.7	12	42.9	10	35.7
Para 1	11	25.0	12	27.3	7	25.0	7	25.0
Para2& greater	26	59.1	22	50.0	9	32.1	11	39.3
P value	0.636				0.826			
Education below high school	34	77.3	33	75.0	22	78.6	21	75.0
High school	10	22.7	11	25.0	6	21.4	7	25.0
P value	0.803				0.752			
First trimester BMI (Mean±SD)	26.9±4.5		24.2±4.2		30.9±5.9		24.3±5.7	
P value	0.005*				0.0001*			
PROM Yes	11	25.0	4	9.1	1	3.6	2	7.1
No	33	75.0	40	90.9	27	96.4	26	92.9
#OR(95%CI); P value	3.33 (0.78-15.5); 0.047*				0.48 (0.01-9.90); 0.553			
Gestational age (weeks) (Mean±SD)	29.5±5.2		29.8±4.1		38.6±1.4		38.4±1.3	
P value	0.764				0.582			

Table 1: Sociodemographic characteristic of placental abruption cases and controls delivered at preterm and term gestations

*Significant difference using Pearson Chi-square test for difference between proportions or student-t-test for difference between two independent means at 0.05 level of significance. OR(95%CI); Odds ratio and its 95% confidence interval.

Regarding first trimester body mass index (BMI), there was a statistical difference in both preterm and term groups with P value of 0.005, and a mean \pm SD of 26.9 ± 4.5 , 24.2 ± 4.2 for preterm cases and controls respectively and a P value of 0.0001 with a mean \pm SD of 30.97 ± 5.9 , 24.3 ± 5.7 for term cases and controls respectively, as shown in figure 1.

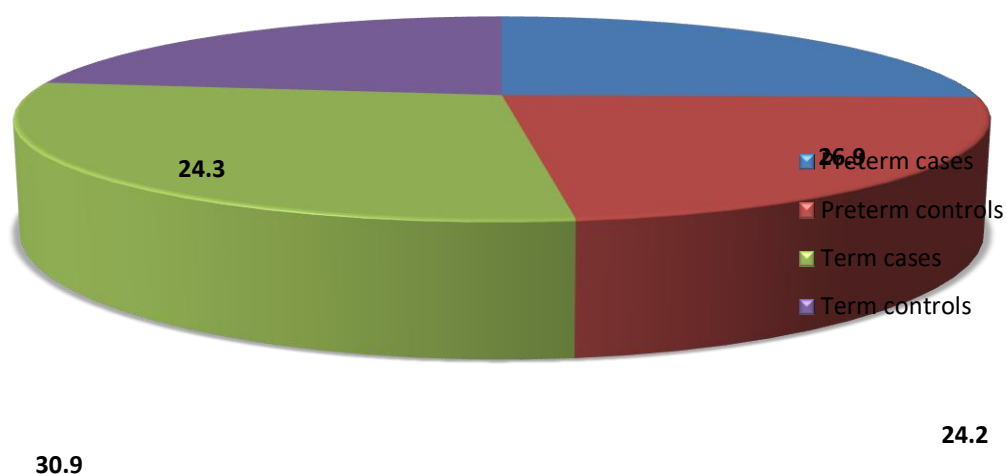


Figure (1): The mean of first trimester BMI in preterm and term placental abruption cases and controls.

The frequency of histological chorioamnionitis was greater in abruption cases group in comparison with control group in both preterm and term gestations and it was more significant in preterm group as shown in figure 2.

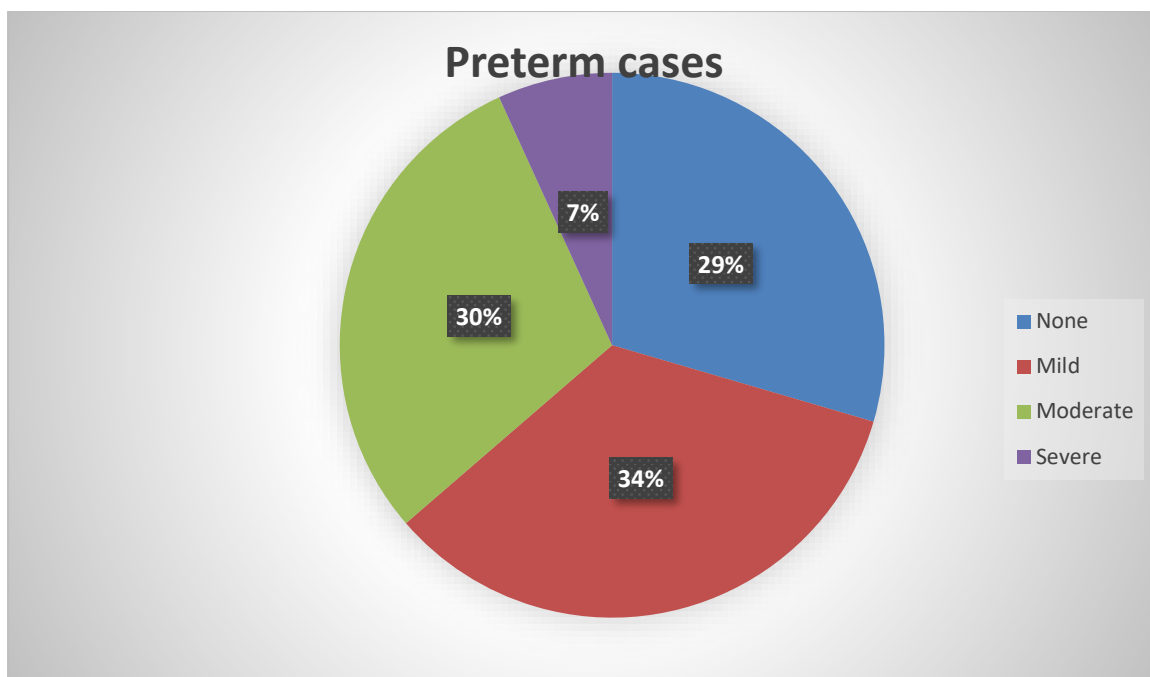


Figure (2): The severity of histologic chorioamnionitis among placental abruption cases and controls in preterm births

Histological chorioamnionitis also more common in term placental abruption cases than term controls OR 3.24, 95% CI (0.96-11.17) as shown in figure 3. In term births we had four cases with severe histological chorioamnionitis all of them with abruption and we had no case in control group. but it did not reach statistical significance also because of small sample size.

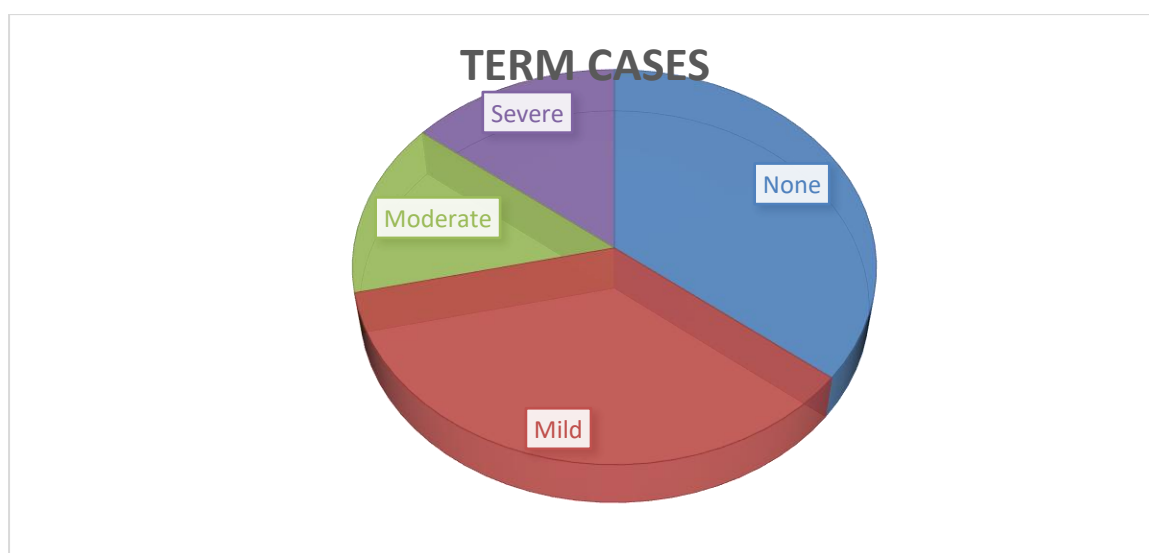


Figure (3) : The severity of histologic chorioamnionitis among placental abruption cases and controls in term birth

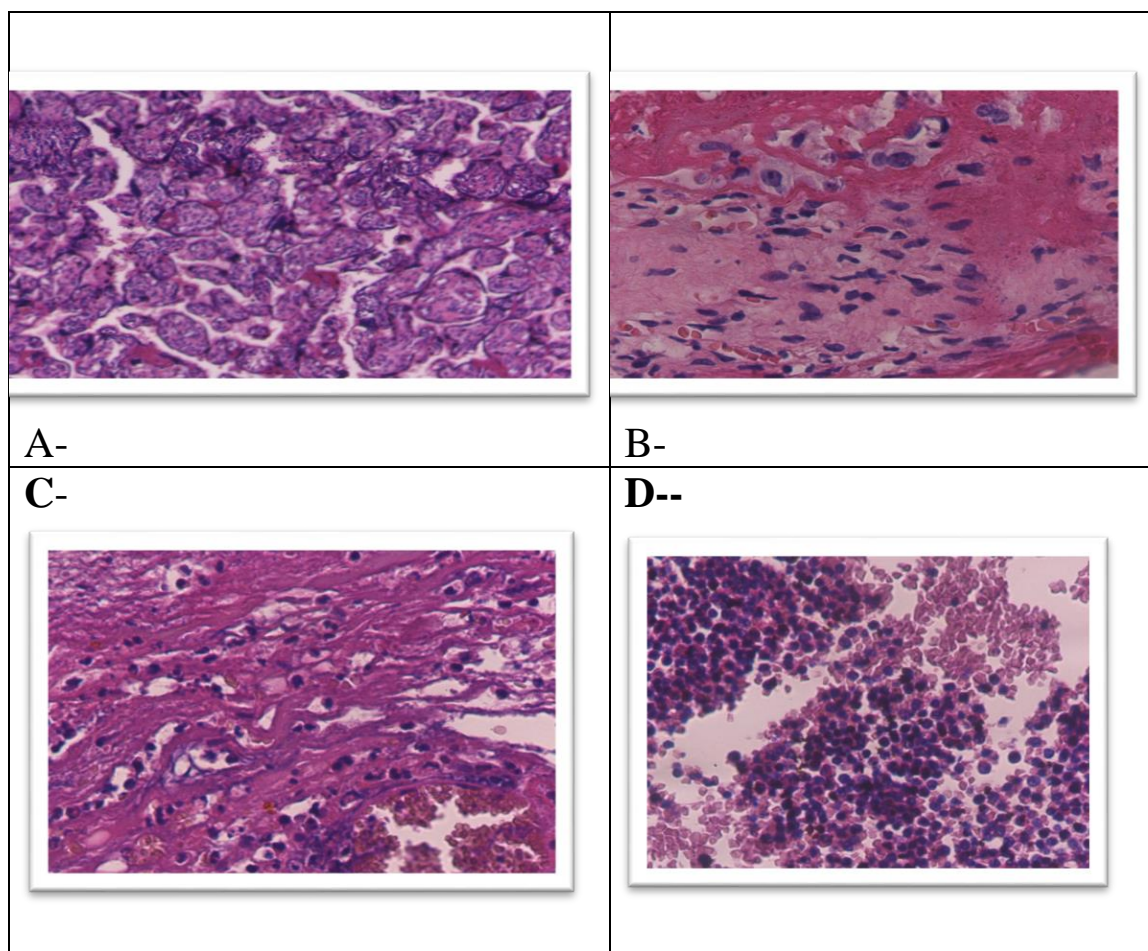


Figure (4): A-Normal placental histology. B- Mild placental histologic chorioamnionitis. C- Moderate placental histologic chorioamnionitis. D- Severe placental histologic chorioamnionitis

Discussion:

Placental abruption is potentially devastating for both mother and fetus and has been associated with stillbirth, preterm delivery, and fetal growth restriction⁽⁷⁾. So identification of its risk factors might improve maternal and fetal conditions. Although many risk factors have been identified, causal pathway remains largely speculative⁽⁸⁾.

This study is a prospective case control study in which a complete histological evaluation of the placentae of both placental abruption cases and their matched controls were done, using standardized methodology with well-defined pathologic criteria for inflammatory lesions.

Maternal age, parity and gestational age were matched between cases and controls for both term and preterm gestations. Regarding maternal education status there is no significant statistical difference between abruption cases and controls.

Regarding first trimester BMI there are statistically significant difference between abruption cases in both term and preterm gestations and control group, at preterm group (P value = 0.005), at term (P value = 0.0001) . This demonstrate that women with abruption had a higher first trimester BMI in both term and preterm births this may suggest that higher maternal weight in early pregnancy is associated with a higher risk of placental abruption .

Our results agree with that of Ray *et al*⁽⁹⁾ who stated that placental dysfunction which may manifest partly as the hypertensive disorders of pregnancy and abruption or infarction of the placenta, occurs more commonly in women with obesity, chronic hypertension, diabetes mellitus, and dyslipidemia , and so women who exhibit features of the metabolic syndrome before pregnancy have a higher graded risk of placental dysfunction including placental abruption and fetal demise .

This study disagree with Becker *et al*⁽¹⁰⁾ who reported that high maternal weight in early pregnancy is associated with a lower risk of placental abruption . We speculate that the placental lesions that manifest as severe chorioamnionitis are indicative of an intense inflammatory process at the interface of the decidua and chorion, which stimulate inflammatory cytokines and chemokines. The result of this cascade of events is destabilization of the uteroplacental interface, culminating in placental abruption, premature rupture of membranes, and preterm labor. Because the development of severe histologic chorioamnionitis takes time, this further provides evidence for abruption as a more chronic process, One potential explanation for our findings is that abruptions elicit an intense production of thrombin from the decidua that in turn leads to a massive recruitment of neutrophils^(11&12) . Therefore, the presence of neutrophils in the chorion may be a manifestation of a pathway that begins with abruption-related hemorrhage,

leading to decidual cell production of tissue factor and eventually conversion of prothrombin to thrombin.

Current study show that the frequency of histologic chorioamnionitis were greater in abruption cases than controls in both term (64.3%) and preterm (70.4 %) births, our findings suggest that more severe inflammatory lesions of the placenta, characterized by neutrophils infiltration of the chorion and amnion, are associated with placental abruption in both preterm and term gestations, with a statistically significant results in preterm births and to lesser extent in term births, we did not reach a statistically significant results in term group probably because of small sample size, and these findings agreed with that of Nath *et al* ⁽⁸⁾ who demonstrated that severe acute inflammatory process are important in term and preterm abruption and concluded that histologic chorioamnionitis is associated with placental abruption, but disagree with this study that the association was strongest in the presence of severe chorioamnionitis at term and, to a lesser extent, at preterm gestations. These observations suggest that the histologic findings in abruption are accompanied by severe inflammation, in both preterm and term gestations.

Ananth *et al*⁽¹³⁾ stated that histologic lesions of the placenta, umbilical cord, and membranes are associated with increased risk of placental abruption in later pregnancy. However, the increased risk associated with placental lesions suggests that prolonged inflammation may be implicated in placental abruption. Also Darby *et al* ⁽¹⁴⁾ concluded that histologic chorioamnionitis and funisitis were present significantly more often in patients with abruption than in control patients (41 versus 4%; P less than .0001), so a significant association exists between preterm placental abruption and histologic chorioamnionitis.

Rana *et a.*,⁽¹⁵⁾ stated that evidence of histologic chorioamnionitis was higher in the abruption group 12/40 (30%), than in the control group 8/35 (22.85%), but the difference was not statistically significant. Suzuki *et al.*, ⁽¹⁶⁾ concluded that the incidence

of preterm labour and prematurity was higher in abruption cases with histological chorioamnionitis than those without chorioamnionitis.

Conclusions: Histologic chorioamnionitis is associated with placental abruption. The association is increased with increasing the severity of chorioamnionitis in preterm, and to lesser extent, in term gestations. These observations suggest that placental abruption are accompanied by placental inflammation, in both preterm and term gestations.

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