Incidence of PROM and the mean gestational age at delivery by severity of histologic chorioamnionitis among placental abruption cases

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Abstract:

Background: When the placenta detaches from the uterine wall prior to delivery, this condition is known as placental abruption. A placental abruption may cause the mother to bleed profusely and deprive the unborn child of oxygen and nourishment. **Patients and methods:** 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 chorioamniontis is then sub- classified into mild, moderate or severe. The association between histologic chorioamnionitis and placental abruption were analyzed in all groups. **Results :**first trimester body mass index (BMI), there was a statistical difference in both preterm and term groups, and a mean ± SD of 26.9 ± 4.5, 24.2 ± 4.2 for preterm cases, Premature rupture of membrane approached statistical significance for preterm gestation with a higher incidence in cases (25%) than controls , the association between histological chorioamnionitis and

placental abruption at preterm gestations OR 7.15, 95% CI (2.55-20.49) was significant. , PROM was more frequent in abruption cases as the severity of chorioamnionitis increased, with PROM presented in 71.4% of abruption cases with severe chorioamnionitis. Among abruption cases there was an apparent trend for earlier delivery in PROM group in comparison with non PROM cases, which was more striking with severe chorioamnionitis. **Conclusion**: Premature rupture of membrane approached statistical significance for preterm gestation with a higher incidence in cases than control, PROM was more frequent in abruption cases as the severity of chorioamnionitis increased, with PROM presented in abruption cases with severe chorioamnionitis.

Keywords: PROM; gestational age; delivery; chorioamnionitis; placental abruption

Introduction

Abruption may occur by haemorrhage into the decidua basalis, which splits, leaving a thin layer adjacent to the myometrium. This dicedual haemorrhage leads to separation, compression, and further bleeding. Alternatively, a spiral artery may rupture, creating a retroplacental haematoma. the diagnosis of placental abruption primarily is a clinical one, ultrasonography may detect only 2% of placental abruption [(1)], Although the signs and symptoms vary considerably[(2)], they are diagnostic in moderate to severe cases, where the clinical picture is usually clear and the management will be dictated by the fetal and maternal conditions,Early grades may be much more difficult to diagnose [(3)].

The Fetal complications as the : The perinatal mortality rate varies from 4.4%-67.3%, depending on neonatal facilities. More than 50% of deaths are stillbirth[(3)],the neonate is frequently premature because it must be delivered prematurely because of fetal distress or severe maternal morbidity. ; Fetal

growth restriction: Is reported in up to 80% infants born before 36 weeks gestation[3]; Congenital malformation: The rate of congenital malformation may be as high as 4.4% (twice that of general population). The rate of major malformation is increased three folds, most involve the CNS[3]. and Neonatal hematologic findings: Fetal anemia result from significant fetal bleeding[3].

Aim of the study: The aim of the study was to Incidence of PROM and the mean gestational age at delivery by severity of histologic chorioamnionitis among placental abruption cases.

Patients and Methods

The Department of Obstetrics and Gynecology at Al-Yarmouk Teaching Hospital conducted the study. Eighty-two cases of term gestations (completed 37 weeks and longer), forty-four cases of preterm gestations (completed 20–36 weeks), and 72 cases of placental abruption diagnosed clinically and/or sonographically were present in the labor ward along with their matched controls (exclusion criteria include placenta previa in present pregnancy and previous history of abruption, multiple pregnancy).

The Al-Yarmouk Teaching Hospital's Department of Obstetrics and Gynecology carried out this prospective case-control study from May 2018 to October 2020, A thorough medical history, including age, parity, education level, smoking history, history of watery vaginal discharge, and gestational age, was gathered from each patient after they gave their informed consent for the study, An obstetrical checkup as well as a general examination that measured height, weight, and determined body mass index (BMI) were performed.

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.

Following collection, every histology specimen was promptly put on a sheet of filter paper and given a brief period of time to stick to it. After trimming off the extra filter paper, the biopsy-containing section was inverted and put in a 4% buffered neutral formaldehyde-saline solution. Following a 24-hour primary fixation period, the biopsy specimen is sliced into about 3-mm-wide strips, with each strip being appropriately positioned within the final wax block to produce perpendicular sections of the placental layers. Hematoxylin and eosin stain was used to evaluate the sections first. Next, the presence and severity of histologic chorioamnionitis were examined on placenta slides.

The placentas underwent a histologic evaluation by a pathologist who was blinded to the abruption status. The pathologist examined each placenta for gross abnormalities and histologic lesions.

The presence of an inflammatory neutrophil infiltration at two or more locations on the chorionic plate and extraplacental membranes was the defining characteristic of histologic chorioamnionitis ,the degree of chorioamnionitis was then sub-classified 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 sub-chorionic 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 : data analysis was done with the SPSS-18 statistical tool (Statistical Packages for Social Sciences, version 18; "PASW" Statistics).

The frequency, percentage, mean, standard deviation, and range (minimum-maximum values) of the data were expressed simply. The calculation of the odds ratio (OR) and its 95% confidence interval (C.I.) was also performed.

The significance of variances in percentages (qualitative data from the patient group and control group) was assessed using the ANOVA test for more than two independent means, the students-t test for differences between two independent means, and the Pearson Chi-square test for proportions. Any P value less than 0.05 was deemed to be statistically significant, and any P value less than 0.01 was deemed to be extremely significant.

Results:

There were 72 placental abruption cases during the study period, of which 44 cases were preterm (61.1%), and 28 cases were term (38.88%).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 ± 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 ± SD of 30.97 ± 5.9, 24.3 ± 5.7 for term cases and controls respectively, as shown in figure 1.

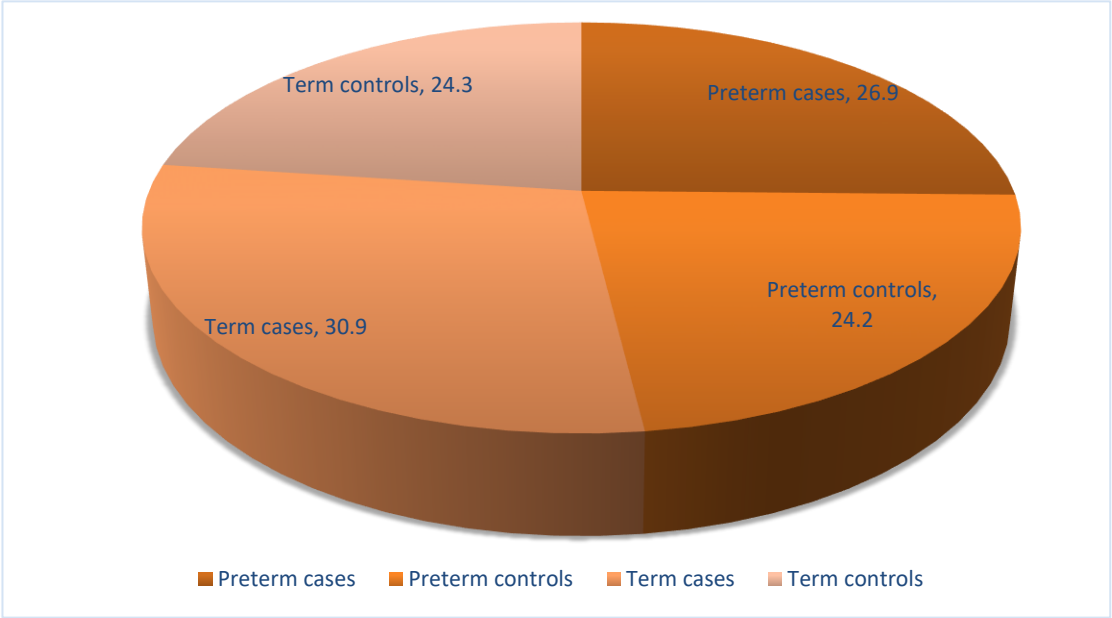

Figure (1): The mean of first trimester BMI in preterm and term placental abruption cases and controls.

Premature rupture of membrane approached statistical significance for preterm gestation with a higher incidence in cases (25%) than controls (9.1%), and a P value 0.047, as shown in figure 2.

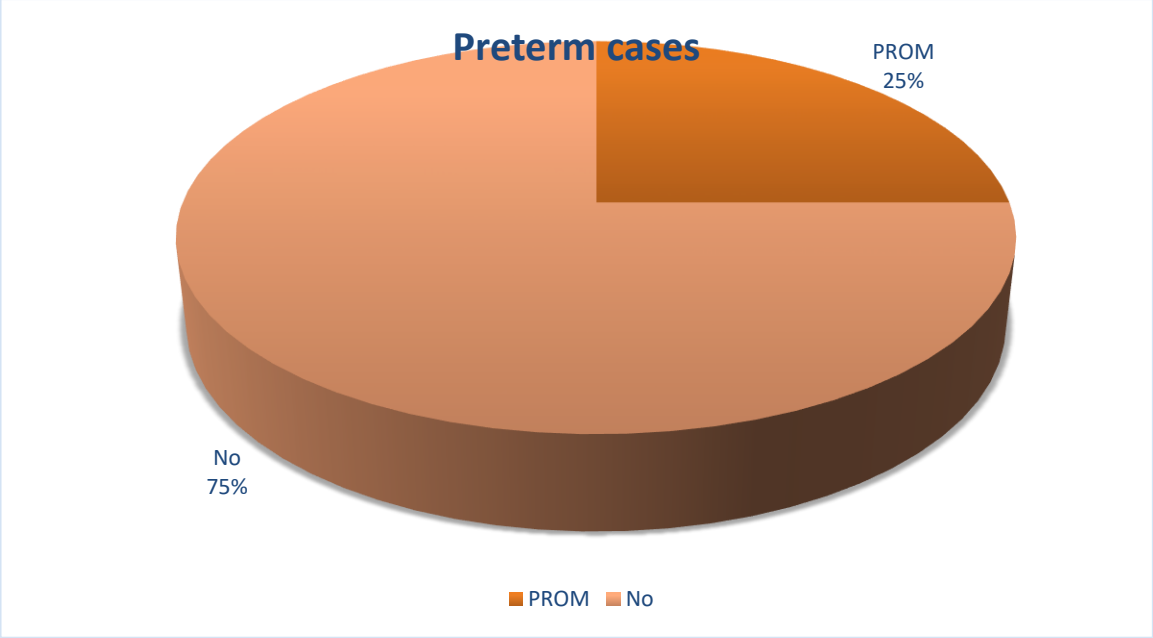

Figure (2): The frequency of PROM in placental abruption cases and controls in preterm and term births

The association between histological chorioamnionitis and placental abruption at preterm gestations OR 7.15, 95% CI (2.55-20.49) was significant. Moderate histological chorioamnionitis was more significant in preterm group, OR 8.25, 95% CI (1.99-39.81), mild chorioamnionitis was also statistically significant OR 6.35, 95% CI (1.79-23.95), regarding severe histological chorioamnionitis in preterm cases with abruption, we had 3 of 4 cases of abruption had severe histological chorioamnionitis, OR 7.62, 95% CI (0.53-411.5), but it did not reach statistical significance probably because of small sample size, as shown in table -1.

Table (1): The association of histologic chorioamnionitis between placental abruption cases and controls in preterm and term gestations

Histological Chorionaminionitis	Preterm births (20-36 week					Term births (37 weeks o longer)				
	Cases (n=44)		Control (n=44)		OR (95%CI	Cases (n=28)		Controls (n=28)		OR (95%CI)
	No	%	N	%		N	%	N	%	
None	13	29.5	33	75.0	-	10	35.7	18	64.3	-
Any	31	70.4	11	25.0	7.15* (2.55-20.49)	18	64.3	10	35.7	3.24 (0.96 11.17)
Mild	15	34.1	6	13.6	6.35* (1.79-23.95)	10	35.7	7	25.0	2.57 (0.63-10.6
Moderate	13	29.5	4	9.1	8.25* (1.99-39.81)	4	14.3	3	10.7	2.40 (0.32-19.3
Severe	3	6.8	1	2.3	7.62 (0.53-411.5)	4	14.3	-	-	-

*Significant difference using Pearson Chi-square test for difference between proportions at 0.05 level of significance.

#OR(95%CI); Odds ratio and its 95% confidence interval

Table (2): Incidence of PROM and the mean gestational age at delivery by severity of histologic chorioamnionitis among placental abruption cases.

Chorionaminionitis	PROM		Gestational age (week		
	No	%	Non-PRO	PROM	P valu
None (n=23)	3	13.1	35.5±3.0	33.5±1.6	0.275
Mild (n=25)	5	20.0	34.2±5.6	33.2±1.5	0.411
Moderate (n=17)	5	29.4	34.4±3.0	33.0±2.3	0.364
Severe (n=7)	5	71.4	32.0±4.4	26.8±2.1	0.048*
P value	0.016		0.539	0.0001*	

*Significant difference using Pearson Chi-square test for proportions or student-t-test for difference between two independent means or ANOVA test for more than two independent means at 0.05 level of significance.

Because PROM has been associated with increased risk of histological chorioamnionitis, we performed a separate analysis of abruption cases and PROM as shown in table 3, PROM was more frequent in abruption cases as the severity of chorioamnionitis increased **(figure-3),** with PROM presented in 71.4% of abruption cases with severe chorioamnionitis.

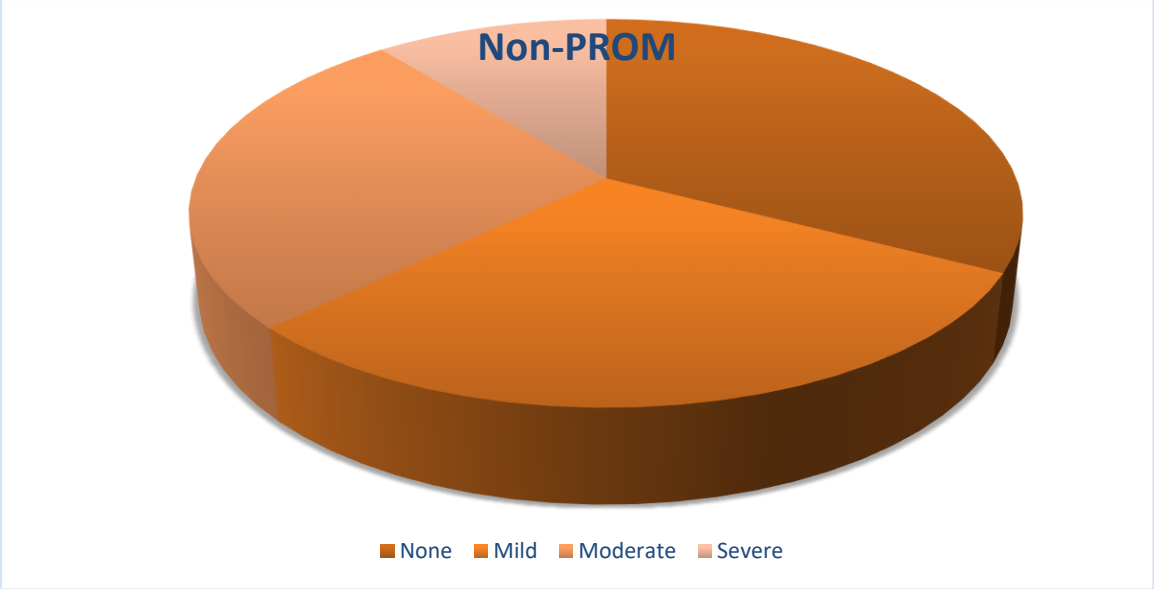

Figure (3): The association of the severity of histologic Chorionamnionitis in placental abruption cases and PROM status.

Among abruption cases there was an apparent trend for earlier delivery in PROM group in comparison with non PROM cases **(Figure-4)**, P value 0.0001, which was more striking with severe chorioamnionitis P value o.048.

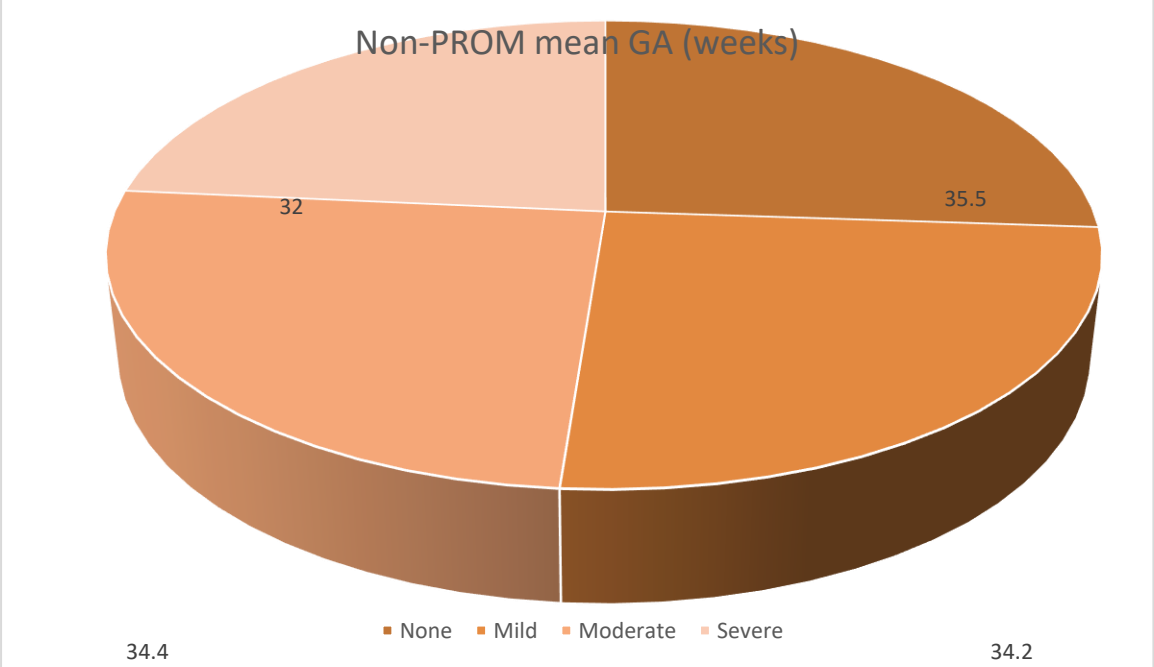

Figure (4): The mean gestational age at delivery in PROM and non-PROM placental abruption cases in association with the severity of histologic chorioamnionitis

Discussion:

Placental abruption is potentially devastating for both mother and fetus and has been associated with stillbirth, preterm delivery, and fetal growth restriction[4].So identification of its risk factors might improve maternal and fetal conditions,Although many risk factors have been identified, causal pathway remains largely speculative[5].

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.,* [6] 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 .

Current study disagree with Becker *et al* [7] who reported that high maternal weight in early pregnancy is associated with a lower risk of placental abruption, Salihu *et al* [8] concluded that obesity is associated with a reduced risk for placental abruption when the weight gain during pregnancy is moderate ,This

may be explained that our population diet with a high energy, nutrient-poor that result in a lack of vitamins and minerals . Data from the National Health and Nutrition Examination Survey III demonstrate that elevated BMI is associated with low micronutrient levels, including folate, vitamin D, vitamin E and others[9]. If obese women, like underweight women, do not have adequate nutrient intake, then we would have expected to see an increased risk of placental abruption, not a decreased risk, because some studies have linked vitamin and mineral deficiencies with abruption[10].

Our study show that PROM status was more frequent in preterm abruption cases than controls as it is present in 25% of preterm cases with abruption,this results agree with that of Nath *et al*[5] who stated that PROM is more frequent in preterm abruption cases than controls.

Ananth *et al* [11] concluded that the risk of abruption was 3.58 fold higher among women with PPROM compared with women with intact membrane and recommended that physicians managing patients with PPROM should be aware that these patients are at increased risk of developing abruption after 24 hours of developing PPROM. So Major *et al*[12]concluded that pregnancies complicated by PROM that are managed expectantly are at significant risk for developing abruption and so regarded PROM a risk factor for placental abruption, while Markhus *et al*[13] suggested that in prelabour preterm rupture of membrane (PPRPM) cases the risk of abruption was not higher than in other preterm births. However, comparing the risk of abruption in PPROM and the total gestational age range, results agreed with previous studies of a higher risk of abruption in PPROM than in total births population.

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[14,15]. 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.

Placental abruption are associated with a thrombin-enhanced expression of IL-8, a potent neutrophil chemoattractant, which leads to a marked infiltration of decidual neutrophils[14,15] . This influx of neutrophils into the decidua is a rich source of proteases that can degrade extracellular matrix, leading to premature rupture of the fetal membranes[15], Therefore, it is difficult to judge definitively whether neutrophil infiltration into the decidu is secondary to vascular disruption or whether it is the primary cause of abruption through inflammation. Others have described apoptotic cell death in the placentae of patients with histologic evidence of chorioamnionitis [16,17]. Mackenzie *et al* [18] concluded that Abruption-generated thrombin promotes PROM by mediating fetal membrane extracellular matrix degradation via enhanced decidual cell matrix metalloproteinase-3 expression.

Ananth *et al*[19] concluded that the risk of abruption in patients with PPROM was higher in the presence of intrauterine infections with rate of 4.81%, while the rate of abruption was 0.83% in women with PPROM without intrauterine infections. Among abruption cases there was an apparent trend for earlier delivery in PROM abruption cases vice non-PROM cases. This pattern of earlier delivery was most striking for severe chorioamnionitis, with delivery

occurring on average 5.2 weeks earlier in PROM cases (P value = 0.048). These data may suggest that inflammation-mediated abruption is not determined by PROM status but that PROM is likely a contributor to the association of inflammation and abruption. These data are in agreement with that of Nath *et al*[(5)]who concluded that abruption cases with PROM who have severe histological chorioamnionitis tend to deliver earlier than those with non-PROM, with delivery occurring on average 4.5 earlier in PROM cases (P value > 0.05).Suzuki *et al* [(18)]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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