Platelet Count and Mean Platelet Volume in First Trimester are the Predictors of Preterm Premature Rupture of Membranes

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Abstract

Background:
Preterm Premature Rupture of Membranes (PPROM) complicates up to 3% of pregnancies and is associated with 30-40% of preterm birth.

Objective:
To find out the values of Platelet Count (PC) and Mean Platelet Volume (MPV) during first trimester of pregnancy to predict preterm premature rupture of membranes (PPROM).

Methods:
This prospective cohort study was conducted on 75 study subjects in Department of Fetomaternal Medicine and Obstetrics and Gynaecology, BSMMU, after taking approval from Institutional Review Board (IRB). Non-random purposive sampling technique was followed. After taking consent and matching eligibility criteria, data were collected from subjects on variables of interest using the structured designed by interview, observation, clinical examination and haematological investigation PC and MPV of subjects at 11 – 13 weeks of gestation. Levels of PC and MPV were documented, and participants were followed until delivery and also advised to report immediately if they experienced symptoms of PPROM. During the follow up, two participants were dropped out. Data were recorded on separate sheets for each participant and analyzed using SPSS 22.0 software.

Result:
In comparison with non PPROM, PPROM had significantly increasedthe level of PC and significantly decreased level of MPV in the first trimester of PPROM. The cut off value of the MPV ≤8 fL and PC ≥294,000/cu.mm. Sensitivity and Specificity of MPV 77.8% and 93.8% and Sensitivity and Specificity of PC were 66.7 % and 70.3%. Subjects with Platelet Count (PC) ≥294000/cu.mm had 3.84 times higher risk to develop PPROM and MPV ≤8fL had 19.73 times the higher risk to have PPROM. The overall accuracy of MPV for detecting PPROM was found to be superior to the Platelet Count (PC).

Conclusion:
Low MPV and high PC at first trimester of pregnancy are predictors of PPROM.

Keywords: Platelet count (PC), Mean platelet volume (MPV), Preterm premature rupture of membrane (PPROM)

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Introduction:

The fetal membranes are the thin tissue that surrounds the fetus during gestation andare critical for maintaining a pregnancy to delivery.[1] In order for successful delivery to occur, rupture of the membrane (ROM) takes place at term. Occasionally, Rupture of Membranes (ROM) occurs before the onset of labour, known as

premature rupture of membranes (PROM), which is not considered to be pathological as it is usually followed by contractions.[2,3] Preterm Premature Rupture of Membranes (PPROM) is defined as rupture of amniotic membranes prior to the completion of 37 weeks of gestation.[4] Preterm Premature Rupture of Membranes (PPROM) complicates up to 3% of pregnancies and is associated with 30%-40% of preterm birth.[5,6] PPROM can result in significant neonatal morbidity and mortality, primarily from prematurity, sepsis, cord prolapse and pulmonary hypoplasia. In addition, there are risk associated with chorioamnionitis and placental abruption.[7] PROM remains a serious challenge for obstetricians, because of its high rate of comorbidity, including infection, cesarean section and other associated problems.[8] Although many aetiological factors may be considered with spontaneous preterm labour and PPROM (previous preterm birth, urinary tract and sexually transmitted infections, previous or current cervical surgical procedure, low socio-economic status and low maternal body mass index, amniocentesis, etc.), the actual cause of membrane weakening and rupture is not known.[3,9-11] Regardless of causes, inflammation is the only pathologic process for a strong causal relation with preterm labour and PPROM has been defined.[9,12-14] The applicability of Platelet Count (PC) and Mean Platelet Volume (MPV) for the clinical and pathophysiological understanding of PPROM has not been investigated. Platelet activation has long been noticed in the pathophysiology of infection and inflammation.[15] Early identification in the first trimester of pregnancy of patient at risk of PPROM is considerably important in reducing adverse perinatal outcomes. Ekin et al conducted a similar study and found that the sensitivity was 58% and 65%, while the specificity was 62% and 44% at the cut-off values of mean platelet volume (MPV) ≤8.6fL and platelet count ≥216410/µL, respectively, in predicting PPROM.[9]

The study aimed to predict Platelet Count (PC) and Mean Platelet Volume (MPV) values from maternal serum during 11-13 weeks of pregnancy, and their subsequent development of preterm premature rupture of membranes.

Methods:

This cohort study was conducted in the Outpatient Department of Fetomaternal Medicine and Obstetrics and Gynaecology of Bangabandhu Sheikh Mujib Medical University (BSMMU) over a period of one year from September 2022 to August 2023. A total of 73 pregnant women at 11-13 weeks of gestation without any diagnosed platelet disorder were enrolled in this study. Pregnant women with fetal anomalies, chronic hypertension, cardiac, renal, liver disease, epilepsy, history of PPROM &cervical incompetence and bicornuate uterus were excluded from this study. The purpose and procedure of the study was explained to the participants and inform written consent was obtained. All the information obtained through interviews, observation, clinical examination and investigations were recorded. All study participants were followed up by regular ANC up to delivery. Platelet Count (PC) and Mean Platelet Volume (MPV) were measured between 11 and 13 weeks, and all the selected women were monitored throughout their pregnancies to assess the potential development of PPROM. Statistical analysis was performed using the Statistical Package for Social Science (SPSS, Chicago, IL, 2001) version 22 software for windows. The results of the study were presented in table and figures. Chi-square test and Fisher's Exact test were done to compare qualitative data and unpaired t-test was done to compare quantitative data. ROC curve of serum platelet count and mean platelet volume to predict PPROM. The p-value <0.05 was considered as statistically significant.

Results:

Mean age of the women with PPROM was 26.96±5.12 years and with non-PPROM was 27.34±5.14. The majority were housewives, constituting 51 participants (69.9%). Additionally, 44 participants (60.3%) had experienced multiple pregnancies, while 69 respondents (94.5%) had a normal Body Mass Index (BMI). There was no significant difference in age, parity, BMI and occupation between PPROM and non-PPROM women (Table-I).

Table-I: Demographic profile of the study participants (N=73)

Demographic characteristics	Total (N=73,100%) no. (%)	PPROM (N=9,12.3%) no. (%)	Non-PPROM (N=64 87.7%) no. (%)	p-value
Age (years)				
≤20	4(5.5)	0(0.0)	4(6.3)	
21 - 25	25(34.2)	0(0.0)	25(39.1)	
26 - 30	27(37.0)	7(77.8)	20(31.3)	
>30	13(13.3)	2(22.2)	15(23.5)	
Mean±SD	30.0±4.74	26.96±5.12	27.34±5.14	0.098
Min-max	18 - 41	26 - 41	18 - 41	
Occupation				
Housewife	51(69.9)	4(44.4)	47(73.4)	0.122
Student	2(2.7)	0(0.0)	2(3.1)	
Service	20(27.4)	5(55.6)	15(23.4)	
BMI(kg/m2)				
<18.5	2(2.7)	2(22.2)	0(0.0)	[a]0.001
18.5-24.9	69(94.5)	7(77.8)	62(96.9)	
>24.9	2(2.7)	0(0.0)	2(3.1)	
Parity				
Primi	29(39.7)	5(55.6)	24(37.5)	[b]0.469
Multipara	44(60.3)	4(44.4)	40(62.5)	
Mode of delivery				
Vaginal Delivery	42(57.5)	5(55.6)	37(57.8)	[b]1.000
Caesarean Section	31(42.5)	4(44.4)	27(42.2)	

[a]Chi-Square test and [b]Fisher's Exact test was done

Pregnant women with platelet count ≥294000 have 3.84 times the risk to have PRPOM than Platelet count <294000 (p=0.055) (Table-II).

Table-II: Platelet count in PPROM Study participants (N=73)

Platelet count (At 11 to 13 weeks)	PPROM (n=9)	Non PPROM (n=64)	Total	RR	p-value
≥294000	6(66.7)	19(29.7)	25(34.2)	3.84	0.055
<294000	3(33.3)	45(70.3)	48(65.8)		

ROC plots of platelet was shown in figure-1. The optimum cut-off level was determined by selecting points of test values that provided the highest Youden Index (sensitivity+specificity-1). The optimum cut-off levels for platelet count is 294000 with sensitivity of 66.7%, specificity of 70.3%, PPV of 24.0% and NPV of 93.8%. The area under the ROC curve was 0.677 (95% CI 0.484–0.870).

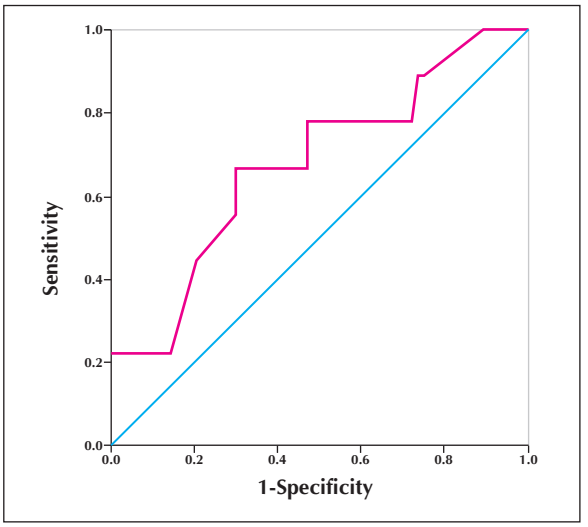

Figure-1: Receiver operating characteristic (ROC) curve of Platelet count (PC) for the prediction of PPROM.

Pregnant women with mean platelet volume ≤8.0 have 19.73 times the risk to have PRPOM than mean platelet volume >8 (p <0.001) (Table-III).

Table-III: Mean platelet volume (MPV) in PPROM Study participants (N=73)

MPV (At 11 to 13 weeks)	PPROM (n=9)	Non PPROM (n=64)	Total	RR	p-value
≤8.0	7(77.8)	4(6.3)	11(15.1)	19.73	<0.001
>8.0	2(22.2)	60(93.7)	62(84.9)		

The optimal cut-off level for Mean Platelet Volume (MPV) was established at 8 fL. Additionally, the area under the receiver operating characteristic (ROC) curve was 0.856, with a 95% confidence interval ranging from 0.730 to 0.982. This resulted in a sensitivity of 77.8%, a specificity of 93.8%, a positive predictive value (PPV) of 98.9%, and a negative predictive value (NPV) of 37.2% (Figure-2).

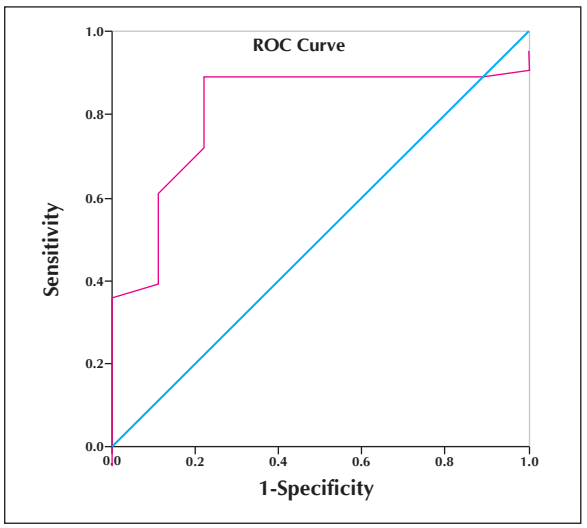

Figure-2: Receiver operating characteristic (ROC) curve of Mean platelet value (MPV) for the prediction of PPROM.

The AUC for MPV (0.894) is significantly higher than that for platelet count (0.677), indicating MPV has a better discriminative ability. MPV has both higher sensitivity (77.8%) and specificity (93.8%) compared to platelet count, suggesting MPV is more effective at correctly identifying both positive and negative cases. The PPV for MPV is very high at 98.9%, meaning it's highly reliable when predicting positive cases. However, its NPV is lower (37.2%), suggesting that a negative MPV result doesn't guarantee absence of the condition. Conversely, platelet count has a high NPV (93.8%) but a low PPV (24.0%), meaning it's less useful in confirming positive cases but more reliable in ruling out negative ones (Table-IV).

Table-IV: Diagnostic values (at first trimester) of Platelet Counts (PC) and Mean Platelet Volume (MPV) in predicting PPROM (N=73)

	Platelet count	MPV
Cut off value	>294000	<8.0
AUC of ROC	0.677(0.484–0.870)	0.894(0.773–1.000)
Sensitivity%	66.7	77.8
Specificity%	70.3	93.8
PPV%	24.0	98.9
NPV%	93.8	37.2

PPV- Positive Predictive Value;
NPV –Negative Predictive Value
AUC- Area Under Curve

Discussion:

Preterm premature rupture of membranes (PPROM) can be predicted by the platelet count and mean platelet volume (MPV) in the first trimester. Although elevated platelet counts were more prevalent in PPROM-affected women, they were not a reliable indicator on their own. In this study, mean age of the women with PPROM was 26.96±5.12 years and with non-PPROM was 27.34±5.14. There was no significant difference in age, parity, BMI and occupation between PPROM and non-PPROM women. There was no significant difference in age, but parity and cesarean delivery was significantly higher in PPROM than control in the study of Ekin et al[9] Kumari et al[16] found no significant age difference between PPROM and non-PPROM women and majority of women with normal BMI. In this study, nine patients (12.3%) developed PPROM, based on maternal outcomes. Of the PPROM cases, 44.45% involved caesarean sections and 55.55% had vaginal births. The non-PPROM group, on the other hand, had 42.18% caesarean sections and 57.82% vaginal births. The PPROM and non-PPROM groups did not significantly differ in their mode of delivery. According to Ekin et al, 39.6% of PPROM patients had a cesarean delivery.[9] In this study, the platelet count (PC) was found to be ≥294,000/cu.mm in 25 patients (34.2%) and <294,000/cu.mm in 48 patients (65.8%). Among the patients with preterm premature rupture of membranes (PPROM), three (33.3%) had a PC <294,000/cu.mm, while six (66.7%) had a PC ≥294,000/cu.mm. The difference was not statistically significant (p>0.05). However, patients with a PC above 294,000/cu.mm had a 3.84 times higher risk of developing PPROM. Additionally, the Mean Platelet Volume (MPV) was ≤8 fL in 11 patients (15.1%) and >8 f Lin 62 patients (84.9%). In the PROM group, two patients (22.2%) had an MPV >8 fL, while seven patients (77.8%) had an MPV ≤8 fL. Those with an MPV below 8 fL had a 19.73 times higher risk of developing PPROM. There was a significant difference between the two groups. Only 3 patients (4.7%) in the non-PPROM group displayed both an elevated platelet count (PC) and a lowered mean platelet volume (MPV). In contrast, 4 patients (44.4%) in the PPROM group exhibited the same combination, indicating that the risk of having both an increased PC and a decreased MPV was 7.54 times higher in the PPROM group.The area under the curve (AUC) of the Receiver Operating Characteristic (ROC)

curve for Platelet Count (PC) in this investigation was 0.677 (95% CI 0.484–0.870). This value indicated that the best threshold for PPROM detection was >294,000/cu.mm, which corresponds to the highest Youden's index. Positive predictive value (PPV) was 24.0%, negative predictive value (NPV) was 93.8%, sensitivity was 66.7%, and specificity was 70.3% at this cutoff. Safaa et al,[17] on the other hand, discovered that the ideal cutoff for PC was ≥270,000/µl, which predicted PPROM with 70% sensitivity, 50% specificity, 64.9% PPV, 67.4% NPV, and 66% accuracy. The area under the curve (AUC) for the Mean Platelet Volume (MPV) ROC curve in this investigation was 0.856 (95% CI 0.730–0.982). With a sensitivity of 77.8%, specificity of 93.8%, positive predictive value (PPV) of 98.9%, and negative predictive value (NPV) of 37.2%, this suggested a cutoff value of less than 8 fL. The ROC analysis conducted by Safaa et al[17] showed that the AUC for MPV was 0.09 (95% CI 0.12–0.05, p<0.001), whereas the AUC for PC was 0.67 (95% CI 0.60–0.70, p<0.001). In their investigation, the ideal MPV cutoff was ≤7.9 fL, which predicted PPROM with 69% sensitivity, 58% specificity, 62.5% PPV, 65.6% NPV, and 64% accuracy. According to Ekin et al,[9] MPV was a better predictor for PPROM, with an AUC of 0.579 (95% CI: 0.536-0.622, p<0.001) for MPV and 0.642 (95% CI: 0.601-0.683, p<0.001) for PC. With a sensitivity of 62% and 44%, a PPV of 56% and 49%, and an NPV of 64% and 60%, the MPV cut-off value was >216 X 10^3/gl.

Conclusions:

In this study, cut off value of Platelet Count (PC) was >294000/cu.mm in prediction of PPROM with sensitivity 66.7% and specificity was 70.3% and at this cut off value was found 3.84 times of more risk to develop PPROM, whereas cut off value of Mean Platelet Volume (MPV) <8 f L in prediction of PPROM with sensitivity 77.8 and specificity 93.8% and having 19.73 times of more risk to develop PPROM. In this study MPV was found to be more efficient as predictor for an early diagnosis of PPROM than PC.

Conflict of Interests: No conflict of interests

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