

To Evaluate Maternal Platelet Indices in Preterm Premature Rupture of Membranes and Their Relation with Adverse Neonatal Outcomes

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Abstract

Preterm premature rupture of membranes is one of the most common issues in daily obstetrics practice. PPRM is associated with 30% of neonatal morbidities and mortalities in preterm delivery. Increased PLT consumption causes activation and increased production of PLT, which causes a hypercoagulable state and microcirculatory defects and vascular reactivity in the placental bed, resulting in placental insufficiency and adverse neonatal outcomes. The present study aimed to determine platelet indices in PPRM patients and to evaluate the association between PLT indices and adverse neonatal outcomes. **Material and methods:** This was a hospital based descriptive study. 130 women with PROM & 130 women without PROM with gestational age between 24 – 36.6 weeks admitted in the labour room for delivery were included in the study. CBC was done for all. Relationship between PLT indices and neonatal outcomes in PPRM cases were analyzed. **Results:** The mean platelet count in women of study group ($224.2 \pm 66.43 \times 10^3/\text{mm}^3$) was lower than mean platelet count in women of control group ($232 \pm 71.58 \times 10^3/\text{mm}^3$). Mean MPV and PDW were significantly more in study group. There was a weak positive correlation existed between Platelet count and APGAR score and birth weight of the baby. A negative correlation existed between MPV and APGAR and birth weight. **Conclusion:** Platelet count, MPV and PDW which are simple, economical and rapid to measure, can be used to predict adverse outcome in PPRM.

Keywords: Maternal Platelet Premature Rupture.

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INTRODUCTION

Preterm premature rupture of membranes (PPROM) is one of the most common and controversial issues in daily obstetrics practice. Premature rupture of membranes (PROM) refers to rupture of foetal membranes prior to the onset of labour and Preterm premature rupture of membranes (PPROM) is defined as spontaneous rupture of foetal membranes prior to 37 weeks of gestation [1]. It affects approximately 3 – 4.5% of all pregnancies [2,3]. PPRM is associated with 30% of neonatal morbidities and mortalities in preterm delivery [4]. A timely and accurate diagnosis of PPRM is critical to optimize pregnancy outcome. Recent studies have shown that the risk of maternal and neonatal infections increases as the time required until delivery increases [5, 6]. However, there is no useful

predictive biomarker of adverse maternal and neonatal outcomes in PPRM.

Normal pregnancy is characterized by an increase in platelet aggregation and a decrease in the number of circulating platelets with gestation. Platelet lifespan declines and the MPV increases minimally during pregnancy. Increased consumption of platelets in the uteroplacental circulation has been suggested to be the explanation of the reduction in the number of circulating platelets [7]. Platelet (PLT) indices, mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT), are determinants of PLT functions, simply assessed by complete blood count (CBC). Currently they are frequently being investigated in a wide variety of clinical conditions. Disturbed PLT functions are implied in hypertension; diabetes; myocardial infarction; cerebrovascular disease; and

some inflammatory diseases, such as systemic lupus erythematosus, inflammatory bowel disease and rheumatoid arthritis [8]. In addition to these, the association between disturbed PLT indices and obstetric conditions, such as recurrent pregnancy loss, first trimester miscarriage, pre-eclampsia, gestational diabetes and preterm labor, have been investigated [9-13].

PLT indices could be useful biomarkers in PPRM cases. Increased PLT consumption causes activation and increased production of PLT, which causes a hypercoagulable state and microcirculatory defects and vascular reactivity in the placental bed, resulting in placental insufficiency and adverse neonatal outcomes [10-13]. Till date very few studies have been done to find association of platelet indices with PPRM. The present study aimed to determine platelet indices (PLT count, MPV, PDW and PCT) in PPRM patients and to evaluate the association between PLT indices and adverse neonatal outcomes, such as low birth weight, APGAR scores < 7 at 5 min, requirement of neonatal intensive care unit (NICU) admission and the development of neonatal sepsis and respiratory distress syndrome (RDS) in PPRM patients.

MATERIAL AND METHODS

This was a hospital based descriptive study carried out in department of Obstetrics and Gynaecology, S.M.S Medical College and attached groups of hospital, Jaipur. Study population was all pregnant woman admitted in the labour room for delivery with gestational age between 24 – 36.6 weeks after applying inclusion and exclusion criteria. Study Group – Women with PROM and Control – Women without PROM.

Sample size was calculated at 80% study power and error of 0.05 assuming the standard deviation of 2.8 fl in MPV among control group as per result of seed article. For minimum detectable mean difference of 1 fl in MPV, 123 patients in each group are required for this study which is further enhanced and rounded off to 130 patients in each group as final sample size expecting 5% drop out/attrition.

Inclusion criteria: singleton live pregnancy of gestational age between 24-36.6 weeks and willing to participate in the study

EXCLUSION CRITERIA

Women with pre-eclampsia, GDM, other medical disorders, IUGR and history of hematopoietic disorders. Institution Review Board & Ethical committee approval was taken prior to commencement of the study. Detailed clinical history, examination, routine investigations and USG were done for all pregnant women with gestational age between 24 – 36.6 weeks, admitted in the labour room. PPRM was

confirmed by: history, observation of pooling of amniotic fluid in posterior fornix of vagina or active leakage of amniotic fluid from cervix and fern test if required. CBC, C reactive protein other investigations were done. Labor was induced in pregnancies complicated with PPRM at and after 34 weeks of gestation. Betamethasone was given for lung maturation to all women. All women were monitored throughout labour and delivery outcomes were noted. Birth weights of neonates, 5 min APGAR score, development of neonatal sepsis, development of neonatal RDS and NICU admission were noted. Data were entered into MS excel sheets and statistically analyzed to find any alterations in PLT indices between the PPRM group and control. We looked for a relationship between PLT indices and neonatal outcomes in PPRM cases.

RESULTS

Socio-demographic profile of the women is shown in Table 1. Majority of the women in study group (63.8%) and control group (73%) were below 25 years. The mean age of women in study group and control group was 23.5±2.36 years and 22.5±2.1 years respectively. Most of women belonged to rural areas (study group-60.8% and control group 73.8%). 53.1% women in study group were non-booked as compared to control group and the difference between two groups was statistically significant (p value 0.04) at p <0.05. Majority of women in both groups were Hindu, literate, belonged to middle socio-economic status according to modified B G Prasad Classification, and had normal BMI and primigravida.

In both study and control group, majority of the women were having gestational age more than 32 weeks and below 36.6 weeks (90.8% in study and 86.2% in control group). Extreme prematurity was seen in 1.5% study as well as in control group. Both the groups were comparable with no significant difference (p value 0.5) (Table 2).

Neonatal outcome is shown in Table 3. NICU admission, RDS and septicemia were significantly more in babies born to women with PPRM than without PPRM.

Table 4 shows CBC parameters. Women with PPRM had slightly more WBC counts than without PPRM (10.92±3.77 vs 10.26±4.36). Similarly neutrophilic count was slightly more in women with PPRM than in women without PPRM (8.79 ± 3.77 vs 7.92 ± 4.31). The difference in WBC count and neutrophil count was statistically not significant. PPRM was also associated with abnormal erythrocyte parameters including anaemia. Mean RDW in study group was 19.89 ± 10.61% and in control group was 15.7 ± 2.74%. RDW was significantly more in study group (p = 0.0000) The mean platelet count in women of study group (224.2 ± 66.43 x10³/mm³) was lower than mean platelet count in women of control group

($232 \pm 71.58 \times 10^3/\text{mm}^3$). Mean MPV was significantly more in study group (11.65 ± 1.04 fl) than in control group (9.98 ± 0.76 fl) ($p=0.0000$). The mean platelet distribution width (PDW) in women of study group was $16.04 \pm 3.12\%$ and in control group it was $14.69 \pm 3.08\%$. The difference in the PDW was statistically significant ($p=0.0005$). The mean plateletcrit (PCT) in women of study group was $0.232 \pm 0.048\%$ and in control group it was $0.207 \pm 0.40\%$. The difference in the PCT was statistically not significant ($p=0.4$).

Correlation between platelet indices and APGAR score and birth weight are shown in Graph 1 to

8. On Pearson's linear regression analysis, there was a weak positive correlation existed between Platelet count and APGAR score ($R=0.105$), and birth weight of the baby ($R=0.014$). The relation was statistically not significant. On Pearson's linear regression analysis, there was a weak negative correlation existed between PDW and APGAR score ($R=-0.126$), and birth weight of the baby ($R=-0.142$), between MPV and APGAR score ($R=0.063$), and birth weight of the baby ($R=-0.089$). There was also a weak negative correlation between PCT and APGAR score ($R=-0.044$), and birth weight of the baby ($R=-0.075$).

Table-1: Socio-demographic profile of the women

Variables	Study group (n = 130)		Control (n = 130)		P value
	No.	%	No.	%	
Age					P = 0.1
<25	83	63.8	95	73.0	Not significant
≥25	47	36.2	35	27.0	
Mean Age	23.5±2.36		22.5±2.1		
Residence					P = 0.3
Urban	51	39.2	44	26.2	Not significant
Rural	79	60.8	86	73.8	
Religion					P = 0.1
Hindu	104	80.0	112	86.2	Not significant
Muslim	26	20.0	18	13.8	
Literacy status					P = 0.1
Literate	81	62.3	93	71.5	Not significant
Illiterate	49	37.7	37	28.5	
Socio-economic status					P = 0.2
Low	30	23.1	41	31.5	Not significant
Middle	91	70.1	78	60.0	
upper	9	6.8	11	8.5	
BMI (Kg/m²)					P = 0.2
<18.5	3	2.3	2	1.5	Not significant
18.5-24.9	102	78.5	90	69.3	
25-29.9	20	15.4	26	20.0	
>29.9	5	3.8	12	9.2	
Gravida					P = 0.2
Gravida 1	73	56.2	81	62.3	Not significant
Gravida ≥2	57	43.8	49	37.7	

Table-2: Distribution according to gestational age

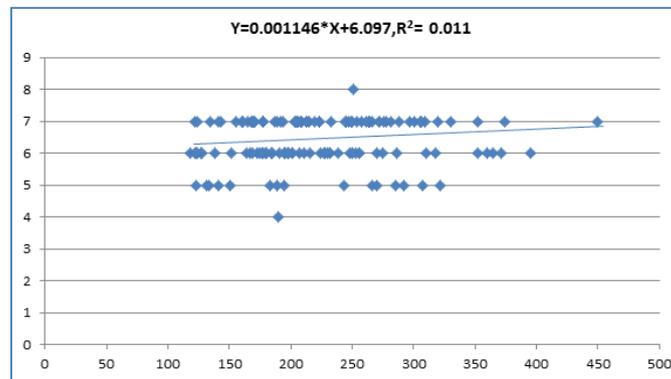
G A (weeks)	Study group		Control		Total		Chi-square P value
	No	%	No	%	No	%	
24-28	2	1.5	2	1.5	4	1.5	Not significant
28-32	10	7.7	16	12.3	26	10.0	
32-36	93	71.5	84	64.6	177	68.1	
36-36.6	25	19.3	28	21.6	53	20.4	
Total	130	100	130	100	260	100	

Table-3: Neonatal outcomes in the study and control groups

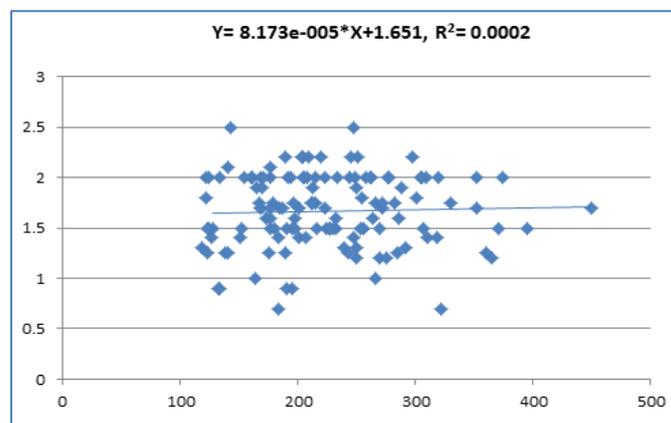
Neonatal outcomes	Study group		Control		P value
	No.	%	No.	%	
Birth weight <1.5	32	24.6	33	25.4	0.8, not significant
≥1.5	98	75.4	97	74.6	
APGAR <7 (5 min)	77	59.1	75	57.7	0.2, not significant
NICU admission	84	64.6	63	48.5	<0.05, significant
RDS	11	13.1	3	4.8	0.04, significant
Septicemia	21	25.0	10	15.9	0.03, significant
Convulsions	4	4.8	5	7.9	0.7, not significant
IVH	3	3.6	2	3.2	0.6, not significant
Hypoglycemia	7	8.3	6	9.5	0.7, not significant
Hypothermia	5	5.9	3	4.7	0.4, not significant
Jaundice	15	17.9	12	19.0	0.5, not significant

Table-4: CBC parameters in the study and control groups

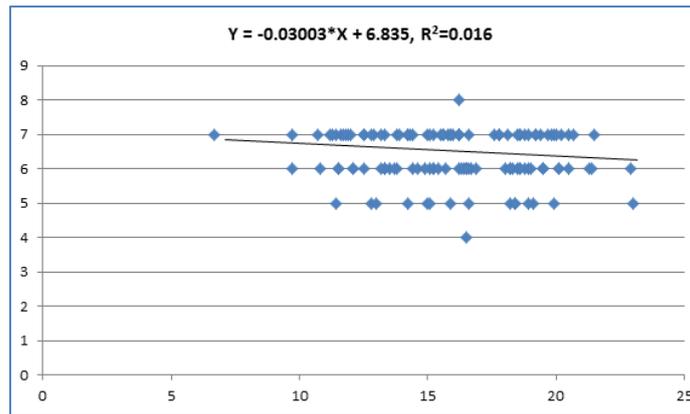
CBC Parameters	Study Group (n = 130)	Control (n = 130)	P value
WBC (x10 ³ /mm ²)	10.92 ± 3.77	10.26 ± 4.36	0.19
Neu (x10 ³ /mm ²)	8.79 ± 3.77	7.92 ± 4.31	0.08
Hgb (g/dl)	10.78 ± 1.69	11.09 ± 1.72	0.14
Hct (%)	33.19 ± 4.56	33.98 ± 4.60	0.16
RDW (%)	19.89 ± 10.61	15.7 ± 2.74	0.0000
Plt (x10 ³ /mm ³)	224.2 ± 66.43	232 ± 71.58	0.3
MPV (fl)	11.65 ± 1.04	9.98 ± 0.76	0.0000
PDW (%)	16.04 ± 3.12	14.69 ± 3.08	0.0005
PCT (%)	0.232 ± 0.048	0.207 ± 0.40	0.4



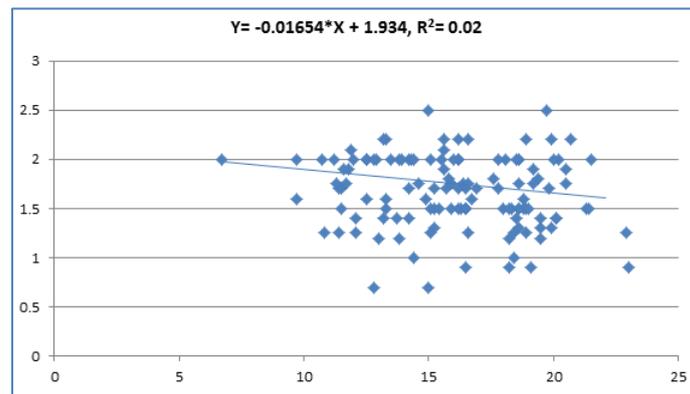
Graph-1: Correlation between platelet count and Apgar score of the babies in PPRM (X axis-Plt, Y axis- Apgar score)



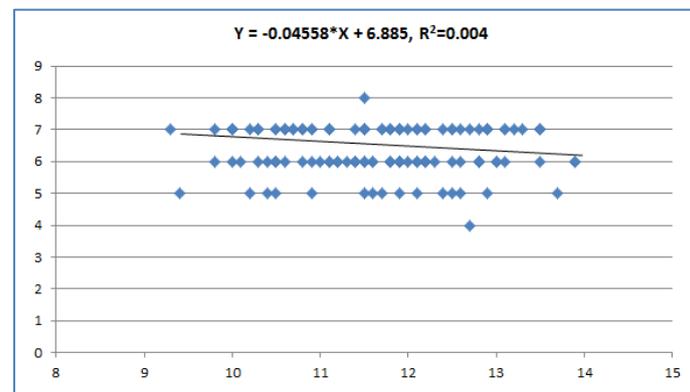
Graph- 2: Correlation between platelet count and birth wt of the babies in PPRM (X axis-Plt, Y axis-Birth wt)



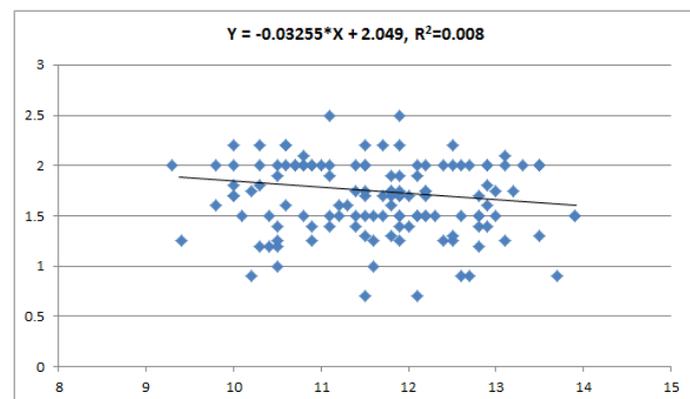
Graph 3: Correlation between maternal PDW and APGAR score of the babies in PPRM (X axis – PDW, Y axis – APGAR score)



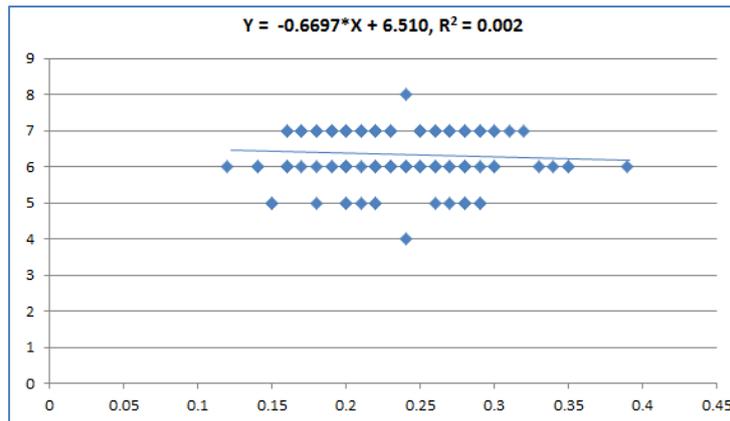
Graph-4: Correlation between maternal PDW and Birth weight of the babies in PPRM (X axis PDW, Y axis Birth Wt)



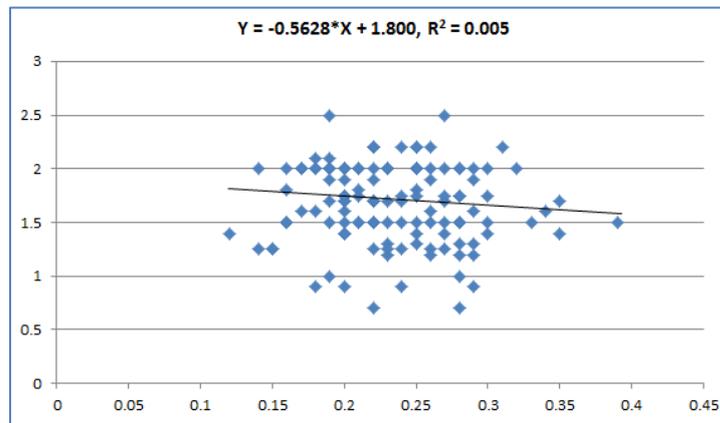
Graph 5: Correlation between maternal MPV and APGAR score of the babies in PPRM (X axis – MPV, Y axis – APGAR score)



Graph-6: Correlation between maternal MPV and Birth weight of the babies in PPRM (X axis – MPV, Y axis – birth wt)



Graph 7: Correlation between maternal PCT and APGAR score of the babies in PPRM (X axis – PCT, Y axis – APGAR score)



Graph-8: Correlation between maternal PCT and birth weight of the babies in PPRM (X axis – PCT, Y axis – birth wt)

DISCUSSION

Disturbed platelet functions have been associated with various obstetrics conditions such as recurrent pregnancy loss, first trimester abortion, pre-eclampsia and preterm labour. So, keeping this in mind the present study was done to evaluate platelet indices (platelet count, mean platelet volume and platelet distribution width) in women with preterm premature rupture of membranes (PPROM) and to find their relation with adverse neonatal outcomes in PPRM such as low birth weight, Low APGAR score, NICU admission, birth asphyxia, neonatal sepsis and early neonatal death.

The mean age of the women 23.5 ± 2.36 Yrs) in our study was lower than that (28.7 ± 2.2 Yrs) observed by Manuck and Varner [14] and (28.7 ± 5.1 Yrs) observed by Toprak *et al.* [15]. This may be due to early marriage which is still prevalent in our state. Women residing in rural areas during pregnancy have been shown to have a slightly more chance to have preterm delivery. Our results were consistent with the results observed by Chang HH *et al.* [16] and Theresia B Temu *et al.* [17]. This may probably be due to women residing in urban area have easy accessibility to health facilities as compared to rural areas. The mean BMI of women in study group was 23.1 ± 2.3 and in control group was 23.8 ± 3.2 . The difference in the BMI

between the two groups was statistically not significant (p value 0.2). The mean BMI of the women in our study (23.5 ± 2.8 kg/m²) was lower than (26.6 ± 7.3 kg/m²) that reported by Manuck and Varner *et al.* [14]. The mean gravidity in our study was lower than reported by Toprak *et al.* [15].

The mean gestational age in our study was 33.8 ± 2.1 weeks which was lower than mean gestational age (35.5 ± 0.8 weeks) observed in the study done by Melamed *et al.* [18]. In study group 84 babies (64.6%) required NICU admission for various reasons while in control group 63 babies (48.5%) required NICU admission. The difference in the NICU admission between two groups was statistically significant. Our results were comparable with that of B. Dunder *et al.* [19] they observed that 58% babies in study group require NICU admission. Requirement of NICU admission was much higher than (30%) observed by Melamed *et al.* [18]. This difference could be because of difference in study design, local pediatric practice and relatively small sample size of our study.

Women with PPRM had slightly more WBC counts than without PPRM (10.92 ± 3.77 vs 10.26 ± 4.36). Similarly neutrophilic count was slightly more in women with PPRM. The difference in WBC count and neutrophil count was statistically not

significant. Similar observation was made by B. Dunder *et al.* [19]. Similarly mean neutrophilic count ($8.79 \pm 3.77 \times 10^3 / \text{mm}^3$) for PPRM in our study was also lower than ($9.94 \pm 3.39 \times 10^3 / \text{mm}^3$) reported by Toprak *et al.* [15], but comparable with the results of B. Dunder *et al.* [19]. They observed a neutrophilic count of $8.7 \times 10^3 / \text{mm}^3$. PPRM was also associated with abnormal erythrocyte parameters including anaemia. Our results were consistent with observations made by J. Liu *et al.* [20] and Obi SN *et al.* [21]. The mean platelet count ($224.2 \pm 66.43 \times 10^3 / \text{mm}^3$) for PPRM in our study was lower than that observed by Toprak *et al.* [15] ($244.5 \pm 60.0 \times 10^3 / \text{mm}^3$) and J. Liu *et al.* [20] ($233.2 \pm 70 \times 10^3 / \text{mm}^3$), but higher than that observed by B. Dunder *et al.* [19] ($2.17 \times 10^3 / \text{mm}^3$). J. Liu *et al.* [20] in their study observed that that women with PPRM had Platelet count of $233.2 \pm 70 \times 10^3 / \text{mm}^3$ which was lower than a platelet count of $274.3 \pm 77.6 \times 10^3 / \text{mm}^3$ in women without PPRM. According to them PPRM was associated with abnormal platelet parameters, including thrombocytopenia, decreased PLT and PDW and increased MPV. In our study mean PDW and MPV were significantly more in women with PPRM than in women without PPRM.

Pregnancy is a hypercoagulable state. The sensitive role of platelets in maintaining the balance between prothrombotic tendency and placental development is vital for the continuation of a pregnancy [22]. Increased platelet volume is a direct indicator of increased platelet synthesis. Increased MPV reflects an increase of active platelets in circulation and in platelet aggregation capacity [23]. Platelets with high MPV are accepted as having more granules containing mediators and being more active. Increased MPV is associated with both arterial and venous vascular pathologies. As pregnancy advances, platelet count decreases, with no significant change in MPV [24]. The number and activities of platelets in complicated pregnancies have been evaluated in a large number of studies. Preeclampsia, premature rupture of membranes (PROM), and IUGR are the most commonly studied pregnancy complications. These studies have reported that increased MPV (and therefore increased platelet activity) increases placental platelet aggregation, causing thrombosis and placental deficiency [25, 26].

Maconi *et al.* [27] have found in PLT and MPV between healthy and nonhealthy pregnant women can be helpful in the differential diagnosis and in the management of complicated pregnancies. In our study women with PPRM had thrombocytopenia and PCT, MPV and PDW were significantly higher in women with PPRM than in women without PPRM. MPV levels might be used as an independent, prognostic marker to predict adverse outcome in PPRM.

Technically a positive correlation existed between maternal platelet count and birth weight ($r = 0.014$) and APGAR score ($r = 0.105$) of the babies in

women with PPRM by using Pearson's correlation coefficient. With increase in maternal platelet count there is increase in birth weight and APGAR score of the babies and vice versa.

A negative correlation existed between maternal PDW and APGAR score ($r = -0.126$) and birth weight ($r = -0.142$) of the babies in women with PPRM by using Pearson's correlation coefficient. With increase in maternal PDW there is decrease in APGAR score and birth weight of the babies and vice versa. A negative correlation existed between maternal MPV and APGAR score ($r = -0.063$) and birth weight ($r = -0.089$) of the babies in women with PPRM by using Pearson's correlation coefficient. A negative correlation also existed between maternal PCT and APGAR score ($r = -0.044$) and birth weight ($r = -0.075$) of the babies in women with PPRM by using Pearson's correlation coefficient.

There were several limitations to the present study. Present study had a small sample size from single centre due to limitation of time. Our centre being a tertiary care centre it caters high risk women referred from all over the state, so result of our study may not represent general population. Finally, as we measured CBC of the women at the time of hospitalization for delivery, serial CBC evaluation may modify the results. Further studies with large sample size are required to validate the role of platelet indices in predicting neonatal outcomes in women with PPRM.

CONCLUSION

This study shows that platelet count decreases while MPV and PDW increases in preterm pregnancy but these changes are more pronounced in PPRM. To conclude, platelet count, MPV and PDW which are simple, economical and rapid to measure, can be used to predict adverse outcome in PPRM.

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