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ACCOUNTS OF ADVERSE NEONATAL EFFECTS IN PRETERM PRELABOR RUPTURE OF MEMBRANES: ANTICIPATING MATERNAL PLATELET INDICES AND C-REACTIVE PROTEIN AS EFFECTIVE BIOMARKERS

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Abstract

Present study aimed at determining maternal platelet indices in preterm prelabor rupture of membranes with adverse neonatal consequences. Comparing maternal C-reactive protein efficacy and platelet indices in predicting outcomes.

Herein, 82 women with preterm prelabor rupture of membranes and 78 women with spontaneous preterm labor were studied. All women undertook complete blood count tests. The group of preterm prelabor rupture of membranes undertook additional C-reactive protein tests. Neonatal outcome data were compiled post-delivery, and results were compared. C-reactive protein efficacy and platelet indices helped in predicting neonatal outcomes in the group of preterm prelabor rupture of membranes using receiver operating characteristic curve analysis.

Women with preterm prelabor rupture of membranes had increased levels of mean platelet volume (8.41 vs. 7.66; p<0.0001), platelet crit (0.223 vs. 0.194; p=0.002), and higher prevalence of early-onset neonatal sepsis (19.5% vs. 2.6%; p<0.001) compared to those with spontaneous preterm labor. In the group of preterm prelabor rupture of membranes, mean platelet volume, platelet crit, and C-reactive protein were significantly associated with respiratory distress syndrome and early-onset neonatal sepsis. The cut-off values mean platelet volume ≥ 8.55fL, platelet crit of ≥0.255%, and C-reactive protein of 5mg/L predicted respiratory distress syndrome with an area under the curve of 0.84, 0.92 and 0.72, the sensitivity of 83%, 91%, and 62%, and specificity of 78.1%, 92.2%, and 68.2%, respectively. The cut-off values of mean platelet volume ≥ 9.05 fL, platelet crit of ≥0.283%, and C-reactive protein of 6mg/L predicted early-onset neonatal sepsis with an area under the curve of 0.86, 0.90 and 0.65, sensitivity of 87.5%, 93%, and 56%, and specificity of 75%, 85%, and 66%, respectively.

Maternal mean platelet volume and platelet crit are useful predictors of neonatal respiratory distress syndrome and early-onset neonatal sepsis in mothers with preterm prelabor rupture of membranes and were better predictors of neonatal outcomes than C-reactive protein.

Keywords: *preterm prelabor,rupture of membranes, respiratory distress syndrome, neonatal sepsis, mean platelet volume.*

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Introduction

Preterm birth is one of the leading causes of perinatal morbidity and mortality worldwide [*Mishra S et al., 2021*]. About 3% of all pregnancies are complicated by preterm prelabor rupture of membranes (PPROM), which is also linked to 40% of preterm births [*Goya M et al., 2013; Cunningham F et al., 2014*]. This increases both maternal and neonatal morbidity and mortality. Early detection of individuals with PPROM and prompt therapy of these patients are critically crucial in avoiding unfavorable maternal and perinatal consequences, as preterm birth is associated with a number of problems. The term "PPROM" refers to the rupture of the fetal membranes spontaneously prior to the 37th week of pregnancy. Preterm Prelabor Rupture of Membranes can happen on its own or as a result of invasive operations such as amniocentesis, fetal surgery, or cerclage implantation.

There are multifarious reasons for the premature rupture of membranes [*Mishra S et al., 2021*]. Around 6-10% of the cases are at risk of having chorioamnionitis; extension of this condition to more than 24 hours elevates the risk to 40% [*Romero R et al., 1992*]. The intensity and prevalence of complications of newborns occurring after PPROM and the membrane rupture's gestational age are inversely related. The most prevalent and dangerous newborn complication at any gestational age is respiratory distress syndrome (RDS). It is defined as an acute pulmonary injury of neonates. Respiratory distress syndrome arises due to the deficiency of lung surfactant relating to prematurity. Early PPROM is frequently accompanied by sepsis, necrotizing enterocolitis (NEC), and intra-ventricular hemorrhage [*Gabbe S et al., 2017*]. The risk of neonatal sepsis is increased two-fold in PPROM compared to premature labor with intact membranes [*Seo K et al., 1992*].

High-risk pregnancies can be identified in many ways, such as the use of clinical, biochemical, and inflammatory markers for the detection of early infection as a result of prematurelabor. The various clinical methods include the identification of epidemiological factors, cervical changes, uterine contractions, and vaginal bleeding [*Deo S et al., 2016*]. For predicting adverse effects relating to PPROM in mothers and neonates, no effective biomarkers are available.

The increased risk of premature delivery is suggested to be effectively identified by one of the biomarkers derived from the maternal serum, i.e., C-reactive protein (CRP). C-reactive protein is a ring-shaped, pentameric, acute-phase protein and consists of five homogenous polypeptides. It is synthesized in the liver with increased levels observed in acute and chronic inflammatory disorders [*Deo S et al., 2016*]. There are conflicting reports on the use of maternal CRP as a predictor for neonatal sepsis, yet it is a valuable marker for early detection [*Hirsch W et al., 1989; Skrablin S et al., 2007; Trochez-Martinez R et al., 2007; van der Heyden J et al., 2010*].

Activation of platelets has been observed in the etiology of infection, inflammation, and malignancy [*Abd El-Fattah A et al., 2022*]. Assessment of complete blood count is done for the platelet indices such as platelet crit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) [*Piazze J et al., 2006; Ekin A et al., 2015; Isık H et al., 2015; Aynıoglu O et al., 2016; Sahbaz A et al., 2016*]. Mean platelet volume is known for indicating the size of the platelets that is considered for platelet activation and function [*Abd El-Fattah A et al., 2022*]. There were several studies that provided a link between MPV and preeclampsia. Ahmed Mohamed Nooh and co-authors (2015) observed that a woman whose PDW and MPVwas elevated during the second and third trimester of pregnancy was more likely to develop preeclampsia. Myatt L. and colleagues (2012) also reported significantly higher MPV in first pregnancies in women who later developed preeclampsia. They also suggested that platelet count could be used to identify women at risk for subclinical vascular dysfunction.

To overcome it
is possible, due to the
uniting the knowledge and
will of all doctors in the world

Investigational studies on the correlation of platelet indices with premature labor, gestational diabetes, and preeclampsia have already been done[*Piazze J et al., 2006; Ekin A et al., 2015; Isık H et al., 2015; Aynıoglu O et al., 2016; Sahbaz A et al., 2016*]. Mean platelet volume has been reported by past studies to be associated with pro-inflammation and pro-thrombosis [*Gasparyan A et al., 2011*]. Activation of platelets arising due to the elevated levels of thrombin after its activation may also suggest premature labor [*Erez O et al., 2008*]. Increased levels of cytokines due to inflammation could be found in systematic circulation as well as maternal-fetal interface [*Turhan N et al., 2000*]. These mediators also cause increased platelet activation and consumption and, in turn, augmented platelet production. This results in morphological alterations in platelets; they become more spherical and have pseudopodia, consequently resulting in alterations in PLT indices [*Vagdatli E et al., 2010*]. Platelet activation leads to a hypercoagulable state which precipitates microcirculatory defects especially in the placental bed, which consequently causes placental dysfunction, the after-effect of which is adverse neonatal outcomes [*Piazze J et al., 2006; Gioia S et al., 2007*].

Thus, for the prediction of PPROM, platelet indices might be used as effective biomarkers. Our study focussed on the platelet indices in detecting PPROM and estimating their association with its detrimental effects in neonates; like APGAR score (Appearance, Pulse, Grimace, Activity, and Respiration) at 1 and 5 minutes, neonatal intensive care unit (NICU) admission, jaundice, NEC, intra-ventricular hemorrhage, respiratory distress syndrome (RDS), early-onset neonatal sepsis and death. We also wanted to compare the efficacy of CRP and the platelet indices in predicting the above adverse outcomes.

Material and methods

The experiment was a potential case study performed in South India from November 2018 to October 2019.

The ethical committee clearance was obtained prior to the enrolment of patients. The purpose of the study was explained to all women, and written informed consent was given to fill up in the language they best understood.

Preterm prelabor rupture of membranes is defined as premature rupture of membranesbefore 37 weeks of gestation. Patients were confirmed to have PPROM by one of the following methods:observation of accumulation of amniotic fluid in the posterior vaginal fornix, amniotic fluid leakage from the cervix, and positivity test for nitrazine paper.

The patients who were confirmed for spontaneous pretermlabor were involved in the study and were affirmed by the following methods: cardiotocography demonstrating at least two contractions in 10 minutes, withcervical length shortening measured clinically or by transvaginal ultrasonography with intactmembranes.

Inclusion criteria: The women having PPROM between 24 to <37weeks of gestation prior to the onset of labor were taken as the study group, and those with spontaneous preterm labor with intact membranes between 24 to <37 weeks were taken as controls.

Exclusion criteria: Women with multiple gestations, medical disorders like gestational diabetes, overt diabetes, gestational hypertension, chronic hypertension, preeclampsia or eclampsia, chronic inflammatory diseases (connective tissue disorders, liver or renal insufficiencies, vasculitis, thrombosis, acute respiratory, urinary or gastrointestinal infections. Further, exclusions of patients were categorized according to the fetuseswith structural abnormalities, chromosomal abnormalities, and intrauterine growth restriction. Those with a history of invasive procedures like cervical cerclage, amniocentesis,andcordocentesis were excluded. Finally, PPROM patients who were managed expectantly (delivered after 37 weeks) were excluded.

Sample size calculation: The sample size was calculated using the formula $n=(Z_{\alpha/2})^2pq/d^2$, where Z is 1.96 (taken from z table), p is the prevalence of RDS, early-onset neonatal sepsis in PPROM patients, q is 1-p, d is the allowable error of 10% and n is the sample size. Previous studies have reported the rate of RDS in <37 weeks of gestation to be between 30-50% [*Nagendra K et al., 1999; Dun-*

dar B et al., 2018] and the rate of early-onset neonatal sepsis to be varying between 10-35% [*Jaiswal A et al., 2017; Dundar B et al., 2018; Sirivunnabood T et al., 2022*]. Assuming the rate of RDS to be around 40% and the rate of early-onset neonatal sepsis of 25% in PPROM (local data), with 5% α error and 95% confidence interval, the sample size achieved was a minimum of 72.

However, during the period of the study, we recruited and analyzed 82 patients from the PPROM group (study group) and 78 patients with spontaneous preterm labor (control group).

Methodology: A structured proforma was prepared for noting down the basic demographic information of the patients, such as the age of the female, parity in pregnancy, previous medical and obstetric history, etc. A complete examination of the general physical, systemic and obstetric being was conducted. Gestational age was defined according to the last menstrual period when it was agreed with the first-trimester ultrasound estimation; otherwise, only the latter was considered.

Management of preterm prelabor rupture of membranes and spontaneous preterm labor: Patients with PPROM and spontaneous preterm received antibiotic ceftriaxone, steroid injection, and neuro-prophylaxis if the gestational age was less than 32 weeks. All the participants were given corticosteroids to attain and assist in the lung maturity of the fetus. In addition, they were given tocolytic drugs with dosages followed according to the pretermlabor protocol at the hospital.

The condition of early-onset neonatal sepsis was confirmed if the preterm newborn showed at

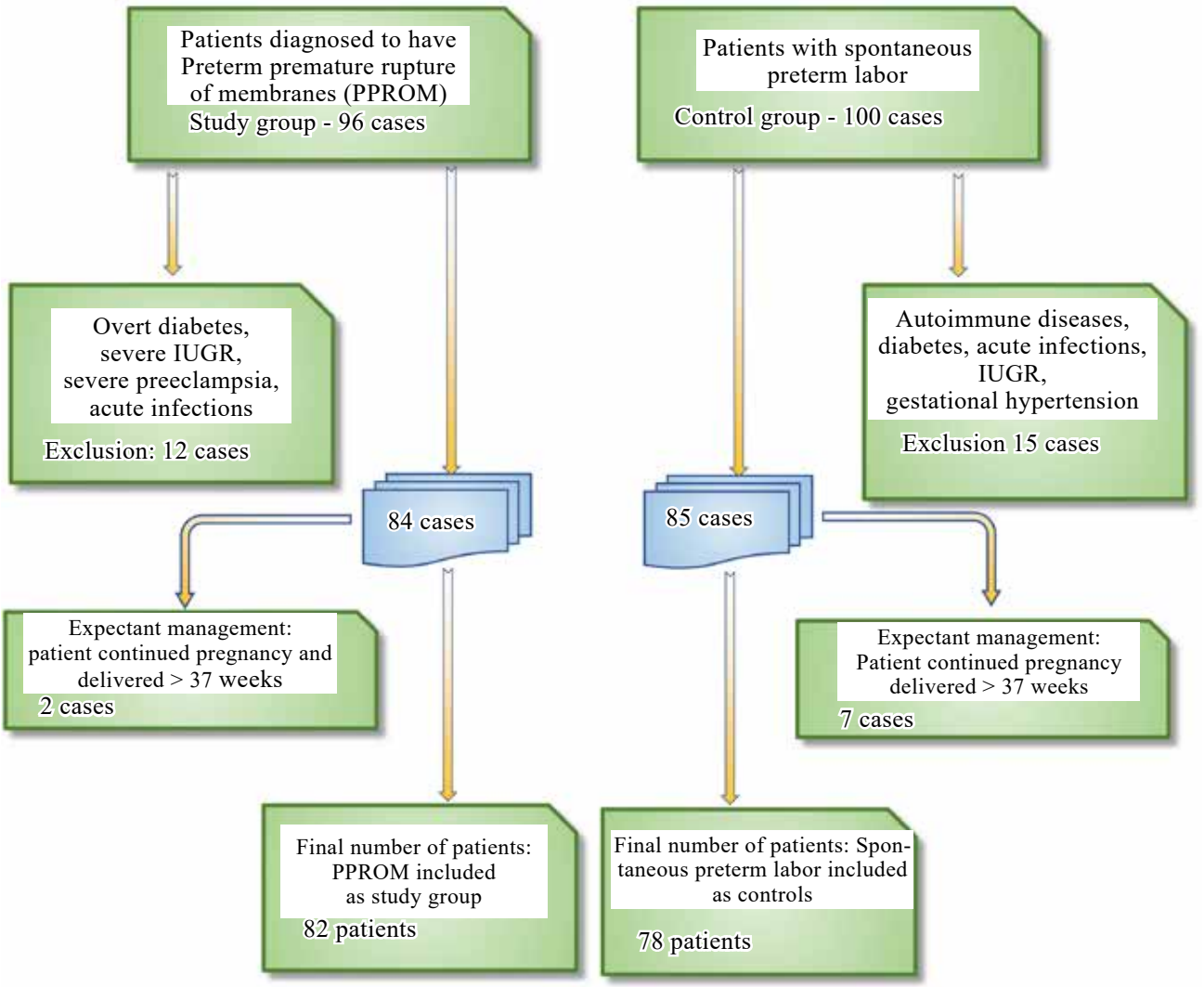

Figure 1: *Flow chart of participants.*

least three of the following features such as; lethargy, shortness of breath, tachypnea (> 70/*min*), bradycardia (heart rate < 90 *bpm*), tachycardia (heart rate > 190 *bpm*), swollen abdomen, temperature fluctuations and, feeding intolerance within 72 hours of admission to NICU. Newborns usually diagnosed with RDS showed the conditions of nasal flaring, grunting respirations, breathing distress, tachypnea, presence of white lung in the chest X-ray, and a sign of air bronchogram.

At the time of admission, all women who had complete blood count parameters like total leucocyte count, hemoglobin (Hb), platelet count (PLT), MPV, PCT, and PDW. Blood samples were taken by venepuncture method and werecollected in tubes coated with tripotassium-ethylene diamine tetraacetic acid to avoid clotting of the samples. In addition to this, the study group had their CRP levels estimated by the immunoturbidimetric method.

The following parameters were noted both in the study and control groups; thegestational age during delivery, mode of delivery, and birthweight of newborns was recorded. Neonatal outcomes such as APGAR score at 1 and 5 min, need for NICU admission (requirement of cardiorespiratory monitoring or assisted ventilation, transient tachypnea of newborn, intravenous antibiotics, birthweight <1.5*kg*), RDS, early-onset neonatal sepsis, intraventricular hemorrhage, NEC, jaundice requiring double surface phototherapy, neonatal death were recorded.

Data analysis: Continuous variables were expressed as mean±standard deviation (SD), whereas categorical variables were expressed as percentages (%). The statistical analysis was conducted using SPSS version 21. The Chi-square test and Mann-witney U test were used to compare categorical variables between the two groups, while the Student's t-test was employed to evaluate continuous numeric variables. For all comparisons, a two-tailed p-value of 0.05 or lower was considered statistically significant. In order to study the diagnostic performance of any marker, a receiver operating characteristic (ROC) curve analysis was carried out, and the area under curve, cut-off values, sensitivity, and specificity were obtained.

Results

A total of 82 PPROM cases and 78 cases with spontaneous pretermlabor as controls were considered after exclusion criteria weretaken into account (Fig. 1).

The basic demographical features are mentioned in table 1. Both the groups were matched in terms of age, parity, gestational age at delivery, and mode of delivery (p>0.05).

Table 1 shows the proportion of patients who received steroids and neuro-prophylaxis among both the groups and were found comparable. They also matched in terms of time interval to delivery and the mode of delivery witha p-value of >0.05. Both the group's basic demographic details and clinical characteristics don't show much difference. Both the groups were matched for time intervals for delivery.

Table 2 mentions the neonatal outcomes where

Table 1.

Demographic and clinical features of PPROM and spontaneous preterm groups

Variables	PPROM (n=82)	Spontaneous preterm (n=78)	p-value
Mean age (in years) (Mean ± SD)	27.62±3.9	27.97±3.66	0.56*
Parity index			
Primigravida (N %)	51(62.7)	41(52.5)	0.17#
Multipara (N %)	31(37.8)	37(47.4)	0.17#
Gestational age at delivery (Mean ± S.D).	33.49±1.43	33.74±1.35	0.37*
<32weeks POG (N %)	26 (31.7)	18 (23.07)	0.2¥
32-33^{+6}weeks (N %)	30 (36.5)	30 (38.4)	
34-36^{+6} weeks (N %)	26 (31.7)	30 (38.4)	
Received steroids (N, %)	64 (78.04)	55 (70.7)	0.35#
Neuro-prophylaxis given (N, %)	20 (24.3)	12 (15.3)	0.56#
Clinical chorioamnionitis (N, %)	6 (7.3)	3 (3.8)	0.095#
Time interval to delivery			
<24 hrs (N, %)	35 (42.6)	38 (48.7)	0.4¥
≥ 24 hrs (N, %)	47 (57.3)	40 (51.2)	
Mode of delivery			
Vaginal delivery (N, %)	31 (37.8)	19 (24.3)	0.06¥
LSCS (N, %)	51 (62.1)	59 (75.6)	

Notes: *Independent sample t-test, #Chi-square test and ¥Mann witney U test; p<0.05 was considered significant. LSCS – lower uterine segment*

significant differences were not found in APGAR scores, NICU admission, the incidence of RDS, NEC, jaundice requiring double surface phototherapy, or neonatal deaths in both groups (p>0.05). PPROM group had a lower mean birth weight than the spontaneous preterm labor group,which was statistically significant(2002±405 vs. 2167±418.7; p=0.05). The incidence of neonatal sepsis in the PPROM group was higher (19.6% vs. 2.5%; p=0.001).

As mentioned in table 3, PCT and MPV values were elevated significantly in the PPROM group as compared to the preterm labor group (8.41±1.06 vs. 7.67±0.73, p<0.0001; 0.223±0.06 vs. 0.193±0.03, p=0.002). However, platelet distribution width, platelet count, hemoglobin and total leukocyte count were almost similar in both groups. Mean C-Reactive protein in PPROM is 5.47±4.6.

We divided the PPROM group into two subgroups; patients who delivered in less than 24 hours since the onset of a leak and the second group of those who delivered in about or more than 24 hours since the leak. There was no significant difference in the CRP values and the platelet indices between the two groups as shown in table 4.

The distinguishing performance of diagnosis relating to MPV, PCT, and CRP in predicting RDS and EONS in the PPROM group was calculated by using the ROC curve analysis.

Among the platelet indices, MPV and PCT were useful in predicting adverse neonatal outcomes such as RDS and neonatal sepsis in PPROM. The same values were not useful in predicting other outcomes. For the diagnosis of RDS, a cut-off of ≥8.55fL for MPV was 83% sensitive, 78.1% spe-

Table 2:

Neonatal outcomes in PPROM and preterm groups

Neonatal outcomes	PPROM (n=82)	Preterm (n=78)	P-value
Birth weight in *grams* (mean±SD)	2002±405	2167±418.7	0.05*¥
<1500*g* (N, %)	10 (12.1)	2 (2.5)	0.06
1500-2500*g* (N, %)	62 (75.6)	63 (80.7)	
>2500*g* (N, %)	10 (12.1)	13 (16.6)	
APGAR score			
1 min- >9 (N, %)	66 (80.48)	64 (82.05)	0.9¥
1min- <9 (N, %)	13 (15.8)	10 (12.8)	
5 mins- <9 (N, %)	3 (3.6)	4 (5.1)	
RDS (N, %)	24 (29.2)	16 (20.5)	0.234#
NEC (N, %)	3 (3.6)	2 (2.5)	0.94#
Jaundice requiring phototherapy (N, %)	44 (53.6)	46 (58.9)	0.56#
NICU admissions (N, %)	32 (39.02)	26 (33.3)	0.68#
NICU stay for >3 days (N, %)	24 (29.2)	14 (17.9)	0.28#
Early-onset Neonatal sepsis (N, %)	16 (19.5)	2 (2.6)	**0.001#**
Neonatal death (N, %)	2 (1.9)	0	0.344#

Notes: **Independent sample t-test, #Chi-square test and ¥Mann-witney U test; p<0.05 was considered significant. RDS- Respiratory distress syndrome (RDS), NICU- neonatal intensive care unit, NEC-necrotizing enterocolitis.*

Table 3.

Complete blood count parameters in PPROM and preterm groups

Blood investigations	PPROM (n=82)	Preterm (n=78)	P value
Platelet indices			
Platelet count (in lakhs) (Mean±SD)	2.42±0.626	2.43±0.56	0.8*
MPV (in *fL*) (Mean±SD)	8.41±1.06	7.67±0.73	**<0.0001***
PCT (in %) (Mean±SD)	0.223±0.06	0.193±0.03	**0.001***
PDW (in %) (Mean±SD)	17.1±1.09	17.26±0.53	0.14*
Haemoglobin (*gm/dl*) (Mean±SD)	10.8± 0.86	10.3± 0.92	0.93
Total leukocyte count (x 10^3)	11.2± 0.72	11.9± 0.82	0.17

Notes: **Independent sample t- test p<0.05 was considered significant.*

***Table 4*:**

Differences in the lab parameters among the PPROM group

Investigations	Time interval till delivery (Total: 51)		p-value
	<24 hrs (n=35)	≥24 hrs (n=47)	
Platelet indices			
Platelet count (in lakhs) (Mean±SD)	2.43±0.65	2.43±0.6	1
MPV (in fL) (Mean±SD)	8.45±0.96	8.55±0.91	0.7
PDW (in %) (Mean±SD)	16.85±1.51	17.12±0.54	0.37
PCT (in %) (Mean±SD)	0.217±0.05	0.214±0.05	0.84
CRP (Mean±SD)	4.92±4.07	5.44±5.06	0.77

Table 5:

ROC analysis of maternal platelet indices and CRP in predicting RDS in PPROM neonates. and predicting early-onset neonatal sepsis in PPROM.

Lab parameters	Mean Platelet Volume (MPV) (*fL*)	Platelet crit (PCT) (*%*)	C- Reactive Protein (CRP) (*mg/L*)
in PPROM neonates.			
Area Under the Curve (**AUC**)	0.84	0.92	0.72
P-value	<0.001	<0.001	0.01
Cut off	8.55	0.255	0
Sensitivity (%)	83	91	62
Specificity (%)	78.1	92.2	68.2
predicting early-onset neonatal sepsis in PPROM.			
AUC	0.86	0.90	0.65
P-value	0.001	0.001	0.04
Cut off	9.05	0.283	6
Sensitivity (%)	87.5	93	56
Specificity (%)	75	85	66

cific, and ≥0.253% for PCT was 91% sensitive and 92.2% specific (Fig. 2 and Table 5).

For the diagnosis of early-onset neonatal sepsis, MPV cut-off of 9.05*fL*was 87.5% sensitive and 93% specific, while PCT cut-off of 0.283% was 93% sensitive and 85% specific.A CRP threshold of 6*mg/L* was only 56% sensitive and 66% specific for predicting early-onset neonatal sepsis, which implies that maternal blood's MPV and PCT values are more efficacious than CRP in predicting adverse neonatal outcomes in the baby (Fig. 3 and Table 5).

Discussion

The major findings of our study defined elevated levels of MPV and PCT values in the PPROM group thanin the control group. The indices were useful in predicting RDS and neonatal sepsis, but not other newborn complications. Platelet indices were superior to CRP in the prediction of adverse outcomes.

The time period between the membrane rupture and delivery poses a significant risk for the emergence of maternal and neonatal issues in PPROM. We divided our PPROM patients into those who delivered in less than 24 hrs and in about or more than 24 hrs. While comparing the various platelet indices among the two subgroups, there was no significant difference between them statistically, with a p-value of >0.05. The levels of CRP were also comparable between the two groups. Thus, the patients who delivered later did not have anyworse laboratory markers, as expected. This might be due to the stringent antibiotic administration to all the patients who had PPROM.

The death of neonates with the condition of PPROM was associated with three reasons: sepsis, prematurity, and pulmonary hypoplasia [*Duff P, 1991*]. When comparing the neonatal outcomes in the preterm labor and the PPROM groups, the early-onset neonatal sepsis rateswere highersig-

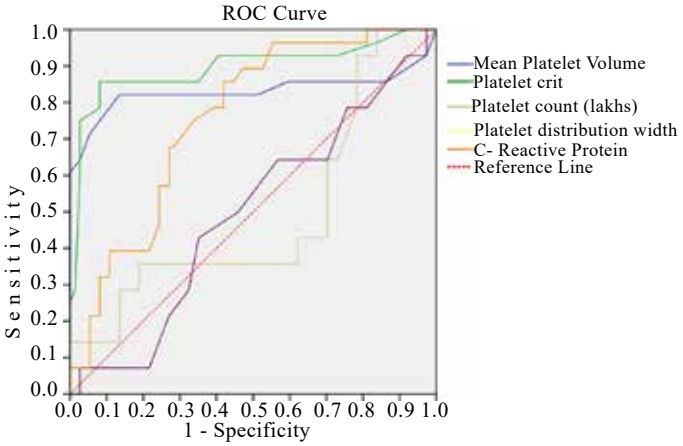

Figure 2: *Receiver operator curve analysis of maternal platelet indices and CRP in predicting RDS in neonates in PPROM*

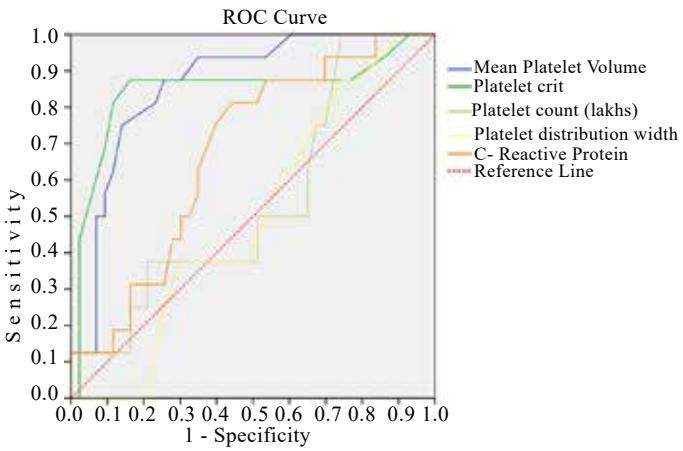

Figure 3. *ROC analysis of maternal platelet indices and CRP in predicting early-onset neonatal sepsis among the PPROM group*

nificantly in the PPROM group. The occurrence and severity of these complications are inversely correlated with gestational age.

In their study Dundar B. and co-authors (2018) observed patients with PPROM had increased MPV, PCT, and anincreased occurrence of neonatal sepsis. Also, we had a similar result in our study where the PCT and MPV levels were significantly raised in the group who had PPROM condition,and neonatal sepsis was more common in this group.

An experimental-control study was conducted in Baghdad by Farhan to determine the value of platelet indices in preterm delivery. They concluded that prematurelabor is correlated with lower levels of MPV and elevated levels of PDW [*Farhan F, 2016*]. A retrospective study was conducted to determine the variations in platelet indices and hemoglobin in threatened preterm labor [*Artunc Ulkumen B et al., 2014*]. They found lower MPV levels and elevated PDW levels, suggesting ahigher degree of inflammation and platelet activation in diseased states.Our study had control groups as patients with preterm labor and intact membranes, which recorded lower MPV and higher PDW, but the values were not significant statistically ($p<0.05$).

Some authors conducted a retrospective study in Turkey to predict the development of subsequent PPROM by evaluating platelet counts and MPV values in the first trimester period [*Ekin A et al., 2015*]. Women who were about to develop PPROM had significantly higher platelet counts and lower MPVvalues in the first trimester, and the accuracy of MPV to detect PPROM was superior to that of platelet counts. The case-control study of Dundar B. and colleagues (2018) in Turkey also studied the relationship between platelet indices and adverse neonatal outcomes. A PCT value of above 0.22% was linkedwith a 5.86-fold increased risk of RDS. A higher PDW score was also correlated with the development of RDS. These results were consistent with our study. For the diagnosis of RDS, a cut-off of ≥8.5*fL* for MPV, ≥0.253% for PCT, and MPV cut-off of ≥9.05*fL*, while PCT cut-off of ≥0.283% for predicting early-onset neonatal sepsis was calculated. These cut-offs had high sensitivity and specificity, which implied that the platelet indices could be used as reliable tests in PPROM to predict adverse outcomes. A prospective case-control study was done in Amritsar, India, to evaluate the role of CRP in PPROM. For the early diagnosis of chorioamnionitis, CRP levels were 100% sensitive but less specific (69.56%). C-reactive protein detected neonatal sepsis with 100% sensitivity [*Aggarwal A, Pahwa S, 2018*]. A similar study in Korea by Jeon, et al [*Jeon J et al., 2014*] concluded that maternal CRP cut-off value of above 1.22 *mg/dL* showed 71% sensitivity and 84% specificity for anticipating neonatal sepsis, and babies in the maternal CRP positive group had more neonatal sepsis (71%) than the group with negative CRP (29%), ($p<0.001$). This was in discordance with our study, where a CRP threshold of 6*mg/L* was only 56% sensitive and 66% specific for predicting early-onset neonatal sepsis.

Most of the patients in PPROM group were referred cases and had received antibiotics.Torbé A. and Kowalski K. (2010) studied maternal serum and vaginal fluid C-reactive protein level to predict early-onset neonatal infection in preterm premature rupture of membranes and concluded that predictive performance of both maternal serum CRP and vaginal fluid CRP was poor. Ourstudy shows that MPV and PCT values were superior to the conventionally used inflammatory marker CRP in predicting early-onset neonatal sepsis.

Limitations: PPROM group had a lower mean birth weight, which was a confounding factor. Our study had a small sample size and involved only a single centre; therefore, our results cannot be extrapolated to the other centres. Further prospective studies with a large sample sizeare required to evaluate the confounding factors contributing to adverse neonatal outcomes.

Conclusion

In summary, the whole study can confirm that the maternal platelet indices such as MPV and PCT had higher levels in the study group of preterm premature rupture of membrane.These platelet indices are also related to the occurrences of adverse neonatal outcomes. C-Reactive protein levels were also tested for their sensitivity and specificity,

which did not give better results. The membrane rupture, along with the time of delivery, is a crucial point to look for in the cases of PPROM.

It is critical to identify the markers to anticipate neonatal problems during expectant treatment and antenatal surveillance.To avoid incidences of neonatal death conditions due to RDS or neonatal sepsis, the platelet indices can be a reliable aid in predicting the adverse outcomes of PPROM. These are slightly more efficacious than the regularly used CRP for diagnosis.

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