THE ROLE OF PLATELET COUNT AND MEAN PLATELET VOLUME DURING FIRST TRIMESTER IN PREDICTION OF PRETERM PREMATURE RUPTURE OF MEMBRANES

By

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ABSTRACT

Background: The fetal membranes are the thin tissue that surround the fetus during gestation, and critical for maintaining a pregnancy to delivery.

Objective: To evaluate the values of platelet count and mean platelet volume (MPV) obtained from maternal serum during pregnancy to predict subsequent preterm premature rupture of membranes (PPROM).

Patients and Methods: This study was a prospective Cohort study that was conducted on 300 cases of pregnant women at Obstetric and gynecological department at El-Hussein University Hospital. All patients met the inclusion criteria and were divided into two groups, Group I (PPROM group) that included 22 pregnant women with history of vaginal fluid leakage and diagnosed as PPROM and Group II (Control group) which included 278 pregnant women with gestational age between 37 - 41 weeks and without any history of complications throughout the pregnancy as a control group.

Results: As regard the area under curve, cutoff and validity of PLT regard detection of PPROM, Significant AUC with cutoff >258 with sensitivity 83.3% and specificity 75.0%. The overall accuracy of MPV for detecting PPROM was found to be superior to platelet count.

Conclusion: MPV is a cheap, rapid and easily applicable test for determining the patients at risk for PPROM. Due to multifactorial origin of PPROM, early detection of all patients with a single test is rather difficult. In order to develop an accurate and efficient method in the estimation of the risk of PPROM, screening strategies combining MPV with other biological markers should be considered.

Keywords: First Trimester, Preterm Premature Rupture of Membranes.

INTRODUCTION

The fetal membranes are the thin tissue that surround the fetus during gestation, and critical for maintaining a pregnancy to delivery. In order for successful delivery to occur, normal rupture of the membrane (ROM) takes place at term. Occasionally, ROM occurs before the onset of labour, known as premature rupture of the membrane (PROM), which is not considered to be pathological as it is usually followed by contractions (*Calvin and Oyen*, 2010). The premature rupture of membrane is considered preterm if occurred before 37 weeks of gestation. So Preterm premature rupture of membranes (PPROM) is defined as rupture of the amniotic membranes prior to the completion of 37 weeks of gestation (*Kale et al., 2010*).

PROM remains a serious challenge for obstetricians, because of its high rate of comorbidity, including infection, cesarean section, and other associated problems (*American College of Obstetricians and Gynecologists, 2016*). Preterm PROM "PPROM", accompanied by preterm birth, is the leading cause of morbidity and mortality in the neonatal period (*Yeh et al., 2017*).

As preterm birth is associated with numerous complications, early identification of patients with an increased risk for PPROM is considerably important in reducing adverse perinatal outcomes. The cause of PPROM is multifactorial and intra-amniotic infection, reduction in membrane collagen content, stretched membranes, vasculopathy in placentation and decidual hemorrhage are considered to be possible mechanisms underlying PPROM. Among these, chronic infection of fetal membranes has a clear role in the initiation and propagation of molecular events leading to PPROM (Ekin et al., 2015).

Previous studies have shown that intrauterine infection triggers a rise of several cytokines in maternal serum as well as amniotic fluid (*Agrawala and Hirsch*, 2012).

Platelet activation has long been noticed in the pathophysiology of infection, inflammation and malignancy. Mean platelet volume (MPV) is a reliable indicator of platelet size that reflects platelet function and activation. Previous studies reported the association of MPV with both pro-thrombosis and proinflammation (*Gasparyan et al.*, 2011).

The aim of this study is to evaluate the values of platelet count and mean platelet volume (MPV) obtained from maternal serum during pregnancy to predict subsequent preterm premature rupture of membranes (PPROM).

PATIENTS AND METHODS

This was a prospective cohort comparative study that was conducted at Obstetric and gynecological department at Sayed Galal and El-hussien University Hospital in the period from June 2019 to January 2020.

Before the start of the study, permission was obtained from the Ethical Committee in the faculty of medicine, Al-Azhar University. Also Informed consent from patients included in the study was obtained.

This study was conducted on 300 of cases attending ANC unit at Sayed Galal and El-Hussien university hospitals, they were divided into two groups:

- **Non-PPROM group:** included 278 pregnant women who delivered without occurrence of PPROM.
- **PPROM group:** included 22 pregnant women who suffered of PPROM.

All the women participating in this study were chosen according to the following criteria:

Inclusion Criteria:

- Pregnant women aged 18 35ys
- Non-complicated singleton pregnancy.

• Gestational age 11 - 14 weeks for the study group at the start of the study.

Exclusion Criteria:

- Women with multiple pregnancies, fetal anomalies.
- Women with pat history of bleeding tendency of Know blood disease.
- Women with chronic hypertension, cardiac, renal or liver diseases, epilepsy and unexplained anemia.
- Presence of any vaginal bleeding of any amount.
- Women with cervical Incompetence, short cervix or on cervical cerclage.

After informed written consent were obtained from all patients included in the study they were subjected to the followings:

- I. Full medical history.
- II. Full general examination.
- III. Ultrasonic examination.
- IV. Routine investigations.
- V. Pregnancy outcomes.

All selected women were observed during the course of pregnancy and after the end of pregnancy in order to assess the following outcomes.

Primary outcomes: Occurrence of PPROM.

Secondary outcomes:

- Time and mode of delivery

- Neonatal APGAR score at 1 and 5 minutes.
- Neonatal ICU admission

Statistical Analysis:

The collected data was revised, coded. tabulated and introduced to a PC using Statistical package for Social Science (SPSS version 20.0 for windows; SPSS Inc, Chicago, IL, 2001). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. Descriptive Statistics: Mean, Standard deviation (± SD) and range for parametric numerical data. and percentage of Frequency nonnumerical data. Student T Test: was used to assess the statistical significance of the difference between two study group means. Chi-Square test (X2): was used to examine the relationship between two qualitative variables. ROC curve: A receiver operating characteristic (ROC), or simply ROC curve, is a graphical plot which illustrates the performance of a binarv classifier system as its discrimination threshold is varied. It is created by plotting the fraction of true positives out of the positives (TPR = true)positive rate) vs. the fraction of false positives out of the negatives (FPR = falsepositive rate), at various threshold settings. TPR is also known as sensitivity (also called recall in some fields), and FPR is one minus the specificity or true negative rate. P>0.05: Non significant (NS). P< 0.05: Significant (S). P<0.01: Highly significant (HS).

RESULTS

Maternal ages were ranging between 19-35 years with mean age 26.89 ± 4.42 , gestational ages (GA) at the beginning of

the study was ranging between 11 - 14 weeks with mean GA 12.3 ± 0.99 while at the end of the study was ranging between

29 – 40 weeks with mean GA 37.3 \pm 2.26. Regarding parity, majority of studied cases were para \leq 2 (49.3%) while 19.4 % were para 3 – 4 times and 2.3% of cases were para more than 4 times. 20% of studied group had previous PROM, 30% had positive FH, 35.7% of studied group had no co-morbidities, 34% had anemia and 18.3% had passive smoker and finally gestational DM was in 12%, only 5.3% had IVF. 12.7% had preterm labor, 7.3% had PPROM, 28% had PPH and 51.3% had NVD and CS was 48.7%. Female babies were 56.3% and male represent 43.7%, NCIU was needed by 19.7% regard survival 3.7% died and 96.3% survived (**Table 1**).

 Table (1): Maternal and gestational ages, clinical and obstetric history, maternal outcome, Neonatal outcome distribution among studied group

| Age: 26.89 ± 4.42 Range 19 – 35 Gestational Age (GA) at beginning: 12.3±0.99 N 11.1 – 14 Gestational Age (GA) at beginning: 11.1 – 14 Mean ± SD 37.3 ± 2.26 Range 37.3 ± 2.26 Gestational Age (GA) at beginning: 37.3 ± 2.26 N % Adment ± SD 37.3 ± 2.26 Range N % PG 37.3 ± 2.26 Statistic Mean ± SD % Statistic Mean ± Statistic M | Variable | | | | | | | | | |
|---|---------------------------|-------|----------------|------------------|-------|--|--|--|--|--|
| | | | | | | | | | | |
| • Range $19-35$ Gestational Age (GA) at beginning: 12.3 ± 0.99 • Mean \pm SD $11-14$ GA at end: 37.3 ± 2.26 • Range 37.3 ± 2.26 • Range $29-40$ • Parity: 87.3 ± 2.26 • Range $29-40$ • PG $23-4$ • PG 37.3 ± 2.26 • NO 240 • NO | | | | 26.89 ± 4.42 | | | | | | |
| Gestational Age (GA) at beginning: 12.3±0.99 Mean ± SD 11 – 14 GA at end: 37.3 ± 2.26 Range 37.3 ± 2.26 Range 37.3 ± 2.26 Range 37.3 ± 2.26 Parity: 37.3 ± 2.26 PG 37.3 ± 2.26 $29 - 40$ $99 - 40$ Parity: 87 $29 - 40$ 99 $3.3 \cdot 4$ 7 2.3 77 7 2.3 7 2.3 7 2.3 7 2.3 7 2.3 7 2.3 7 2.3 7 2.3 7 7.3 7 7 87 90 900 30.0 900 30.0 900 30.0 FH 90 88 94.7 92.7 | | | | | | | | | | |
| | | 17 55 | | | | | | | | |
| • Range $11-14$ GA at end: 37.3 ± 2.26 • Range $29-40$ Parity: N $\%$ • PG 87 29.0 ≤ 2 87 29.0 • 3 - 4 58 19.4 • 3 - 4 58 19.4 • > 4 7 2.3 • Total 300 100.0 Previous PROM • NO 240 80.0 • NO 240 80.0 90 30.0 FH • NO 210 70.0 • PS 90 30.0 30.0 Itemp • NO 210 70.0 FH • NO 210 70.0 PG • VES 90 30.0 Itemp • NO 202 33.7 Preterm • No 262 83.3 <td></td> <td>12.3</td> <td>±0.99</td> | | 12.3 | ±0.99 | | | | | | | |
| GA at end: 37.3 ± 2.26 Range 37.3 ± 2.26 Parity: N 96 Parity: 87 29.0 • ≤ 2 148 49.3 • $3 \cdot 4$ 58 19.4 • 2 7 2.3 • Total 7 2.3 Previous PROM • NO 240 80.0 FH 90 300 100.0 FH • NO 210 70.0 FH • NO 210 70.0 FH • NO 107 35.7 • Passive smoker 55 18.3 • Risks and co-morbidity • NO 107 35.7 • Passive smoker 55 18.3 • Gestational DM 36 12.0 • No 262 87.3 Preterm • No 262 87.3 • Yes 38 12.7 • No 216 72.0 • Yes 84 28.0 MODE • No 216 72.0 • Yes <td></td> <td colspan="9">Range</td> | | Range | | | | | | | | |
| Range $29-40$ Parity: N % • PG 87 29.0 • ≤ 2 148 49.3 • $3 \cdot 4$ 58 19.4 • > 4 58 19.4 • > 4 7 2.3 • Total 7 2.3 Previous PROM • NO 240 80.0 Previous PROM • YES 60 20.0 FH • NO 210 70.0 FH • NO 107 35.7 • Passive smoker 55 18.3 • NO 107 35.7 • Passive smoker 55 18.3 • NO 107 35.7 • Passive smoker 55 18.3 • • No 22.0 7.3 Preterm • No 27.7 27.7 | 0 | | | | | | | | | |
| • Range $29-40$ Parity: N % • PG 87 29.0 • ≤ 2 148 49.3 • $3 \cdot 4$ 58 19.4 • > 4 58 19.4 • > 4 7 2.3 • Total 300 100.0 Previous PROM • NO 240 80.0 FH • NO 240 80.0 FH • NO 210 70.0 FH • NO 107 35.7 • NO 107 35.7 • Passive smoker 55 18.3 12.0 • NO 107 35.7 • Passive smoker 55 18.3 12.0 • NO 107 35.7 • Passive smoker 55 18.3 12.0 • No 222 7.3 14.6 Preterm • No 277 < | Mean ± SD | 37.3 | ± 2.26 | | | | | | | |
| Parity: N % • ≤ 2 87 29.0 • ≤ 2 148 49.3 • ≤ 2 148 49.3 • > 4 58 19.4 • > 4 7 2.3 • Total 7 2.3 • Total 7 2.3 • NO 240 80.0 Previous PROM • NO 210 70.0 FH • YES 60 20.0 FH • YES 90 30.0 FR • NO 107 35.7 • Passive smoker 55 18.3 • NO 107 35.7 • Passive smoker 55 18.3 • O 102 34.0 IVF • -VE 284 94.7 Preterm • No 262 <t< td=""><td>Range</td><td colspan="7"></td></t<> | Range | | | | | | | | | |
| • PG 87 29.0 • ≤ 2 148 49.3 • $3 \cdot 4$ 58 19.4 • > 4 7 2.3 • Total 300 100.0 Previous PROM • NO 240 80.0 • NO 240 80.0 0 FH • NO 210 70.0 FH • NO 210 70.0 FH • NO 107 35.7 • Passive smoker 55 18.3 • NO 107 35.7 • Passive smoker 55 18.3 • NO 107 35.7 • Passive smoker 55 18.3 • • VE 284 94.7 IVF • · VE 284 94.7 • · · No 262 87.3 Preterm • No 278 92.7 | 8 | | | | | | | | | |
| • PG 87 29.0 • ≤ 2 148 49.3 • $3 \cdot 4$ 58 19.4 • > 4 7 2.3 • Total 300 100.0 Previous PROM • NO 240 80.0 • NO 240 80.0 0 FH • NO 210 70.0 FH • NO 210 70.0 FH • NO 107 35.7 • Passive smoker 55 18.3 • NO 107 35.7 • Passive smoker 55 18.3 • NO 107 35.7 • Passive smoker 55 18.3 • • VE 284 94.7 IVF • · VE 284 94.7 • · · No 262 87.3 Preterm • No 278 92.7 | Parity: | | | - | - | | | | | |
| • ≤ 2 148 49.3 • $3 \cdot 4$ 58 19.4 • > 4 7 2.3 • Total 300 100.0 Previous PROM • NO 240 80.0 FH • NO 240 80.0 FH • NO 210 70.0 FH • NO 210 70.0 FH • NO 107 35.7 • Passive smoker 55 18.3 • NO 107 35.7 • Passive smoker 55 18.3 • Sectational DM 36 12.0 • No 102 34.0 IVF • ·VE 284 94.7 • ·VE 284 94.7 • ·VE 284 94.7 • ·VE 284 94.7 • ·VE 16 5.3 Preterm • No 216 72.0< | | | | 87 | 29.0 | | | | | |
| | | | | | | | | | | |
| | • <u>3-4</u> | 58 | 19.4 | | | | | | | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | ■ >4 | 7 | 2.3 | | | | | | | |
| Previous PROM · YES 60 20.0 FH · NO 210 70.0 · YES 90 30.0 Risks and co-morbidity · NO 107 35.7 · Passive smoker 55 18.3 · Gestational DM 36 12.0 · Anemia 102 34.0 IVF · · VE 284 94.7 Preterm · · · VE 16 5.3 Preterm · No 262 87.3 · Yes 38 12.7 PROM · No 278 92.7 · Yes 38 12.7 PPROM · No 216 72.0 · Yes 84 28.0 MODE · NVD 154 51.3 · CS 146 48.7 | Total | | | 300 | 100.0 | | | | | |
| • YES 60 20.0 FH • NO 210 70.0 • YES 90 30.0 Risks and co-morbidity • NO 107 35.7 • Passive smoker 55 18.3 • Gestational DM 36 12.0 • Anemia 102 34.0 IVF • -VE 284 94.7 • -VE 284 94.7 • +VE 16 5.3 Preterm • No 262 87.3 • No 278 92.7 • No 278 92.7 • No 216 72.0 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 Baby sex • | | • | NO | 240 | 80.0 | | | | | |
| FH • YES 90 30.0 Risks and co-morbidity • NO 107 35.7 • Passive smoker 55 18.3 • Gestational DM 36 12.0 • Anemia 102 34.0 IVF • -VE 284 94.7 • VF 284 94.7 • VE 284 94.7 • VE 284 94.7 • VE 284 94.7 • VE 16 5.3 Preterm • No 262 87.3 • Yes 38 12.7 PROM Yes 38 12.7 • No 278 92.7 • No 216 72.0 • Yes 84 28.0 MODE • No 216 72.0 • Yes 84 28.0 131 MODE • CS 146 48.7 • Baby sex • Male 131 43.7 • Female | Previous PROM | • | YES | 60 | 20.0 | | | | | |
| • YES 90 30.0 Risks and co-morbidity • NO 107 35.7 • Passive smoker 55 18.3 • Gestational DM 36 12.0 • Anemia 102 34.0 IVF • -VE 284 94.7 • -VE 284 94.7 • -VE 284 94.7 • -VE 284 94.7 • -VE 16 5.3 Preterm • No 262 87.3 • No 278 92.7 PPROM Yes 38 12.7 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • NVD 154 51.3 • Female 169 56.3 NICU • | | | NO | 210 | 70.0 | | | | | |
| Risks and co-morbidity Passive smoker 55 18.3 • Gestational DM 36 12.0 • Anemia 102 34.0 • VE 284 94.7 • -VE 284 94.7 • +VE 16 5.3 Preterm • No 262 87.3 • Preterm • No 278 92.7 • Pres 22 7.3 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 • Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | FH | • | YES | 90 | 30.0 | | | | | |
| Risks and co-morbidity • Gestational DM 36 12.0 • Anemia 102 34.0 • VE 284 94.7 • -VE 284 94.7 • +VE 16 5.3 Preterm • No 262 87.3 • Yes 38 12.7 PROM • Yes 38 12.7 PROM • No 262 87.3 • Yes 38 12.7 PROM • Yes 38 12.7 PROM • No 278 92.7 • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | | • | NO | 107 | 35.7 | | | | | |
| Risks and co-morbidity • Gestational DM 36 12.0 • Anemia 102 34.0 • VE 284 94.7 • -VE 284 94.7 • +VE 16 5.3 Preterm • No 262 87.3 • Yes 38 12.7 PROM • Yes 38 12.7 PROM • No 262 87.3 • Yes 38 12.7 PROM • Yes 38 12.7 PROM • No 278 92.7 • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | D (1) 1 1 1 1 (1) | • | Passive smoker | 55 | 18.3 | | | | | |
| IVF • -VE 284 94.7 • +VE 16 5.3 Preterm • No 262 87.3 • Yes 38 12.7 PPROM • No 278 92.7 • Yes 22 7.3 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 Baby sex • Male 131 43.7 • Not 241 80.3 NICU • Needed 59 19.7 | Risks and co-morbidity | • | | 36 | 12.0 | | | | | |
| IVF +VE 16 5.3 Preterm No 262 87.3 • Yes 38 12.7 PPROM • No 278 92.7 • No 278 92.7 • Yes 22 7.3 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | | • | Anemia | 102 | 34.0 | | | | | |
| IVF +VE 16 5.3 Preterm No 262 87.3 • Yes 38 12.7 PPROM • No 278 92.7 • No 278 92.7 • Yes 22 7.3 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | | • | -VE | 284 | 94.7 | | | | | |
| • No 262 87.3 • Yes 38 12.7 • No 278 92.7 • Yes 22 7.3 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 Baby sex • Male 131 43.7 NICU • Not 241 80.3 • Needed 59 19.7 | IVE | • | +VE | | 5.3 | | | | | |
| • Yes 38 12.7 PPROM • No 278 92.7 • Yes 22 7.3 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | D (| • | No | 262 | 87.3 | | | | | |
| • No 278 92.7 • Yes 22 7.3 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | Preterm | • | Yes | 38 | | | | | | |
| • Yes 22 7.3 PPH • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | | • | | | | | | | | |
| • No 216 72.0 • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | PPROM | • | | | | | | | | |
| • Yes 84 28.0 MODE • NVD 154 51.3 • CS 146 48.7 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | DDU | • | | | | | | | | |
| MODE • NVD 154 51.3 • CS 146 48.7 • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | РРН | • | | | | | | | | |
| MODE • CS 146 48.7 Baby sex • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 | MODE | • | | | | | | | | |
| • Male 131 43.7 • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 • Survived 289 96.3 | MODE | • | | | | | | | | |
| Baby sex • Female 169 56.3 NICU • Not 241 80.3 • Needed 59 19.7 • Survived 289 96.3 | | | | | | | | | | |
| • Not 241 80.3 • Needed 59 19.7 • Survived 289 96.3 | Baby sex | | | | | | | | | |
| NICU • Needed 59 19.7 • Survived 289 96.3 | | | | | | | | | | |
| • Survivad 280 06.3 | NICU | | | | | | | | | |
| | | | Survived | 289 | 96.3 | | | | | |
| Mortality Died 11 3.7 | Mortality | | | | | | | | | |

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| Total | | 300 | 100.0 |
|--|------------|-----------------|--------------------|
| Age was significantly higher among | PLT was | s significantly | higher among |
| PROM cases but GA at the end was | PPROM c | ases but MPV | was significantly |
| significantly lower at PPROM group and | lower amo | ong PPROM ca | uses with no other |
| there was no significant difference | significan | ce between gro | ups (Table 2). |
| between groups regard GA at beginning. | - | - | - |

| Table (2): | Comparison between | ı both studied | l group | as regard | maternal, | gestational |
|-------------------|--------------------|----------------|---------|-----------|-----------|-------------|
| | ages and LAB paran | neters | | | | |

| Variable | No PPROM group (N = 278) | PPROM group (N = 22) | P - value |
|--------------|-----------------------------|-------------------------|-----------|
| Age | 26.74 ± 4.37 | 29.09 ± 4.56 | 0.016* |
| GA beginning | 12.28 ± 0.96 | 12.5 ± 1.26 | 0.327 |
| GA end | 37.81 ± 1.32 | 30.81 ± 1.59 | 0.00** |
| HB | 11.39±1.46 | 11.25±1.39 | 0.647 |
| WBCs | 8.42±1.11 | 8.1±1.66 | 0.179 |
| PLT | 245.24±41.46 | 285.13±50.11 | 0.00** |
| MPV | 9.07±0.45 | 8.51±0.34 | 0.00** |
| INR | 1.04±0.06 | 1.06±0.09 | 0.090 |
| Cr | 1.02±0.11 | 1.01±0.12 | 0.803 |

Previous PROM and positive family history were significantly positive correlated with PPROM cases with no other significant association or difference (Table 3).

| Table (3): | Comparison | between | both | studied | group | as | regard | clinical | and | obstetric |
|-------------------|------------|---------|------|---------|-------|----|--------|----------|-----|-----------|
| | history | | | | | | | | | |

| | Variable | | No PPROM group | PPROM group | X2 | Р |
|---------------|-----------------|---|----------------|-------------|-------|--------|
| | PG | Ν | 79 | 8 | | |
| | rG | % | 28.4% | 36.4% | | |
| | ≤2 | Ν | 142 | 6 | | |
| Douity | <u><u> </u></u> | % | 51.1% | 27.3% | 6.25 | 0.081 |
| Parity | 3-4 | Ν | 50 | 8 | 0.25 | 0.081 |
| | 3-4 | % | 18.0% | 36.4% | | |
| | > 4 | Ν | 7 | 0 | | |
| | >4 | % | 2.5% | 0.0% | | |
| | No | Ν | 233 | 7 | | |
| Previous PROM | INO | % | 83.8% | 31.8% | 34.44 | 0.00** |
| Previous PROM | Var | Ν | 45 | 15 | 34.44 | 0.00** |
| | Yes | % | 16.2% | 68.2% | | |
| | No | Ν | 202 | 8 | | |
| | | % | 72.7% | 36.4% | 10 50 | 0.00** |
| FH | Yes | Ν | 76 | 14 | 12.79 | 0.00** |
| | | % | 27.3% | 63.6% | | |
| | No | Ν | 101 | 6 | | |
| | | % | 36.3% | 27.3% | | |
| | | N | 48 | 7 | | |
| D : 1 | Passive smoker | % | 17.3% | 31.8% | 6.0 | 0.11 |
| Risk | DM | N | 36 | 0 | 6.0 | 0.11 |
| | DM | % | 12.9% | 0.0% | | |
| | | N | 93 | 9 | | |
| | Anemia | % | 33.5% | 40.9% | 1 | |
| | NI- | Ν | 263 | 21 | | |
| | No | % | 94.6% | 95.5% | 0.020 | 0.97 |
| IVF | Vag | Ν | 15 | 1 | 0.029 | 0.86 |
| | Yes | % | 5.4% | 4.5% | 7 | |

Preterm was significantly associated with PPROM also PPH was significantly associated with PPROM and CS as mode of delivery was significantly associated with PPROM. Birth weight and APGAR

score were significantly lower among PPROM cases and NICU also baby mortality were significantly associated with PPROM (**Table 4**).

| | Variable | | No PPROM group (N = 278) | PPROM group (N = 22) | P - value | |
|-------------------|--------------|-----|-----------------------------|-------------------------|-----------|---------|
| | No | Ν | 262 | 0 | | |
| Preterm | INO | % | 94.2% | 0.0% | 0.00** | |
| Preterm | Yes | Ν | 16 | 22 | 0.00*** | |
| | res | % | 5.8% | 100.0% | | |
| | No | Ν | 206 | 10 | | |
| PPH | INO | % | 74.1% | 45.5% | 0.004* | |
| rгп | Yes | Ν | 72 | 12 | 0.004* | |
| | res | % | 25.9% | 54.5% | | |
| | | Ν | 150 | 4 | | |
| Mode | NVD | % | 54.0% | 18.2% | 0.001** | |
| wiode | CS | Ν | 128 | 18 | 0.001*** | |
| | | % | 46.0% | 81.8% | | |
| Birtl | h weight (gn | n) | 3025.64±298.36 | 2015.9±226.45 | 0.00** | |
| | R score at 1 | | 7.19±0.84 | 6.27±1.24 | 0.00** | |
| APGA | R score at 5 | min | 8.59±0.73 | 7.72±1.38 | 0.00** | |
| | M | Ν | 125 | 6 | | |
| Baby | М | % | 45.0% | 27.3% | 0.107 | |
| gender | Б | Ν | 153 | 16 | 0.107 | |
| - | F | % | 55.0% | 72.7% | | |
| | N | Ν | 234 | 7 | | |
| NICU admission | No | % | 84.2% | 31.8% | .0.001* | |
| | V | Ν | 44 | 15 | <0.001* | |
| | Yes | % | 15.8% | 68.2% | 7 | |
| Mortality | Dial | Ν | 7 | 4 | | |
| | Died | % | 2.5% | 18.2% | -0.001* | |
| | Survived | | | 271 | 18 | <0.001* |
| | | % | 97.5% | 81.8% | 1 | |

 Table (4):
 Comparison between both studied group as regard maternal outcome and neonatal outcomes

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ROC Curve for PLT cutoff regards PPROM

Significant AUC with cutoff >258 with sensitivity 83.3% and specificity 75.0% (Figure 1).

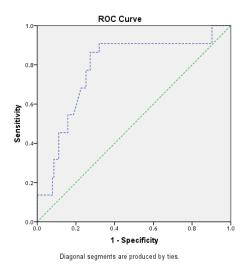


Figure (1): Area under curve, cutoff and validity of PLT and MPV regard detection of PPROM

| ſ | A 200 | Cutoff | D | 95% Confid | ence Interval | Sensitivity | Specificity |
|---|-------|--------|--------|-------------|---------------|-------------|-------------|
| | Area | Cuton | Γ | Lower Bound | Upper Bound | Sensitivity | specificity |
| | 0.783 | >258 | 0.00** | 0.680 | 0.885 | 83.3% | 75.0% |

ROC Curve for MPV cutoff regards PPROM

Significant AUC with cut off (Figure 2).

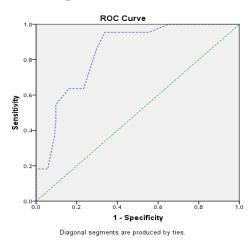


Figure (2): Area under curve, cutoff and validity of MPV regard detection of PPROM

| Amoo | Cutoff | D | 95% Confide | ence Interval | Sensitivity | Specificity |
|-------|--------|--------|-------------|---------------|-------------|-------------|
| Area | Cuton | Г | Lower Bound | Upper Bound | Sensitivity | specificity |
| 0.841 | <8.75 | 0.00** | 0.774 | 0.908 | 87.0% | 68.5% |

DISCUSSION

As regard age and gestational age distribution among the studied groups, the mean of the age was 26.89 ± 4.42 with minimum 19 and maximum 35 years; the Gestational age at the beginning was distributed as 12.3 ± 0.99 and at the end 37.3 ± 2.26 . In this study, majority of parity was ≤ 2 as it was represented 49.3% followed by 29.0% then 3-4 with 19.4% and finally >4 with 2.3%.

The study by *Al Riyami et al.* (2013) revealed that in order to reduce the risk of PPROM in future pregnancies, especially at extreme gestational age. In addition, the findings showed that women aged 30 years and older and nulliparous women were noted to be at an increased risk of extreme PPROM.

The obtained results by *Guseinova and Khodzhaeva* (2019) revealed a higher incidence of PPROM at 22-36 weeks gestation in first-time pregnant women, whereas PB with intact fetal membranes and term delivery were found among multiparous women. Most pregnant women with PB as a result of PPROM were in the most active reproductive age of 25-30 years (60%).

According to the results of the study of foreign scientists *Hailemariam et al.* (2017) and *Ibishi and Isjanovska* (2015), it was revealed that the peak of occurrence of PPROM in incomplete pregnancy in 43% of cases was noted at the age of 26-30 years.

In the study by *Lorthe et al.* (2018), it is concluded that with PPROM at 22–25 weeks' gestation, overall and for each GA at PPROM, nearly half of the fetuses were delivered within the first week. Obstetric management appears to be strongly influenced by GA at PPROM Overall. Also, PPROM at 22–25 weeks was associated with high frequencies of perinatal mortality and morbidity.

Both perinatal and childhood prognosis, related to all fetuses or to live born infants, significantly improved with advancing GA at PPROM. PROM is one of the causes of increased maternal and perinatal morbidity and mortality. The cause may not be known, but multiple risk factors abound (Lawan et al., 2019). As regard the clinical and obstetric history distribution, 20% of studied group had previous PROM, 30% had positive FH, 35.7% of studied group had no comorbidities, 34% had anemia and 18.3% had passive smoker and finally gestational DM was in 12%, only 5.3% had IVF.

Lawan et al. (2019) in his study found that past obstetric performance is an important risk factor for PROM, and in keeping with other studies, we found previous history of PROM to be highly predictive of subsequent PROM which supported our results.

In consistent with our study, *Caughey* et al. (2010) found that the risk of recurrence of PROM ranges from 16% to 32% when compared with 4% in women with previously uncomplicated pregnancy.

The recurrence of PROM may be associated with an underlying pathology or unforeseen genetic factor that has persisted in the subsequent pregnancies. A proper evaluation in to the possible cause of PROM and its subsequent elimination may change the course of future pregnancies. *Bouvier et al.* (2019) and *Whynott et al.* (2017) in their study confirmed the most known risk factors for PPROM, such as BMI <18.5 kg/m2, history of PPROM or prematurity, nulliparity, multiple pregnancies, low level of education, and infections. These results, as well as the percentage of PPROM (2.7%).

The American Association of Obstetricians and Gynecologists cited data according to which PPROM with history of PB increases the risk of "recurrence" of PPROM by 16-32% (American College of Obstetricians and Gynecologists, 2016).

According to the maternal outcome distribution among studied group, 12.7% had preterm labor, 7.3% had PPROM, 28% had PPH and 51.3% had NVD and CS was 48.7% and as regard the baby outcome distribution, female baby were 56.3% and male represent 43.7%, NCIU was needed by 19.7% regard survival 3.7% died and 96.3% survived.

Online with our study results, three retrospective studies, *Palmer et al.* (2017) and *Beckmann et al.* (2010) have shown that maternal outcomes (chorioamnionitis, mode of delivery) and neonatal outcomes (hospitalization in intensive care units, respiratory distress syndrome, intraventricular hemorrhage).

PROM accounts for 25-40% of all preterm deliveries that increase the risk of neonatal morbidity by 75%. In addition, improvement in survival may be associated with adverse long term sequels needing more treatment and NICU hospitalization. In accordance with our study, *Afrasiabi et al. (2014)* reported that there were 489 babies hospitalized in NICU for 1 to 54 days; 28.42% born were preterm, 308 with birth weight <2500

gram and 170 with birth weight between 2500 and 4000 gram.

In our study, age was significantly higher among PROM cases but GA at the end was significantly lower at PPROM group and there was no significant difference between groups regard GA at the beginning. In the study by Ibrahiem et (2020),there was statistically al. significant difference between the two groups as regards gestational age at latency delivery and period with significant increase in study group than The latency time between control. PPROM and delivery seems to be a key point to improve perinatal morbidity and mortality. Increase of this period could help attending physicians in PPROM management.

In agreement with those studies, *Luzi et al.* (2018) study showed a statistically significant increase (p = 0.04) of delivery gestational age.

The study by *Nageeb et al.* (2020) which supports our results found that the gestational age at ROM was significantly lower and the latent period was significantly shorter in patients delivering before 34 weeks of gestation (p-values <0.001).

As regard our study, Previous PROM and positive family history were significantly positive correlated with PPROM cases with no other significant association or difference.

In accordance with our study results, Assefa et al. (2018), Choudhary et al. (2015) and Tarek et al. (2012) showed that previous PROM to be the strongest risk factor for premature ruptures of membranes. Women who had previous PROM were 4.45 more likely to develop PROM with AOR 4.45 (CI: 1.87, 10.6). This might be due to untreated genitourinary infection and a short cervical length. In addition, obstetric problems are recurrent by nature.

In our study, preterm was significantly associated with PPROM also PPH was significantly associated with PPROM and CS as mode of delivery was significantly associated with PPROM. In the study by *Ibrahiem et al. (2020)*, there was statistically highly significant difference between the two groups regarding spontaneous delivery and cesarean section (CS) with low incidence of CS among study group (27.2%) and high incidence of CS among control group (44.1%) unlike our study results.

Our study is counteracting a study by *Kunze et al. (2016)* conducted on 1026 cases with PROM. In their study they reported a cesarean section rate of (27 %).

Our study showed that birth weight and APGAR score were significantly lower among PPROM cases and NICU also baby mortality were significantly associated with PPROM. The study by *Nageeb et al. (2020)* found that The Apgar score at 1 and 5 minutes as well as the birth weight were significantly lower in the group delivering before 34 weeks of gestation (p-values <0.001).

PROM accounts for 25-40% of all preterm deliveries that increase the risk of neonatal morbidity by 75%. In addition, improvement in survival may be associated with adverse long term sequels needing more treatment and NICU hospitalization. In accordance with our study, *Ibrahiem et al. (2020)* revealed significant relation between length of

neonatal NICU stay and maternal PROM. *Afrasiabi et al. (2014)* reported that there were 489 babies hospitalized in NICU for 1 to 54 days; 28.42% born were preterm, 308 with birth weight <2500 gram and 170 with birth weight between 2500 and 4000 gram. There was a (P=0.001) and significant relation between length of neonatal NICU stay and maternal PROM.

PLT was significantly higher among PPROM cases but MPV was significantly lower among PPROM cases with no other significance between groups. Tzur et al. (2013) investigated maternal leukocyte count in the first trimester of pregnancy and the risk for development of obstetric complications. In their study, a significant association observed between was leukocytosis during the first trimester and PPROM. According to these reports, it is evident that there is a strong relevance between levels of inflammation markers and occurrence of PPROM as a result of up regulated secretion by cytokines.

There are few reports about the relationship between MPV and morbidities among large cohorts of premature newborns. *Cekmez et al.* (2013) found that elevated MPV measured within2 h of birth was associated with BPD, IVH, and NEC using univariate analysis in 44 BPD, 42 IVH, and 21 NEC preterm newborns, but they did not perform multivariate analysis.

As regard the area under curve, cutoff and validity of PLT regard detection of PPROM, Significant AUC with cutoff >258 with sensitivity 83.3% and specificity 75.0%.

In the study by Ekin et al. (2015), The cut-off values of MPV ≤ 8.6 fL and platelet count $\geq 216 \times 103/\mu$ L predicted PPROM

with a sensitivity of 58% and 65%, a specificity of 62% and 44%, a positive predictive value of 56% and 49%, a negative predictive value of 64% and 60%, positive likelihood ratio of 1.56 and 1.16 and negative likelihood ratio of 0.66 and 0.8, respectively.

The overall accuracy of MPV for detecting PPROM was found to be platelet superior to count. Early identification in the first trimester of pregnancy of patients at risk of PPROM is great importance as preventive of interventions could be offered to these patients. The estimated detection rates of PPROM were mostly based on maternal characteristics and obstetric history. Among these, history of an earlier preterm labor or PPROM is the strongest risk factor (Toprak et al., 2017).

Early MPV decrement with a high platelet count in the prediction of PPROM can be explained by reactive thrombocytosis. It is a benign form of thrombocytosis secondary to medical or surgical conditions. According to this, there is an inverse relation between platelet count and MPV (*Ekin et al.*, 2015).

Approximately one half of PPROM cases are associated with intraamniotic infection, which are mostly subclinical in of nature. In cases intra-amniotic proinflammatory infection, and immunoregulatory cytokines are produced within the uterine cavity and then they reach the maternal circulation. Overproduction of cytokines, such as interleukin (IL)-4, IL-6 and tumor necrosis factor. influence platelet characteristics interfering by with megakaryopoiesis and subsequent release of predominantly small platelets from the bone marrow. Another evidence was about thrombopoietin, which is the major hormone that regulates platelet production by acting at earlier stages of megakaryopoiesis (*Nageeb et al., 2020*).

CONCLUSION

This is a second study that measures the predictability of PPROM with platelet count and MPV in maternal serum during the first trimester. We found that plasma MPV could be used as a more efficient indicator for an early diagnosis of PPROM than platelet count. Thus, our study can serve as a reference data for clinical practice in detecting those asymptomatic women with subclinical intra-amniotic infection at increased risk for PPROM and subsequent preterm delivery. MPV is a cheap, rapid and easily applicable test for determining the patients at risk for PPROM. Due to multifactorial origin of PPROM, early detection of all patients with a single test is rather difficult. In order to develop an accurate and efficient method in the estimation of the risk of PPROM, screening strategies combining MPV with other biological markers should be considered.

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دور عدد ومتوسط حجم الصفائح الدموية خلال الثلث الأول من الحمل في توقع التمزق المبكر لأغشية المحيطة بالجنين إبراهيم عبد الرحمن عبد الفتاح، عبد المنعم محمد زكريا، باسم رجب عبد العزيز، عمرو أحمد رزق*

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خلفية البحث: الأغشية الرقيق التى تحيط بالجنين مهم جدا للحف الخ على الجنين حتى تمام الحمل. ولحدوث الولادة الطبيعية بمرورة صحيحه يجب أن يحدث التمزق لهذه الأغشية فى ميعاد محدد عن اكتمال نمو الجنين.

الهدف من البحث: تقييم قيم عدد الصفائح الدموية و حجم الصفائح الدموية و حجم الصفائح الدموية و حجم الصفائح الدموية المستخلصة من دم الأمهات ودور ها فى توقع حدوث تَمَرُقُ الأَعْشِيَّةِ المُبْتَسَر المُبَكْر.

المريضات وطرق البحث: كانت هذه الدراسة عبارة عن دراسة جماعية استطلاعية أجريت على 300 حالة من النساء الحوامل في قسم النساء والولادة بمستشفى الحسين الجامعي. استوفى جميع المرضى معايير التضمين وتم تقسيمهم إلى مجموعتين ، المجموعة الأولى: وتشمل 22 من السيدات الحوامل لديهم تاريخ مرضي لحدوث تسرب لسوائل عن طريق المهبل قبل الأسبوع السابع والتلاثين وتم تشخيصه على أنه تمَزُقُ الأَغْشِيَّةِ المُبْتَسَر المُبَكُر . المجموعة الثانية: وتشمل 27 من السيدات الحوامل مع عمر حمل يتراوح بين 75 – 41 أسبوع مع عدم وجود أى تاريخ مرضاي له مشاكل او مضاعات خلال فترة الحمل.

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نت المج البحث: فيما يتعلق بالمنطقة الواقعة تحت المنحنى والقطع وصلحية الكشف عن تمزق الأغشية المبتسر المبكر فيما يتعلق بالكشف عن تمزق الأغشية المبتسر المبكر، فإن AUC مهم مع قطع> 258 مع حساسية 83.3٪ ونوعية 75.0٪. تم العثور على الدقة الكلية لحجم الصفائح الدموية للكشف عن تمزق الأغشية المبتسر المبكر لتكون أعلى من عدد الصفائح الدموية.

الإستنتاج: يمكن استخدام متوسط حجم المسفائح الدموية البلازمي كمؤشر أكثر كفاءة للتشخيص المبكر للتمزق الأغشية المبتسر المبكر من عدد الصفائح الدموية وذلك مقارنة بعدد الصفائح الدموية. حيث يمكن استخدامها لتشخيص وجود التهابات وعدوات بكتيرية داخل السائل الأمنيوسي.

الكلمات الدالة: تمرزق الأغشية المبتسر المبكر, عدد المسفائح الدموية, حجم الصفائح الدموية,