*Asian Research Journal of Gynaecology and Obstetrics*

***Volume 7, Issue 1, Page 94-105, 2024; Article no.ARJGO.115845***

# Risk Factors of Premature Rupture of the Membranes: Case Control Study

**Salwa Benkia [a++*], Nagat Bettamer [b++], Amna Attia Fadel [a++], Enas R. Haleis [a++] and Tamadur Abdelnabi Abubakr [c#]**

*[a] Department of Obstetrics and Gynecology, Benghazi Medical Center, Faculty of Medicine, University of Benghazi, Libya.*
*[b] Department of Obstetrics and Gynecology, Al-Jamhoria Hospital, Faculty of Medicine, University of Benghazi, Libya.*
*[c] Benghazi Medical Center, Libya.*

***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

***Article Information***

**Open Peer Review History:**
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/115845

***Original Research Article***

***Received: 07/02/2024***
***Accepted: 10/04/2024***
***Published: 23/04/2024***

## ABSTRACT

**Background:** premature rupture of the membranes is a common condition with large contribution to preterm delivery and serious maternal and fetal morbidities. Aims: To investigate the risk factors of preterm premature rupture of membrane.
**Methods:** Case–control study included a review of records of sample cases delivered in Benghazi medical center during the year 2021. Statistical analysis was done using SPSS 23.0 with appropriate tests.
**Results:** A total of 120 participants were enrolled with 60 patients in each group. Maternal age was statistically significant only when considering categories. The rate of mothers in advanced maternal age was in case group,23.3% and for the control group, 43.3%. Also, a higher proportion of

*[++] Consultant;*
*[#] SHO;*
**Corresponding author: E-mail: alzwai2010@yahoo.com;*

nullipara among a group of cases; 30.0% and Control; 13.3%, higher rate of mothers with previous caesarean was found among case group (31.7% against 10.0%), vaginal discharge was reported among all of cases (100.0%) while rate among controls was only 45.0% and high CRP was reported only among case group in a proportion of 23.3% but not among the control group. Those differences were all statistically significant. Blood group and Rhesus factor, history of abortion among controls, urinary tract infection, early pregnancy bleeding and male fetus had statistically insignificant differences.

**Conclusion and Recommendations:** Premature rupture of the membranes is associated with primiparity, history of vaginal discharge and clinical as well as laboratory manifestations of inflammation and further multicenter prospective study to verify outcomes of premature rupture of membranes are recommended.

*Keywords: Risk factors of premature rupture; preterm prelabor rupture; genital infections; maternal inflammatory; prevent preterm birth; preterm births.*

## 1. INTRODUCTION

"Preterm prelabor rupture of the membranes (PPROM) is defined as rupture of the fetal membranes prior to 37 weeks of completed gestation. This significant obstetric problem occurs in about 3-4% of all pregnancies and is directly associated with 40% to 50% of all preterm births" [1, 2].

"It increases the risk of prematurity and leads to several other perinatal and neonatal complications, including a 1 to 2 percent risk of fetal death" [3].

"One of the most common complications of preterm PROM is early delivery. The latent period, which is the time from membrane rupture until delivery, generally is inversely proportional to the gestational age at which PROM occurs" [3].

"When PROM occurs too early, surviving neonates may develop sequelae such as malpresentation, cord compression, oligohydramnios, necrotizing enterocolitis, neurologic impairment, intraventricular haemorrhage, and respiratory distress syndrome" [3].

"The number of pPROM cases exceeds that of preeclampsia and gestational diabetes and other iatrogenic preterm births. In addition, neonatal mortality and morbidities are higher in pPROM group than any other subclasses of preterm births. Yet, pPROM is an often -ignored and understudied adverse outcome of pregnancy. Despite remarkable improvements in prenatal care over the past three decades, rates of pPROM and subsequent preterm delivery have worsened" [4].

"Regarding the pathophysiology of PROM, almost half of all preterm births are caused or triggered by an inflammatory process at the feto-maternal interface resulting in preterm labour or rupture of membranes with or without chorioamnionitis ("first inflammatory hit"). Preterm babies have highly vulnerable body surfaces and immature organ systems. They are postnatally confronted with a drastically altered antigen exposure including hospital-specific microbes, artificial devices, drugs, nutritional antigens, and hypoxia or hyperoxia ("second inflammatory hit")" [5].

"The diagnosis of PROM requires a thorough history, physical examination, and selected laboratory studies. Patients often report a sudden gush of fluid with continued leakage. Physicians should ask whether the patient is contracting, bleeding vaginally, has had intercourse recently, or has a fever. It is important to verify the patient's estimated due date because this information will direct subsequent treatment" [1].

"The physician should perform a speculum examination to evaluate if any cervical dilation and effacement are present. When preterm PROM is suspected, it is important to avoid performing a digital cervical examination; such examinations have been shown to increase morbidity and mortality" [1].

"If PROM occurs during term, immediate delivery is recommended, as it is associated with a significantly lower perinatal morbidity rate than expectant management" [6–9].

"However, the management of women with preterm PROM (PPROM), accounting for 40% of the total preterm deliveries, is somewhat

controversial. Immediate delivery may lead to complications resulting from fetal immaturity, but expectant management is associated with risks such as placenta abruptio, infection, fetal distress, and umbilical cord prolapse, causing a medical dilemma" [7, 10, 11].

"In early PPROM, defined as PROM before 34.0 weeks of gestation, expectant management is strongly recommended because of adverse neonatal outcomes from prematurity. In a study by Ekin et al., although complications such as chorioamnionitis and placental abruption were increased, the overall adverse pregnancy outcomes were decreased in women managed expectantly" [12].

"The optimal management of late PPROM, defined as PROM between 34.0 weeks and 36.6 weeks of gestation, remains inconclusive. Therefore, the management of late PPROM should be determined on the basis of a comprehensive acknowledgment of the risk of infection and possible complications from premature delivery. According to the 2018 American College of Obstetricians and Gynecologists (ACOG) guidelines, expectant management, including a combination therapy of intravenous ampicillin and erythromycin, administration of antenatal corticosteroids until 34.0 weeks of gestation and group B Streptococcus prophylaxis, is strongly recommended" [6, 13].

"The guidelines recommend prompt delivery after 34.0 weeks of gestation. However, the Cochrane review mentioned the lack of clinical evidence to support these guidelines" [7, 13].

## 2. REVIEW OF THE LITERATURE

"The etiology of PPROM is unclear. PPROM may be caused by cervical incompetence, genital infections, and uterine abnormality. Some studies have shown that a history of PPROM, race, smoking status, poor nutrition, and genital infection are risk factors for PPROM" [14].

"The etiologies of genital infection include *Chlamydia trachomatis* (CT), *Ureaplasma urealyticum* (UU), *Candida albicans*, syphilis, *Neisseria gonorrhoea* (NG), group B streptococci (GBS), herpes simplex virus (HSV), and bacterial vaginosis (BV)" [15].

"Genital infections might cause a release of cytokines and other inflammatory mediators that may weaken the membrane and cause PPROM. Studies by Chow and Blas showed that CT infection was associated with the occurrence of PPROM" [16, 17].

"Pregnant women with BV more readily developed PPROM than women without BV" [16 – 19].

"Candidiasis infection in pregnant women with PPROM is controversial, and a recent study showed that the treatments for candidiasis might reduce the incidence of PPROM" [20].

"Pregnant women who were infected with NG had a six-time higher risk of developing PPROM than women without NG infection. GBS might cause the activation of inflammatory cells in fetal membranes, which could lead to PPROM" [18, 21].

According to Bouvier D et al (2019) "The specific risk factors for PPROM were body mass index (BMI) <18.5 kg/m$^2$, history of PPROM, nulliparity, gestational diabetes, and low level of education". [22]

Watts DH et al (1991) [23] determined "CRP levels serially from 22 weeks' gestation until delivery in healthy pregnant women without antepartum complications; the median hs-CRP values ranged from 0.7–0.9 mg/dL for women who were not in labour and showed no significant change in serum levels of hs- CRP according to the gestational age".

Moghaddam Banaem L et al (2012) [24] found "a significant relationship between elevated maternal serum hs-CRP levels in the first 20 weeks of pregnancy and the later occurrence of preterm premature rupture of membranes (PPROM) andpreterm birth as well".

Nevertheless, a recent meta-analysis by Etyang AK et al [25] showed that "the sensitivity and specificity for CRP ≥ 20 mg/L (5 studies, 252 participants) was 59% (95% CI 48-69) and 83% (95% CI 74-89) respectively". So, the use of CRP for predicting PPROM is limited.

### 2.1 Aims of the Study

To investigate the demographic and clinical risk factors for preterm premature

rupture membranes among the Libyan patients.

## 3. METHODOLOGY

### 3.1 Design of Study and Settings

Case control study in mothers admitted for delivery to labour room in Al Jamhoria hospital / Benghazi medical center BMC during the period of the year 2021.

### 3.2 Groups of the Study

Group of cases were randomly selected cases of preterm premature rupture of the membranes.

Group of controls were mothers delivered normally without significant complications at the same time.

### 3.3 Data Synthesis

Review of records for all patients with premature rupture of the membrane deliveries according to preformed data sheet includes data related to demographic and personal characteristics, past history, the present delivery.

### 3.4 Variables

Maternal age Parity
Blood group Rh factor status
History of obstetric conditions.
History of vaginal discharge
History of urinary tract infection.
History of early pregnancy bleeding.
Vital signs
CRP (c-reactive protein)

### 3.5 Statistical Analysis

Data were analyzed using the statistical package for social science (SPSS) version 23. Descriptive statistics as frequency and percentage.

Inferential statistics were used when needed Chi-square($X^2$), t test and Mann-Whitney U test to find the difference in the distribution of the variables between the two groups, *P*-value were considered significant when ≤ 0.05.

Data were presented in form of tables and figures, which were the figures done by Microsoft Excel 2010.

## 4. RESULTS AND DISCUSSION

A total of 120 participants were enrolled with 60 patients in each group. All of the cases in case group were diagnosed with a history of painless leaking and positive speculum examination.

### 4.1 Demographic and Other Risk Factors

Maternal age tends to be lower among cases and the rate of advanced maternal age is higher among controls. The difference was statistically significant. See Fig. 1 and Table 1.

Parity is also less among cases and a higher proportion of nullipara among this group. The difference was statistically significant. See Fig. 2 and Table 2.

Larger proportion of mothers with a history of abortion among controls, but the difference was not statistically significant. See Table 3.

Higher rate of mothers with previous was found among case group. The difference was statistically significant. See Table 4.

### 4.2 Clinical Characteristics

Most of cases (41/60; 68.3%) had duration of leaking < 72 hours.

**Table 1. Group and advanced maternal age**

| | | | Advanced maternal age | | |
|---|---|---|---|---|---|
| | | | **Yes** | **No** | **Total** |
| **Group** | **Case** | Count | 14 | 46 | 60 |
| | | % within Group | 23.3% | 76.7% | 100.0% |
| | **Control** | Count | 26 | 34 | 60 |
| | | % within Group | 43.3% | 56.7% | 100.0% |
| **Total** | | Count | 40 | 80 | 120 |
| | | % within Group | 33.3% | 66.7% | 100.0% |

*Pearson Chi-Square; 5.400; P = 0.020*

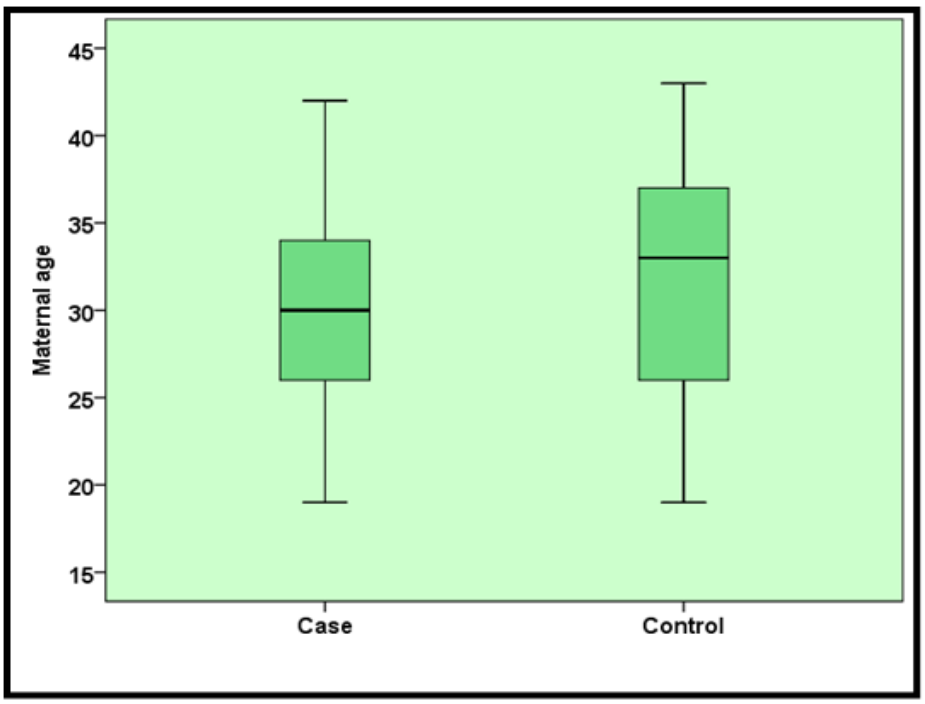


**Fig. 1. Comparison of maternal age across study groups**
*Case; Mean 30.53 (SD 5.622), Median 30.00 Range19 - 42*
*Control; Mean 31.92 (SD 6.692), Median 33.00 Range 19 - 43*

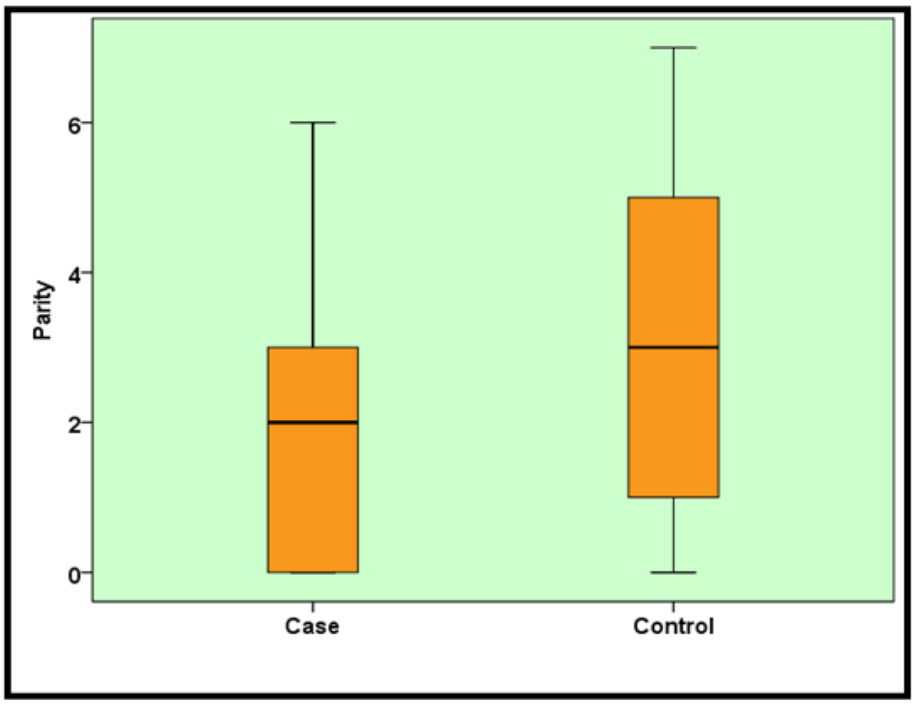


**Fig. 2. Comparison of parity across study groups**
*Case; Mean 1.83 (SD 1.719), Median 2.00 Range 0 - 6*
*Control; Mean 3.07 (SD 2.193), Median 3.00, Range 0 - 7*
*Mann-Whitney U; 1212.5, P 0.002*

**Table 2. Group and primi**

| | | | Primi | | |
|---|---|---|---|---|---|
| | | | **Yes** | **No** | **Total** |
| **Group** | **Case** | Count | 18 | 42 | 60 |
| | | % within Group | 30.0% | 70.0% | 100.0% |
| | **Control** | Count | 8 | 52 | 60 |
| | | % within Group | 13.3% | 86.7% | 100.0% |
| **Total** | | Count | 26 | 94 | 120 |
| | | % within Group | 21.7% | 78.3% | 100.0% |
| *Pearson Chi-Square; 4.910 0.027* | | | | | |

**Table 3. Group and any abortions**

| | | | Any abortions | | |
|---|---|---|---|---|---|
| | | | **Yes** | **No** | **Total** |
| **Group** | **Case** | Count | 16 | 44 | 60 |
| | | % within Group | 26.7% | 73.3% | 100.0% |
| | **Control** | Count | 19 | 41 | 60 |
| | | % within Group | 31.7% | 68.3% | 100.0% |
| **Total** | | Count | 35 | 85 | 120 |
| | | % within Group | 29.2% | 70.8% | 100.0% |
| | | *Pearson Chi-Square* | *.363* | *0.547* | |

**Table 4. Group and any previous scars**

| | | | Any previous scars | | |
|---|---|---|---|---|---|
| | | | **Yes** | **No** | **Total** |
| **Group** | **Case** | Count | 19 | 41 | 60 |
| | | % within Group | 31.7% | 68.3% | 100.0% |
| | **Control** | Count | 6 | 54 | 60 |
| | | % within Group | 10.0% | 90.0% | 100.0% |
| **Total** | | Count | 25 | 95 | 120 |
| | | % within Group | 20.8% | 79.2% | 100.0% |
| *Pearson Chi-Square;8.539;P = 0.003* | | | | | |

**Table 5. Group and Maternal blood group**

| | | | Maternal blood group | | | | |
|---|---|---|---|---|---|---|---|
| | | | **A** | **B** | **AB** | **O** | **Total** |
| **Group** | **Case** | Count | 24 | 11 | 1 | 24 | 60 |
| | | % within Group | 40.0% | 18.3% | 1.7% | 40.0% | 100.0% |
| | **Control** | Count | 31 | 9 | 2 | 18 | 60 |
| | | % within Group | 51.7% | 15.0% | 3.3% | 30.0% | 100.0% |
| **Total** | | Count | 55 | 20 | 3 | 42 | 120 |
| | | % within Group | 45.8% | 16.7% | 2.5% | 35.0% | 100.0% |
| | | *Pearson Chi-Square* | *2.281* | *0.516* | | | |

Gestational diabetes was reported only among cases in small proportion. The difference was statistically insignificant. See Table 7.

Vaginal discharge was reported among cases in higher rates than controls. The difference was statistically significant. See Table 8.

Urinary tract infection and also early pregnancy bleeding were reported in higher rate among cases, but the difference was not statistically significant.See Tables 9 and 10.

Fever and tachycardia were only documented among cases not in controls. The difference was statistically significant. See Figs. 3 and 4.

CRP was only elevated among case group but not in control group. The difference was statistically significant. See Table 11.

### 4.3 Gender of the Baby

Male gender of the neonate is higher among case group than in control group. The difference w PPROM has unclear etiology. PPROM may be caused by multiple of factors that involve inflammatory conditions [14].

The present study investigated total of enrolled 120 participants with 60 patients in each group. All of the cases in case group were diagnosed with history of painless leaking and positive speculum examination.

**Table 6. Group and maternal Rh**

| | | | Maternal Rh | | |
|---|---|---|---|---|---|
| | | | **Rh +** | **Rh -** | **Total** |
| **Group** | **Case** | Count | 55 | 5 | 60 |
| | | % within Group | 91.7% | 8.3% | 100.0% |
| | **Control** | Count | 53 | 7 | 60 |
| | | % within Group | 88.3% | 11.7% | 100.0% |
| **Total** | | Count | 108 | 12 | 120 |
| | | % within Group | 90.0% | 10.0% | 100.0% |
| | | *Pearson Chi-Square* | *0.370* | *0.543* | |

**Table 7. Group and GDM**

| | | | GDM | | |
|---|---|---|---|---|---|
| | | | **GDM** | **No GDM** | **Total** |
| **Group** | **Case** | Count | 2 | 58 | 60 |
| | | % within Group | 3.3% | 96.7% | 100.0% |
| | **Control** | Count | 0 | 60 | 60 |
| | | % within Group | 0.0% | 100.0% | 100.0% |
| **Total** | | Count | 2 | 118 | 120 |
| | | % within Group | 1.7% | 98.3% | 100.0% |
| | | *Fisher's exact test P = 0.496* | | | |

**Table 8. Group and vaginal discharge**

| | | | Vaginal discharge | | |
|---|---|---|---|---|---|
| | | | **Reported** | **Not reported** | **Total** |
| **Group** | **Case** | Count | 60 | 0 | 60 |
| | | % within Group | 100.0% | 0.0% | 100.0% |
| | **Control** | Count | 27 | 33 | 60 |
| | | % within Group | 45.0% | 55.0% | 100.0% |
| **Total** | | Count | 87 | 33 | 120 |
| | | % within Group | 72.5% | 27.5% | 100.0% |
| | | *Pearson Chi-Square* | *45.517* | *P <0.001* | |

**Table 9. Group and UTI**

| | | | UTI | | |
|---|---|---|---|---|---|
| | | | **Reported** | **Not reported** | **Total** |
| **Group** | **Case** | Count | 22 | 38 | 60 |
| | | % within Group | 36.7% | 63.3% | 100.0% |
| | **Control** | Count | 18 | 42 | 60 |
| | | % within Group | 30.0% | 70.0% | 100.0% |
| **Total** | | Count | 40 | 80 | 120 |
| | | % within Group | 33.3% | 66.7% | 100.0% |
| | | *Pearson Chi-Square* | *0.600* | *P = 0.439* | |

**Table 10. Group and early pregnancy bleeding**

| | | | Bleeding | | |
|---|---|---|---|---|---|
| | | | Reported | Not reported | Total |
| **Group** | **Case** | Count | 3 | 57 | 60 |
| | | % within Group | 5.0% | 95.0% | 100.0% |
| | **Control** | Count | 0 | 60 | 60 |
| | | % within Group | 0.0% | 100.0% | 100.0% |
| **Total** | | Count | 3 | 117 | 120 |
| | | % within Group | 2.5% | 97.5% | 100.0% |

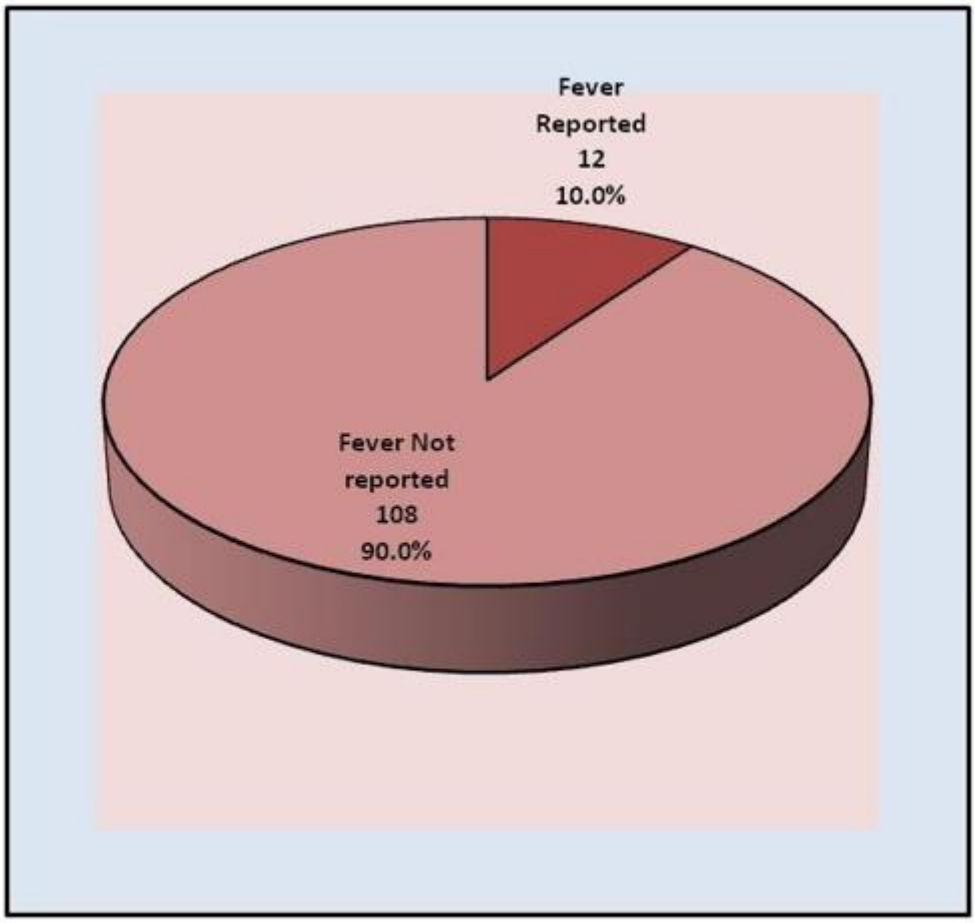


**Fig. 3. Distribution of PROM cases according to fever**
*X 2 = 13.3, P < 0.001*

**Table 11. Group and high CRP**

| | | | CRP High | | |
|---|---|---|---|---|---|
| | | | YES | NO | Total |
| | **Case** | Count | 14 | 46 | 60 |
| | | % within Group | 23.3% | 76.7% | 100.0% |
| | **Control** | Count | 0 | 60 | 60 |
| **Group** | | % within Group | 0.0% | 100.0% | 100.0% |
| | | Count | 14 | 106 | 120 |
| **Total** | | % within Group | 11.7% | 88.3% | 100.0% |

*Pearson Chi-Square 15.849 P <0.001*

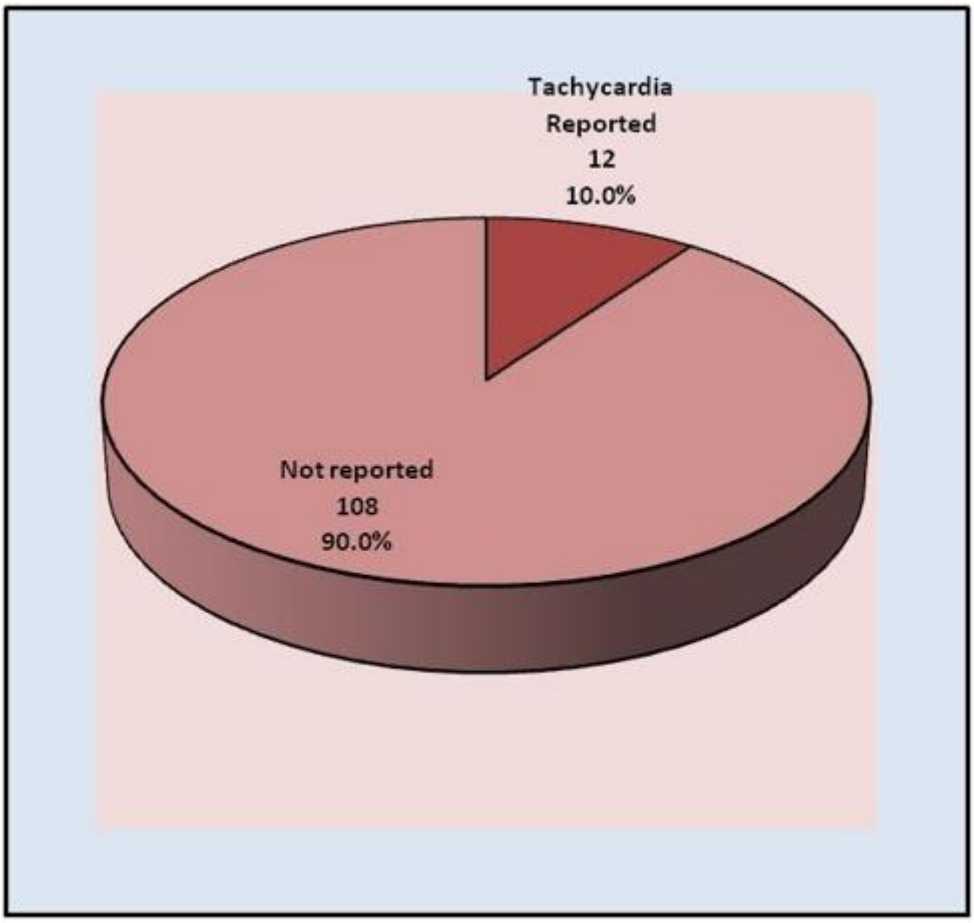


**Fig. 4. Distribution of PROM cases according to tachycardia**
*X 2 = 13.3, P < 0.001*

**Table 12. Group and Gender of the baby**

| | | | Gender | | |
|---|---|---|---|---|---|
| | | | **Male** | **Female** | **Total** |
| **Group** | **Case** | Count | 42 | 18 | 60 |
| | | % within Group | 70.0% | 30.0% | 100.0% |
| | **Control** | Count | 33 | 27 | 60 |
| | | % within Group | 55.0% | 45.0% | 100.0% |
| **Total** | | Count | 75 | 45 | 120 |
| | | % within Group | 62.5% | 37.5% | 100.0% |
| | | *Pearson Chi-Square* | *2.880* | *P = 0.09* | |

Maternal age tends to be lower among cases and rate of advanced maternal age is higher among controls; Case group: Mean 30.53 years (SD 5.622), Median 30.00 and for Control group: Mean 31.92 years (SD 6.692), *P* 0.180. The difference was statistically significant only when considering categories. The rate was in Case, 23.3% and for Control group, 43.3%*; P* = 0.020 Parity is also less among cases and a higher proportion of nullipara among this group. Case; 30.0% and Control; 13.3%. the difference is satatistically significant; *P* = 0.027. This confirms the finding of Bouvier D et al [22] which concluded primiparity as a risk factor for PPROM.

Also comparison of parity as a scale parameter showed significant difference, Casegroup; Mean 1.83 (SD 1.719) and in Control group; Mean 3.07 (SD2.193). The difference was statistically significant *; P* = 0.002. The cause of this association is not yet clear. Anyhow, immune relatedmechanisms may partially explain this.

Larger proportion of mothers with history of abortion among controls, but the difference was not statistically significant.

Higher rate of mothers with previous caesarean was found among case group (31.7% against 10.0%). The difference was statistically significant; *P* = 0.003.

Maternal blood group and maternal Rh factor didn't show any significant association.

Regarding clinical characteristics, most of cases (41/60; 68.3%) had duration of leaking < 72 hours.

Gestational diabetes was reported only among cases in small proportion. The difference was statistically insignificant. This is discordant with Bouvier D et al (2019) [22] which stated GDM as a risk factor for PPROM. The smaller sample size and the probably under diagnosed GDM might be the cause.

Vaginal discharge was reported among all of cases (100.0%) while rate among controls was only 45.0%. The difference was statistically significant (*P* < 0.001). this is concordant with several studies demonstrated that genital infections might cause a release of cytokines and other inflammatory mediators that may weaken the membrane and cause PPROM. Pregnant women with BV more readily developed PPROM than women without BV [15 – 19].

As a consequence of infection, fever and tachycardia were only documented among cases (20.0% for each) not in controls. The difference wasstatistically significant (*P* < 0.001).

Regarding CRP which is known inflammatory marker for several conditions and at cut-off level of 10 mg/L it was reported only among case group in a proportion of 23.3% but not among control group; *P* <0.001. this is concordant with Moghaddam Banaem L et al (2012) [24] and Kahyaoğlu S et al (2014) [25]. Anyhow, the sensitivity and specificity by the present study seems less than described by Etyang AK et al [25] in their meta-analysis. This might put limitation for the reliability of use of CRP.

Urinary tract infection and also early pregnancy bleeding were reported in higher rate among cases, but the difference was not statistically significant.

Male gender of the neonate was higher among case group than in control group (70.0% versus 55.0%). The difference anyhow, was not statistically significant.

The limitations of the present study included retrospective design and difficulty in gathering complete data. Further large multicenter studies with prospective design and use of high sensitivity (hs) CRP as well as other inflammatory markers in sum to clinical predictors and outcome utility estimation are to be considered.

## 5. CONCLUSION AND FUTURE RECOMMENDATIONS

### 5.1 Conclusion

Premature rupture of the membranes is associated with primiparity, history of vaginal discharge and clinical as well as laboratory manifestations of inflammation.

### 5.2 Recommendations

Enhancing clinical and laboratory evaluating of primigravida mothers before within the time before term to expect PPROM and avoid complications.

Multicenter prospective study to verify risk factors and outcomes of premature rupture of the membrane cases in the Libyan population.

## CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Naeye RL, Peters EC. Causes and consequences of premature rupture of fetal membranes. Lancet. 1980;1(8161):192–194.

2. Mercer BM, Crouse DT, Goldenberg RL, et al. The antibiotic treatment of PPROM study: systemic maternal and fetal markers and perinatal outcomes. American Journal of Obstetrics and Gynecology. 2012;206(2)
3. Medina TM, Hill DA. Preterm premature rupture of membranes: diagnosis and management. Am Fam Physician. 2006 Feb 15;73(4):659-64. PMID: 16506709.
4. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet. 2008;371(9606):75–84.
5. Humberg A, Fortmann I, Siller B, Kopp MV, Herting E, Göpel W, Härtel C; German Neonatal Network, German Center for Lung Research and Priming Immunity at the beginning of life (PRIMAL) Consortium. Preterm birth and sustained inflammation: consequences for the neonate. Semin Immunopathol. 2020;42 (4):451-468.
DOI: 10.1007/s00281-020-00803-2. Epub 2020 Jul 13. PMID: 32661735; PMCID: PMC7508934.
6. Committee on Practice Bulletins-Obstetrics. ACOG practice bulletin No. 188: prelabor rupture of membranes. Obstet Gynecol. 2018;131:e1–14.
7. Bond DM, Middleton P, Levett KM, van der Ham DP, Crowther CA, Buchanan SL, et al. Planned early birth versus expectant management for women with preterm prelabour rupture of membranes prior to 37 weeks' gestation for improving pregnancy outcome. Cochrane Database Syst Rev. 2017;3:CD004735.
8. Chandra I, Sun L. Third trimester preterm and term premature rupture of membranes: is there any difference in maternal characteristics and pregnancy outcomes? J Chin Med Assoc. 2017;80: 657–661.
9. Morris JM, Roberts CL, Bowen JR, Patterson JA, Bond DM, Algert CS, et al. Immediate delivery compared with expectant management after preterm pre-labour rupture of the membranes close to term (PPROMT trial): A randomised controlled trial. Lancet. 2016;387:444–452.
10. Ramsey PS, Nuthalapaty FS, Lu G, Ramin S, Nuthalapaty ES, Ramin KD. Contemporary management of preterm premature rupture of membranes (PPROM): a survey of maternal-fetal medicine providers. Am J Obstet Gynecol. 2004;191:1497–1502.
11. Goldenberg RL, Nelson KG, Davis RO, Koski J. Delay in delivery: Influence of gestational age and the duration of delay on perinatal outcome. Obstet Gynecol. 1984;64:480–484.
12. Ekin A, Gezer C, Taner CE, Ozeren M, Uyar I, Gulhan I. Risk factors and perinatal outcomes associated with latency in preterm premature rupture of membranes between 24 and 34 weeks of gestation. Arch Gynecol Obstet. 2014;290: 449–455.
13. Tsakiridis I, Mamopoulos A, Chalkia-Prapa EM, Athanasiadis A, Dagklis
14. T. Preterm premature rupture of membranes: a review of 3 national guidelines. Obstet Gynecol Surv. 2018;73: 368–375.
15. Luo X, Pan J, Wang L, Wang P, Zhang M, Liu M, et al. Epigenetic regulation of lncRNA connects ubiquitin-proteasome system with infection- inflammation in preterm births and preterm premature rupture of membranes. BMC Pregnancy Childbirth. 2015;15:35.
16. Ferrazzi E, Muggiasca ML, Fabbri E, Fontana P, Castoldi F, Lista G, et al. Assessment of fetal inflammatory syndrome by “classical” markers in the management of preterm labor: A possible lesson from metabolomics and system biology. J Matern Fetal Neonatal Med. 2012;25:54–61.
17. Chow JM, Kang MS, Samuel MC, Bolan G. Assessment of the association of *Chlamydia trachomatis* infection and adverse perinatal outcomes with the use of population-based chlamydia case report registries and birth records. Public Health Rep. 2009;124(Suppl 2):24–30.
18. Blas MM, Canchihuaman FA, Alva IE, Hawes SE. Pregnancy outcomes in women infected with *Chlamydia trachomatis*: A population-based cohort study in Washington State. Sex Transm Infect. 2007;83:314–8.
19. Li W, Han L, Yu P, Ma C, Wu X, Moore JE, et al. Molecular characterization of skin microbiota between cancer cachexia patients and healthy volunteers. Microb Ecol. 2014;67:679–89.
20. Ganor-Paz Y, Kailer D, Shechter-Maor G, Regev R, Fejgin MD, Biron- Shental T, et al. Obstetric and neonatal outcomes after preterm premature rupture of membranes among women carrying group B

streptococcus. Int J Gynaecol Obstet. 2015;129:13–6.
21. Roberts CL, Rickard K, Kotsiou G, Morris JM. Treatment of asymptomatic vaginal candidiasis in pregnancy to prevent preterm birth: An open-label pilot randomized controlled trial. BMC Pregnancy Childbirth. 2011;11:18.
22. Mercer BM. Preterm premature rupture of the membranes: Diagnosis and management. Clin Perinatol. 2004;31:765–82, vi.
23. Forest JC, Blanchon L, Bujold E, Pereira B, Bernard N, Gallot D, Sapin V, Giguère Y. Risk Factors and Outcomes of Preterm Premature Rupture of Membranes in a Cohort of 6968 Pregnant Women Prospectively Recruited. J Clin Med. 2019;8(11):1987
24. Watts DH, Krohn MA, Wener MH, Eschenbach DA. C-reactive protein in normal pregnancy. Obstet Gynecol. 1991;77:176–80.
25. Moghaddam Banaem L, Mohamadi B, Asghari Jaafarabadi M, Aliyan Moghadam N. Maternal serum C-reactive protein in early pregnancy and occurrence of preterm premature rupture of membranes and preterm birth. J Obstet Gynaecol Res. 2012;38:780–6.
26. Kahyaoğlu S, Timur H, Eren R, Kahyaoğlu I, Eyi EG, Engin-Üstün Y. Can maternal serum C-reactive protein levels predict successful labour induction with intravenous oxytocin in term pregnancies complicated with premature rupture of the membranes? A cross-sectional study. J Turk Ger Gynecol Assoc. 2014;15(1):36-40.
27. Etyang AK, Omuse G, Mukaindo AM, Temmerman M. Maternal inflammatory markers for chorioamnionitis in preterm prelabour rupture of membranes: a systematic review and meta-analysis of diagnostic test accuracy studies. Syst Rev. 2020;9(1):141.



*Peer-review history:*
*The peer review history for this paper can be accessed here:*
*https://www.sdiarticle5.com/review-history/115845*