



The role of C-reactive protein in the diagnosis of preterm premature rupture of membrane

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Abstract

Background:Preterm birth is the leading cause of neonatal mortality and morbidity in the developed countries. Preterm labor is also the most common reason for antenatal hospitalization of pregnant women, which is associated with socio-economical burdens to the society.

Aim of the Study: The study aimed at evaluating the role of CRP in in the perdition of PPRM and PID in pregnant women

Patients and methods: This is a comparative study that was conducted in the Department of Obstetrics and Gynecology of Salah Al-Din General Hospital from 1st of December 2021 through April 2022.The study included 50 pregnant women presented with PPRM and attending the department of Obstetrics and Gynecology who had Singleton viable pregnancy with a gestational age ranging from 28- 36⁺⁶ weeks depending on accurate last menstrual period and / or by early ultrasonography. They were informed about the nature of the study and verbal consent was obtained from them. The study also included 50 pregnant women without any complaint as control groups. Detailed history was obtained. General and systemic examinations were done. Blood samples collected from each subject enrolled in this study for determination of ESR, WBCs counts and C-reactive protein.

Results:The study revealed that the mean of CRP was elevated significantly in women with PPRM (11.76 mg/dl) as compared with the control group (4.34 mg/dl) at P. value <0.05. The study also showed that the high mean of WBC and ESR recorded among PPRM women as compared with the control group.The study showed that, 40% of PPRM women in the current study were with short cervical length , 30% were with Low socioeconomic conditions, 30% with uterine overdistension, 20% with Previous preterm birth, 16% with Sexually transmitted infections, , 18% with Vaginal bleeding and 6% were Smoker.

Conclusion:The study concluded that The study revealed that the mean of CRP, WBC and ESR recorded among PPRM women as compared with the control group.

Keywords: PPRO: CRP; WBC;ESR; Pregnancy; Preterm.

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Introduction

Preterm birth is the leading cause of neonatal mortality and morbidity in the developed countries. Preterm labor is also the most

common reason for antenatal hospitalization of pregnant women, which is associated with socio-economical burdens to the society⁽¹⁾. Preterm birth is defined by WHO as birth before

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the 36 weeks and 6days of gestation or before 259 days, counting from the first day of the last menstrual period⁽²⁾.Preterm prelabour rupture of membranes (PPROM) is one of the major factors that have been found to correlate with adverse pregnancy outcome¹⁻⁸. It remains a critically important clinical and public health problem. PPRM is a leading cause of preterm delivery with a third of all preterm births resulting from preterm PROM¹⁽³⁾. It is associated with considerable increase in adverse maternal, foetal and neonatal risk. The adverse perinatal outcome following preterm delivery is huge, accounting for up to 70% of perinatal mortality worldwide⁽⁴⁾.The cause of preterm PROM is unknown but the pathophysiology appears to be multifactorial. In any given patient one or more pathophysiologic processes may be evident. Choriodecidual infection or inflammation appears to play an important role in aetiology of preterm PROM, with rupture of membranes being attributed to increasing physical stress that weakens it⁽⁵⁾. Recent evidence suggests that membrane rupture is also related to biochemical processes such as abnormalities in collagen structure and formation as well as increased oxidative stress⁽⁶⁾.C-reactive protein is an acute phase protein widely used as an indicator of infectious or inflammatory conditions. Traditionally it has been used as an adjunctive test for inflammation and as a marker of disease activity. Though sensitive, its nonspecific nature imposes limitation on its clinical use. Currently C-reactive protein is used in the management of chorioamnionitis, preterm premature rupture of membranes, pelvic inflammatory disease, and urinary tract infection⁽⁷⁾. Interestingly, several obstetric conditions such as pre-eclampsia and gestational diabetes are now known to have an underlying inflammatory basis and there is an emerging role of C-reactive protein testing in managing these diseases. Additionally C-reactive protein testing has an established place in management of several

acute abdominal conditions. C-reactive protein (CRP), an acute phase reactant in the innate immune response, is a nonspecific biomarker of inflammation⁽⁸⁾. In acute inflammation, CRP levels increase rapidly and dramatically, exceeding normal levels (<1.0 µg/mL) within 6 hours of infection/injury and peaking around 48 hours at levels exceeding 500 µg/mL⁽⁹⁾. Although CRP's causal role in inflammation and cardiovascular disease remains controversial,¹² modest and sustained elevations (3.0-10.0 µg/mL) have been associated with a large number of medical conditions,obesity,and normal pregnancy^(10,11).The study aimed at evaluating the role of CRP in in the perdition of PPRM and in pregnant women

Patients and Methods

Study design

This is a comparative study that was conducted in the Department of Obstetrics and Gynecology of Salah Al-Din General Hospital from 1st of December 2021 through April 2022.

3.1.1. Patients

The study included 50 pregnant women presented with PPRM and attending the department of Obstetrics and Gynecology who had Singleton viable pregnancy with a gestational age ranging from 28- 36⁺⁶ weeks depending on accurate last menstrual period and / or by early ultrasonography. They were informed about the nature of the study and verbal consent was obtained from them. and 50 pregnant women without any complaint as control groups

Ethical approval

The protocol for this study was approved by the Scientific Committee at Tikrit University - College of Medicine, and the agreement of the attendance to Salah Al-Din General for collecting the sample from the patients was approved via the Directorate of Tikrit Health. Each patient was educated about the research, filled out a questionnaire, and signed a consent form to participate in the study.

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3.1.3. Exclusion Criteria

- ☒ Acute infection like UTI, Covid-19 and Fever
- ☒ Multiple pregnancies.
- ☒ Fetal compromise or with known fetal malformation.
- ☒ Chorioamnionitis
- ☒ Preexisting medical disease including thyroid, liver, renal, or hypertensive disease.
- ☒ Abnormal placentation or history of cervical pathology.

Methods

Detailed history was obtained. General and systemic examinations were done. Sterile vaginal speculum examination for assessment of cervical state (dilatation and effacement), pooling of amniotic fluid in the vagina, and nitrazine paper test was done to confirm the diagnosis of preterm premature rupture of membrane

Five ml of blood sample was taken by vein puncture from each subject enrolled in this study. Blood samples were divided in to 3 tubes, 1.5 ml of blood added to tubes containing sodium citrate as anticoagulant for

determination of ESR by specialized instrument as manufacture instruction. The second part, 1.5 ml of blood was put in test tube containing anticoagulant EDTA and used for assessment of complete blood count (WBCs counts) test using Swelab autoanalyzer (Switzerland) . The second part of sample was 2 ml placed in plane tubes left for 30 minutes at 37 °C then were centrifuged at 3000 rpm for 15 minutes then the clot was removed and the remain re-centrifuged at 3000 rpm for 10 min and the obtained sera were then aspirated using automatic micropipette and transferred into clean test tubes for determination of C-reactive protein by immunofluorescence technique (ichroma, Korea) according to manufacture instruction.

4. Results

The study included:

- 1- 50 pregnant women presented with PPRM
- 2- 50 Pregnant women presented with PID
- 3- 50 pregnant women without any complaint as control groups

Table 1 shows demographic and clinical characteristics of the study population **Table 4.1:General characteristics of PPRM women and the control group**

Variables	Preterm (n:50)	Labor	Control (n:50)	group	P. value
Age (Mean±SD)	33.1±4.81		32.5±4.12		NS
BMI	25.8±3.3		25.1±4.7		NS
Parity, median (Range)	2 (1–5)		2 (1–4)		NS
Residence (rural)	58%		60%		NS

The study revealed that the mean of CRP was elevated significantly in women with PPRM (11.76 mg/dl) as compared with the control group (4.34 mg/dl) at P. value <0.05. The study

also showed that the high mean of WBC and ESR recorded among PPRM women as compared with the control group (P<0.05), (Table 2).



Table 2: Level of C-reactive protein in PPROM and the control group

Parameters		PPROM group	Control group	P. value
CRP level	Mean	11.76	4.34	<0.05
	SD	0.61	0.34	
WBCs	Mean	8.34	4.67	<0.05
	SD	1.23	0.83	
ESR	Mean	17.5	8.46	<0.05
	SD	1.78	1.11	

The study showed that, 40% of PPROM women in the current study were with short cervical

length, 30% were with Low socioeconomic conditions, 20% with Previous preterm birth, 16% with Sexually transmitted infections, 18% with Vaginal bleeding, 6% were Smoker, and 30% with uterine overdistension

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Table 3. Distribution of PPRM women according to risk factors

Risk Factors	No.	%
Low socioeconomic conditions	15	30
Sexually transmitted infections	8	16
Previous preterm birth	10	20
Vaginal bleeding	9	18
Smoking	3	6
Short cervical length	20	40
uterine overdistension	15	30



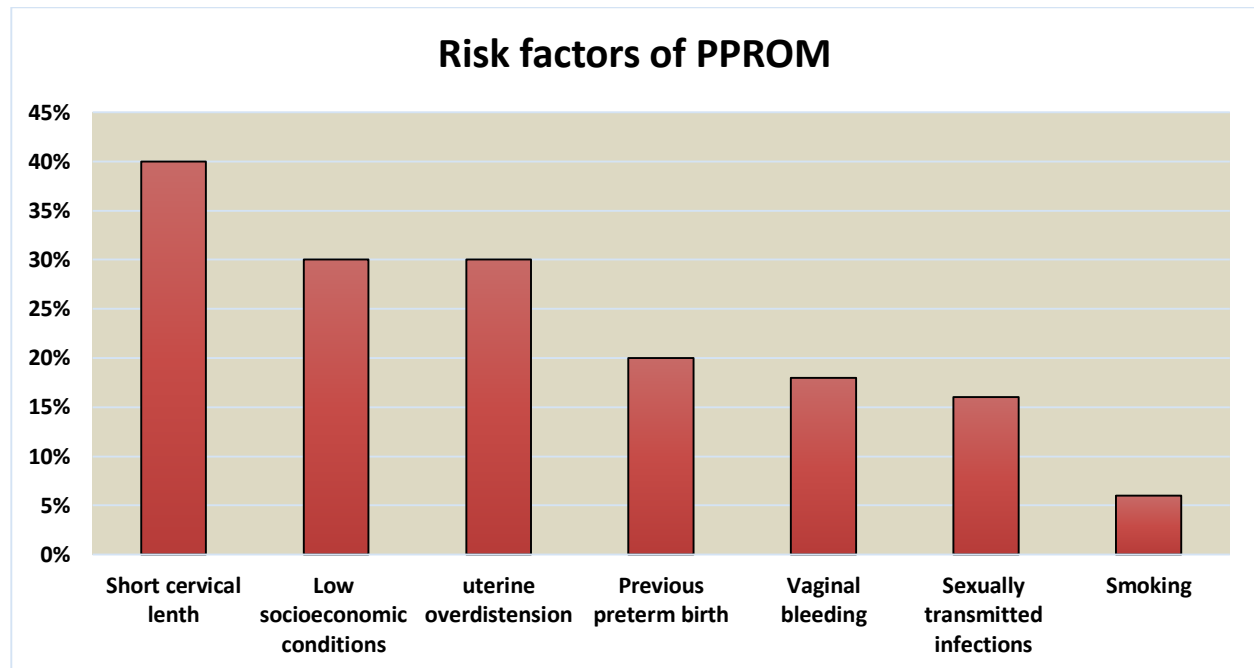


Figure 1: Distribution of PPRM women according to risk factors

Discussion

The study revealed that the mean of CRP was elevated significantly in women with PPRM (11.76 mg/dl) as compared with the control group (4.34 mg/dl) at P. value <0.05. The study also showed that the high mean of WBC and ESR recorded among PPRM women as compared with the control group (P<0.05), (Table 2). The prediction and early diagnosis of chorioamnionitis among women with PPRM is a controversial issue, but has high clinical value to prevent maternal and fetal complications. In the present study, the value of ESR, WBC, and CRP in predicting chorioamnionitis was investigated. The maternal serum level of CRP before termination of pregnancy was found to be the most accurate test for diagnosis of chorioamnionitis among women with PPRM. The results are consistent with those of Thornburg *et al.*⁽¹²⁾, but contrary to other studies^(13,14). In evaluations of amniotic fluid, clinical findings and laboratory tests may be used differentiate between chorioamnionitis and other conditions such as cervicitis, urinary

tract infection, cystitis, herpes infection, pelvic inflammatory disease, and vaginitis. Inflammatory markers such as IL-6, IL-8, and tumor necrosis factor (TNF) in amniotic fluid and maternal serum have been reported as the most potent diagnostic factors, whenever and wherever there is a need for an acute response^(15,16,17). Another study reported that maternal CRP is an appropriate index for predicting acute chorioamnionitis, and a better predictor than WBC count⁽¹²⁾, as. Clearly, both CRP and WBC count increase in unspecific inflammatory conditions⁽¹⁸⁾, however, the findings in the present study indicated that CRP might be a more specific predictor for differential clinical diagnosis of chorioamnionitis as compared with WBC count.

Inflammatory response varies depending on the cause of disease. For example, WBC count is used for the evaluation of microbial infections, whereas CRP is used only as a marker of inflammation, which may not be microbial in nature. However, continued assessment of WBC kinetics is important for



decision making on the type of diagnosis and treatment⁽¹⁹⁾.

Sereepapong et al⁽²⁰⁾ found that maternal serum levels of CRP, WBC count, and neutrophil count had poor diagnostic ability for histologically diagnosed chorioamnionitis. That finding is similar to the present results in terms of WBC count; however, maternal CRP and WBC levels were significantly higher among women with chorioamnionitis in the present study. This discrepancy may be due to differences in patient selection, the method of diagnosis of chorioamnionitis, or the study population.

The study showed that, 40% of PPRM women in the current study were with short cervical length, 30% were with Low socioeconomic conditions, 20% with Previous preterm birth, 16% with Sexually transmitted infections, 18% with Vaginal bleeding, 6% were Smoker, and 30% with uterine overdistension PPRM can result from a physiologic weakening of the membranes combined with the forces caused by uterine contractions. Different studies indicated that intramniotic infection is commonly associated with PPRM in addition to short cervical length, vaginal bleeding, uterine overdistension, nutritional deficiencies of copper and ascorbic acid, connective tissue disorders, and low socioeconomic status^(21,22). Despite a variety of etiologies, often there is no obvious cause that is identified in a patient who presents with PROM⁽²³⁾.

Conclusions

The study revealed that the mean of CRP, WBC and ESR recorded among PPRM and PID women as compared with the control group and short cervical length, Low socioeconomic conditions,, Sexually transmitted infections, Vaginal bleeding, uterine overdistension all were risk factors PPRM

Thus, there is a need to search for simpler methods with sufficient sensitivity to determine inflammatory status of PPRM and CRP should be used as a screening tool for the differential

diagnosis and prediction of chorioamnionitis and PID

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