Ministry of Higher Education and Scientific Research

Diyala University College of medicine

CRP Titre in Correlation with preterm premature rupture of membrane

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بسم ميحرلا نمحرلا هللا

)هُوَ الَّذِي بَعَثَ فِي الْأُمِّيِّينَ سَوُون م مِهُمُ تَلْهُو لَهُيْمْ َتَمهِ يَتْلُكَِهييمْ يَتُعَههيهُمُ

انْكِلْمبَ يَانْحِكْهَهْ يَإْنُ ِْمنُوا مِنُ قْبُمُ نْفِي ضْهْمِلٍ مُبْنيٍ(.

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سورة اجلمعة، آية: 2".

الخلفية: الولادة المبكرة هي السبب الرئيسي لوفيات واعتلال المواليد الجدد في البلدان المتقدمة. المخاض المبكر هو أيظا السبب الاكثر شيوعاً لدخول النساء الحوامل المستشفى قبل الولادة.

الهدف من الدراسة : تقييم دور CRP في PPROM قبل الولادة .

المرضى والأساليب: هذه دراسة مقارنة أجريت في قسم أمراض النساء والتوليد في مستشفى البتول التعليمي، في الفترة من ٢٩ تشرين الثاني ٢٠٢٢ حتى ١٠ أبريل ٢٠٢٣ .
شملت الدراسة ٥٠ مرأة خضعن لل PPROM وتم ابلاغهم بطبيعة الدراسة وتم الحصول على موافقة شفهية منهم، وشملت الدراسة أيظاً ٥٠ مرأة حامل دون أي شكوى كمجموعات ضابطة.

النتائج : كشفت الدراسة ان متوسط CRP كان مرتفعا بشكل ملحوظ لدى النساء المصابات ب PPROM.
)١١,٧٦ مجم/ديسيلتر) مقارنة بالمجموعة الضابطة (٤,٣٤ مجم/ديسيلتر) عند قيمة0.05>p.
كانت ٤٠٪ من نساء PPROM في الدراسة الحالية يعانين من طول عنق الرحم القصير، و٣٠٪ يعانون من ظروف اجتماعية واقتصادية منخفضة، و٢٠٪ مع الولادة المبكرة السابقة، و١٦٪ مع الأمراض المنقولة جنسيا، و١٨٪ مع نزيف مهبلي، و٦٪ كانو مدخنين

الاستنتاج: هناك ارتباط قوي بين المستوى المرتفع من CRP و .PPROM يمكن استخدام CRP أثناء الحمل للفحص التنبؤي للكشف عن الالتهابات التي تسبب تقلص الرحم المبكر وبالتالي التدخل المبكر والرعاية المكثفة قبل الولادة للحد من الاعتلال والوفيات في الفترة المحيطة بالولادة.

Abstract

Background: Preterm delivery is a worldwide public health problem, and it occurs in approximately 6–12% of all pregnancies, Preterm prelabor rupture of membranes is defined as amniotic fluid leakage before 37 weeks of gestation, and it represents approximately 30–40% of all preterm deliveries. PPROM is responsible for a substantial proportion of adverse neonatal complications associated with gestational age and risk of infection. C-reactive protein is an acute-phase reactant, and the CRP level has been reported to be slightly elevated in pregnant women.

Aim: this study aimed to CRP titre in correlation with PPROM.

Subject and methods: The current study is cross section study type was carried out in Albatool Hospital ,Diyala from 29th of November 2022 to the 10th of April 2023.The samples study design was by simple random sampling.

Results: the total sample of study was (100), the control case and preterm case was (50) for each, the mean of CRP was elevated significantly in women with PPROM (11.76 mg/dl) as compared with the control group (4.34 mg/di) at P. value <0.05. The study also showed that the high mean of WBC and ESR recorded among PROM women as compared with the control group (P<0.05). 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 over distension.

Conclusions: There is a strong association between the elevated level of CRP a sensitive biomarker and prediction of premature uterine contractions. Measurement of the level of C-reactive protein during pregnancy can be used as a predictive screening biomarker for detection of subclinical infections that cause preterm uterine contraction and hence early intervention and intensive antenatal care to reduce the peri-natal morbidity and mortality. There was high percentage of cases of PPROM with short cervical length.

Keyword: maternal, C-reactive protein, neonatal infection, premature uterine contractions, premature delivery, preterm delivery.

Acknowledgment

By the name of Allah, we start our project and I am thankful to Allah for helping me to complete this project and giving us the power and determination to do it faithfully and honestly.

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Lists of tables and figures

Introduction

Serum C-reactive protein (CRP) is an acute-phase protein that shows increased expression in the presence of infection, injury and inflammation, the utility of CRP level measurement in obstetrics and gynecology has been extensively studied [1].

Previous studies reported that the CRP levels in women with normal pregnancy were similar to those in non-pregnant women , whereas later studies showed that the CRP levels were slightly higher in normal pregnancy than in a non-pregnant state , CRP elevation is observed as early as at 4 weeks of gestation in normal pregnancy, and higher CRP levels in early pregnancy are associated with increased risks of preterm delivery, gestational diabetes, low birth weight and preeclampsia [2].

Elevated CRP in mid-pregnancy is associated with preterm labor, gestational diabetes mellitus, preeclampsia, urgent cesarean delivery and low Apgar scores, maternal and umbilical cord CRP levels are higher in cases of idiopathic intrauterine growth restriction than in appropriate for gestational age cases, among women with preterm premature rupture of the membranes (ROM), or preterm labor, maternal CRP level is a predictor of intrauterine or neonatal infection, Cord blood CRP level is associated with the duration of labor rather than the delivery mode, and measurement of cord blood CRP, and of neonatal CRP levels, can be performed to detect neonatal infection or sepsis [3].

However, maternal CRP at labor and delivery in term pregnancy has not been well studied thus far. In addition, the relevance of maternal CRP levels to neonatal infection in term pregnancy is less clear than in preterm ROM [4].

Preterm delivery is a worldwide public health problem, and it occurs in approximately 6–12% of all pregnancies , Preterm prelabor rupture of membranes (PPROM) is defined as amniotic fluid leakage before 37 weeks of gestation, and it represents approximately 30–40% of all preterm deliveries. PPROM is responsible for a substantial proportion of adverse neonatal complications associated with gestational age and risk of infection [4].

Microbial invasion of the amniotic cavity (MIAC) is identified in 30–40% of PPROM, particularly at early gestational ages , The presence of microorganisms activates an inflammatory response in the amniotic cavity, which is associated with early gestational age at delivery and a shorter latency to delivery [5].

The active management of PPROM in the Czech Republic provides a short latency from membrane rupture to delivery in women with a PPROM diagnosis. This management scheme provides unique information on the subgroup of women presenting MIAC We previously demonstrated that women with MIAC exhibited the greatest intra-amniotic inflammation , Similar results were observed in the fetal inflammatory response in the umbilical cord using interleukin (IL)-6 assessments, Pregnancies complicated with MIAC exhibit the highest incidence of the subsequent development of early onset sepsis in newborns [6].

Notably, no differences were observed in the inflammatory responses in the amniotic cavity or fetal compartment in women with MIAC alone compared to a negative infectious group. Previous data suggest that the presence of MIAC represents the worse infectious scenario associated with the earliest gestational age at PPROM and the highest inflammatory response in amniotic fluid and umbilical cord, therefore, the antenatal prediction of women with MIAC is crucial to improve the clinical management of women presenting with PPROM [7].

Evaluation of 27 biomarkers using a multiplex approach revealed differences in the concentration of IL-18, IL-1β and monocyte chemotactic protein-1 (MCP-1) in maternal serum between PPROM women with or without MIAC. Notably, these differences were only observed prior to 32 weeks of gestation, However, this multiplex approach did not consider CRP in the analysis [8].

Maternal serum CRP has been proposed as a marker of infection and inflammation in several diseases and MIAC. CRP ex. No significant differences were reported when CRP levels were compared between

PPROM women with or without MIAC , To our knowledge, there are no previous studies evaluating the role of maternal CRP based on the presence of MIAC [9].

It is clinically important to evaluate the role of CRP as a predictor of the worst infectious conditions, such as the occurrence of MIAC, because the information for maternal CRP associated with infection might induce changes in the management of PPROM in most clinical settings, Whether gestational age influences the predictive value of CRP for infectious conditions should also be investigated [10].

Methods

Ethical and Approval Consideration: Permission was taken from patients to fill the information required and they were assured regarding the confidentiality of their responses. The Reason of the study was explained and only those who agreed to participate are included in the study.

Study Population: The study was performed among patients at Albatool Hospital , Diyala.

Study design: The current study is cross section study type was carried out in Albatool Hospital ,Diyala from 29th of November 2022 to the 10th of April 2023.The samples study design was by simple random sampling.

Sample technique and data collection: Trained very well to interview the questionnaire carefully and in scientific way. Respondents were assured that the information obtained would be confidential and used only for statistical purposes.

Questionnaire and Interview: the questionnaire used for data collection was designated in (English) language.

Data Analysis and Presentation: All data management and analysis was done by using SPSS statistical methods. Data have been represented b suitable tables and figures.

The sample: The sample was 100 from patients in Albatool Hospital.

Results

The study included:

1. 50 pregnant women presented with PPROM

2. 50 pregnant women without any complaint as control groups

Table 1: General characteristics of PROM women and the control group

Variables	Preterm (n:50)	Control Group (n:50)	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 PPROM (11.76 mg/dl) as compared with the control group (4.34 mg/di) at P. value <0.05. The study also showed that the high mean of WBC and ESR recorded among PROM women as compared with the control group (P<0.05), (Table 2).

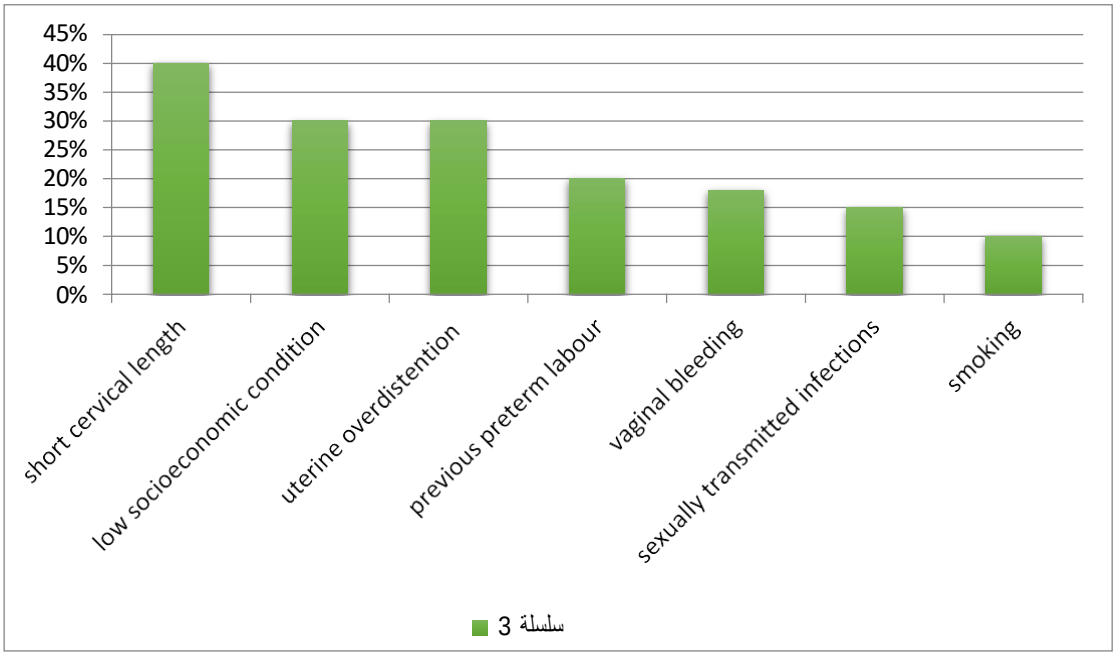
Table 2: Level of C-reactive protein in PPROM and the control group

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 over distension

Table 3. Distribution of PPRM women according to risk factors

Risk Factors	No.	%
Low socioeconomic condition	15	30
Sexually transmitted infection	8	16
Previous preterm birth	10	20
Vaginal bleeding	9	18
Smoking	3	6
Short cervical length	20	40
Uterine over distention	15	30



Discussion

Form the total sample of study was (100), preterm cases was (50) and control cases was (50), in this study the mean-SD of preterm cases 33.1 - 4.81 and for control group 32.5-4.12, and the BMI for preterm 25.8- 3.3 and control group was 25.1- 4.7. The study revealed that the mean of CRP was elevated significantly in women with PPROM (11.76 mg/dl) as compared with the control group (4.34 mg/di) at P. value < 0.05.

The study also showed that the high mean of WBC and ESR recorded among PROM women as compared with the control group (P < 0.05).

The main finding of study was conducted in Hradec Kralove, Czech [13], was the weak association between maternal serum CRP and the occurrence of MIAC, even when different gestational ages were considered. Only CRP levels above the 95th percentile in PPROM below 32 weeks of gestation accurately predicted the occurrence of MIAC. Unfortunately, this low sensitivity prevents the application of this finding in a clinical setting.

A lack of association was also observed when evaluating maternal serum CRP between PPROM women with or without MIAC [18]. Nephelometry, turbidimetry with standard sensitivity [19] and high sensitivity CRP nephelometry with lower limits of detection below 1.0 mg/L were used to measure CRP. The variation in CRP results must be expected when different analytical techniques for CRP evaluation are used Nevertheless, it is unlikely that these variations affected the results of these studies [20].

In the present 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 over distension.

While in another study was conducted in Shizuoka, Japan [21], that about 33% of PPROM women with short cervical length, 10% were with Low socioeconomic conditions, 46% with Previous preterm birth, 13% with Sexually transmitted infections, 26% with Vaginal bleeding, 14% were Smoker, and 38% with uterine over distension.

Conclusions

There is a strong association between the elevated level of CRP a sensitive biomarker and prediction of premature uterine contractions.

Measurement of the level of C-reactive protein during pregnancy can be used as a predictive screening biomarker for detection of subclinical infections that cause preterm uterine contraction and hence early intervention and intensive antenatal care to reduce the peri-natal morbidity and mortality.

There was high percentage of cases of PPROM with short cervical length.

Recommendations

1. Considering the importance of this subject, it is hopeful that the results of this research can be used for promoting further studies regarding CRP and its relationship with pregnancy complications and also other important factors relating CRP such as nutrition, infections, economical and social situations.
2. This study can be used as infrastructure to build other studies in the field of premature uterine contractions.
3. Women at risk for preterm labor should be encouraged to participate in studies aiming at early detection and treatment of premature labour.
4. Future research on molecular biological techniques with high sensitivity and specificity may allow the development of multiple marker tests for the prediction of PTB in asymptomatic and symptomatic at-risk women. This may ultimately be simple and cost-effective enough to introduce as a low-risk screening program.

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