ORIGINAL ARTICLE

Diagnostic accuracy of CRP in Chorioamnionitis in women presenting with PROM near term

SANA NAZEEF[1], JAMSHID FEROZE[2], ATTKA MARYAM[3], NATASHA BUSHRA[4], WAJIHA RIZWAN[5], TAYYIBA WASIM[6], SHAZIA HAIDER[7], SANA AMIN[8]

[1,8]PGR, Department of Gynae and obstetrics Services Institute of medical sciences Lahore
[2]Associate Professor, Department of Gynae and obstetrics Services Institute of medical sciences Lahore
[3]Assistant Professor, Department Of radiology, Rashid Latif medical college Lahore
[4,5,7]Assistant Professor, Department of Gynae and obstetrics Services Institute of medical sciences Lahore
[6]Professor, Department of Gynae and obstetrics Services Institute of medical sciences Lahore
Correspondence to Dr. Natasha Bushra, Email: natashausman5@hotmail.com

ABSTRACT

Background: Chorioamnionitis or intra-amniotic infection is an acute inflammation of the membranes and chorion of the placenta, typically due to ascending poly-microbial bacterial infection in the setting of membrane rupture. The infection can occur when bacteria that are normally present in the vagina ascend into the uterus, where the fetus is located.

Aim: To determine the diagnostic accuracy of C-reactive protein for diagnosis of chorioamnionitis in patients presenting with premature rupture of membranes near term taking histopathology as gold standard.

Methods: It was cross sectional study conducted in Gynecology and Obstetrics Unit II, Services Hospital Lahore for duration of 6 months from 31-8-2019 to 5-3-2020. Total 148 females who fulfilled selection criteria was enrolled in this study from emergency. Blood sample was collected and sent to the laboratory of the hospital for assessment of CPR level. Reports were assessed and if CRP. If CRP>6ml, then patients were labeled as positive. Then patients underwent delivery through cesarean section. Placenta and amniotic membranes were sent for histopathological evaluation.

Results: The average age of women was 26.8 2± 2.98 years. Mean gestational age of women in this study was 39.15±1.41 weeks. Sensitivity and specificity of CRP was 86.84% and 85.29% respectively while PPV and NPV was 95.19% and 65.91% respectively, overall diagnostic accuracy was 86.49%.

Conclusion: C-reactive protein for diagnosis of chorioamnionitis has diagnostic accuracy of 86.49% in patients presenting with PROM near term taking histopathology as gold standard.

Keywords: Diagnostic, Accuracy, C-reactive protein, Chorioamnionitis, premature, Rupture, Membranes

INTRODUCTION

Acute infection of the chorion and membranes of placenta followed by ruptured of membranes is commonly seen and the most common reason identified is infection.[1] thhe microbes are ascended by lower genital tract into the uterus where they affect the intra uterine environment causing infection.[2, 3] Presence of chorioamnionitis was detected in about 66% females with PROM[4].

Chorioamnionitis also increases the rate of cesarean delivery. Approximately 8% of women who have a cesarean delivery had developed a wound infection, and about 1% develop a pelvic abscess. Maternal mortality due to infection is very rare. Babies who delivered to mothers with chorioamnionitis can have serious complications[5].

In few cases, the sequele of infection followed by chorioamnionitis is lethal when the infection is in preterm pregnancy that may lead to iatrogenic delivery. The criteria to diagnose chorioamnionitis has fever the most prodromal sign followed by Uterine fundal tenderness[6]. Other important features may include Maternal tachycardia and change in colour of liquor or purulent discharge[7].

After diagnosing rupture of membranes, risk assessment of patient is crucial step in management.[8] The clinical criteria should be linked with laboratory criteria that may include Maternal leukocytosis in > 80% of cases of cases of clinical chorioamnionitis. Although only raised TLC may not be considered a reason to plan intervention as it may be raised in labour or after use of steroids.[9] Other blood test like C-reactive protein (CRP) Amniotic fluid testing Amniocentesis and histopathology[10].

It has been reported that the maternal serum CRP to identify the presence of amniotic membrane inflammation with microbial invasion, had sensitivity of 47%, specificity of 96%.[2] One study showed that the sensitivity and specificity 77.77% and 100% respectively.[11] While another study found that sensitivity was about 76.9% for chorioamnionitis, determined by CRP and specificity was 31.9%[12].

This study is very important to determine the diagnostic accuracy of C-reactive protein to assist diagnosing chorioamnionitis in patients who present after PROMs near term. Literature has reported that CRP can be a good alternative for histopathological assessment after delivery. CRP can help to predict chorioamnionitis before delivery and can help to plan appropriate management and preventive measures. But controversial results have been observed in literature regarding accuracy of CRP for prediction of chorioamnionitis in females with PROM. This will help us to predict whether CRP is good alternative and can be implemented in local set-up. This will also help us to improve our practice.

Received on 05-11-2020
Accepted on 13-02-2021

MATERIALS AND METHODS

Study Design: It was a cross sectional study which was conducted in Obstetrics & Gynecology department, Services Hospital, Lahore from 31-8-2019 to 5-3-2020. Sample size of 148 cases is calculated with confidence level of 95%, taking 66% as expected percentage of chorioamnionitis[4] and sensitivity of CRP i.e., 76.9% with margin of error 13% and specificity of CRP i.e., 31.9% with 13% margin of error by non-probability, consecutive sampling. 18-40 years of females, with parity <5 presenting at gestational age >36 weeks within 6 hours of PROM were included in the study. Females already diagnosed with chorioamnionitis before PROM (clinical examination), placental complication (morbidly adherent placenta or placental abruption), chronic or gestational hypertension (BP≥140/90mHg), proteinuria (≥+1 on dipstick method), diabetes, urinary tract infection (clinical examination), these were not enrolled in the study

Data Collection Procedure: Total 148 females fulfilling selection criteria presented in emergency Department of Obstetrics & Gynecology, Services Hospital, Lahore were enrolled in study. Informed consent of selected females was taken. Demographics details (name, age, gestational age, parity, BMI) were noted. Blood sample was collected through a 3cc disposable syringe under aseptic measures. All sample were sent to the laboratory of the hospital for assessment of CPR level. Reports were assessed and if CRP. If CRP>6ml, then patients were labeled as positive. Then patients underwent delivery through cesarean section. Placenta and amniotic membranes were sent for histopathological evaluation. If inflammation present and PMN >15/HPF, then patents were confirmed as positive (as per operational definition). Patients were managed as per standard protocol and designed proforma was filled

Data Analysis: SPSS version 21 was used for statistical Analysis. Quantitative variables like age, gestational age, BMI and duration of PROM were calculated as mean and standard deviation. Qualitative variables like chorioamnionitis (on CRP and clinical examination), was presented as frequency and percentage. Parity was also presented as frequency. Data was stratified for age, gestational age, BMI, parity and duration of PROM. Sensitivity , specificity , positive predictive value and negative predictive value was calculated and diagnostic accuracy of CRP was measured taking clinical examination as gold standard for each strata.

RESULTS

The mean age of women was 26.82±2.98 years. There were 54(36.5%) women with 0 parity, 59(39.9%) with 1 parity, 30(20.3%) with 2 parity and 5 (3.4%) with 3 parity. In descriptive statistics for BMI the mean age of patients was 28.8±1.59 years. Minimum and maximum age of patients was 26 and 32 years. In study of descriptive statistics for duration of prom the mean age of patients was 4.87±0.90 years. There were 104(70.3%) women with positive Chorioamnionitis on CRP while 44(29.7%) women had negative Chorioamnionitis on CRP. There were 114(77%) women with positive Chorioamnionitis on histopathology while 34(23%) women had negative Chorioamnionitis on histopathology. Sensitivity and specificity of CRP was 86.84% and 85.29% respectively and PPV and NPV was 95.19% and 65.91% respectively, overall diagnostic accuracy was 86.49% (Table 2).

Sensitivity of 75% and specificity of 100% was seen in 20-25 years, whereas among 26-30 years the sensitivity and specificity was 89.66% and 77.78%, whereas sensitivity of 100% and specificity of 0% was seen in age group of 31-36 years respectively. The PPV and NPV in the age 20-25 years was 100% and 71.43%, in strata of 26-30 years the PPV and NPV was 95.12% and 60.87% and the PPV and NPV in the group of 31-36 years was 75% and 0%the diagnostic accuracy was 84.62%, 87.62% and 75% in all three groups respectively.

Sensitivity and specificity of 85.23 and 84.62% was seen in the gestational age group of 38-40 weeks while in the gestational age of 41-42 weeks the sensitivity and specificity was 92.31% and 87.5%. In the gestational age group of 38-40 weeks value for PPV and NPV was 94.94% and 62.86% respectively while in the gestational age group of 41-42 weeks the values of PPV and NPV was 96% and 77.78% respectively. The diagnostic accuracy of both the groups was 85.09% and 91.18%.

Sensitivity and specificity of 85.37% and 93.55% was seen in the parity group of 0-1 while in the parity group of 2-3 the sensitivity and specificity was 90.63% and 0%. In the parity group of 0-1 value for PPV and NPV was 97.22% and 70.73% respectively while in the parity group of 2-3 the values of PPV and NPV was 90.63% and 0% respectively. The diagnostic accuracy of both the groups was 87.61% and 82.86%.

Sensitivity and specificity of 89.55% and 96.3% was seen in the BMI group of 26-29 while in the BMI group of 30-32 the sensitivity and specificity was 82.98% and 42.86%. In the BMI group of 26-29 the values for PPV and NPV were 98.36%% and 78.79% respectively while in the BMI group of 30-32 the values of PPV and NPV was 90.7% and 27.27% respectively. The diagnostic accuracy of both the groups was 91.49% and 77.78%.

In the Duration of PROM group of 4 the Sensitivity and specificity was 84.31% and 90%, in the duration of PROM group 5 the sensitivity and specificity was 88.24% and 62.5%, whereas sensitivity of 89.13% and specificity of 100% was seen in duration of PROM group of 6 respectively. The PPV and NPV in the PROM duration group of 4 was 95.56% and 69.23%, in the PROM duration group of 5 the PPV and NPV was 83.33% and 71.43% and the PPV and NPV in the PROM duration group of 6 was 100% and 54.55%the diagnostic accuracy was 85.92%, 80% and 90.38% in all three groups respectively (Table 3).

Table 1: Demographic characteristics of study population

Characteristics	Mean	SD	Minimum	Maximum
Maternal age (years)	26.82	2.98	20.00	36.00
Gestational age of Women (Weeks)	39.15	1.41	37.00	42.00
BMI	28.8	1.59	26.00	32.00
Duration of PROM	4.87	0.90	4.00	6.00

Table-2: Diagnostic Accuracy of CRP for diagnosis of Chorioamnionitis

		Histopathology		Total
		Positive	Negative	
CRP	Positive	99(86.8%)	5(14.7%)	104
	Negative	15(13.2%)	29(85.3%)	44
Total		114	34	148

	Value	CI (95%)
Sensitivity	86.84%	(79.42, 91.86[1])
Specificity	85.29%	(69.87, 93.55[1])
Positive Predictive Value	95.19%	(89.24, 97.93[1])
Negative Predictive Value	65.91%	(51.14, 78.12[1])
Diagnostic Accuracy	86.49%	(80.05, 91.08[1])

Table-3: Diagnostic Accuracy of CRP for diagnosis of Chorioamnionitis stratified for duration of PROM

Duration	CRP	histopathology	
		Positive	Negative
4.00	Positive	43(84.3%)	2(10.0%)
	Negative	8(15.7%)	18(90.0%)
5.00	Positive	15(88.2%)	3(37.5%)
	Negative	2(11.8%)	5(62.5%)
6.00	Positive	41(89.1%)	0(0.0%)
	Negative	5(10.9%)	6(100.0%)

	4		5		6	
	Value	CI (95%)	Value	CI (95%)	Value	CI (95%)
Sensitivity	84.31%	(71.99, 91.83[1])	88.24%	(65.66, 96.71[1])	89.13%	(76.96, 95.27[1])
Specificity	90%	(69.9, 97.21[1])	62.5%	(30.57, 86.32[1])	100%	(60.97, 100[1])
PPV	95.56%	(85.17, 98.77[1])	83.33%	(60.78, 94.16[1])	100%	(91.43, 100[1])
NPV	69.23%	(50.01, 83.5[1])	71.43%	(35.89, 91.78[1])	54.55%	(28.01, 78.73[1])
DA	85.92%	(75.98, 92.17[1])	80%	(60.87, 91.14[1])	90.38%	(79.39, 95.82[1])

DISCUSSION

C reactive protein is a clinical marker which is produced in response to inflammation in the body. Woman presenting with vaginal leaking can have elevated C reactive protein which may be considered a non invasive parameter to detect underlying infection[13,14].

There has been enough studies with inconclusive evidence about role of CRP in patients with PROM[15]. Initially study by Romero group in 1996 indicate relation of infection related complications in women with PROM with raised CRP[16]. Several other studies confirmed this finding later[17], but still trial by Cobo et al. failed to depict any role of CRP and no significant difference in woman with PROM at term[18].

However, CRP is aprotein marker released in response to acute inflammation which is sensitive but at the same time it has non specific role to identify underlying inflammation [19]. Pre labour rupture of membranes is a condition in which obstetricians need to outweigh the risk of chorioamnionitis versus planning delivery to limit the risk of infection to new born and such markers may help in solving the diagnostic dilemma of such cases[20].

Vaginal rupture of membranes at preterm gestation is managed in expectant way to avoid complications of pre term delivery but role of more reliable diagnostic test like CRP is at or near term where the risk of underlying infection in continuing pregnancy may risk the baby due to microbial invasion of amniotic cavity. Such non invasive test are useful markers to timely decide the timing of delivery. This acute phase protein C-reactive protein has raised value in less than 24 hours that makes it an easy way to diagnose early stage infective process.

According to Aggarwal et al 2018 [21] majority of patients in study groups belong to gestational age between 29-34 weeks while in our study mean gestational age was 39.15 and maximum number of women were in the gestational age group of 38-40 weeks. The results are in commensurate with the previous studies.[3] Latent period directly proportional to incidence of Chorioamnionitis with increase in latent period, there is increase in incidence of Chorioamnionitis and correlation is better with histological chorioamnionitis then clinical CAM. Aggarwal et al[21] found that in identifying clinical Chorioamnionitis, CRP level is more sensitive (100%) but less specific (69.56%). The positive predictive value was found to be 22.22% and negative predictive value was 100%. While in our study sensitivity of CRP was 86.84% and specificity was 85.29%, positive predictive value was 95.19% and negative predictive value was 65.91% which is almost similar to the findings of above mentioned study. Our findings were also in accordance with other studies[23].

Chorioamnionitis is a condition affecting pregnancy and if left untreated may lead to pelvic infection and sepsis. It may lead to infertility due to microbial invasion of organism leading to tubo-ovarian abscess. There are certain fetal risk associated with chorioamnionitis which may lead to neonatal infection, meningitis and perinatal mortality. ORACLE trial emphasized on the need of antibiotics to minimize complications[24] accurate diagnosis and timely intervention can reduce the risk of both maternal and fetal sequel of complications.

CONCLUSION

It is concluded from the present study that CRP is the earliest and most reliable diagnostic marker. It has the diagnostic accuracy for diagnosis of chorioamnionitis was 86.49% in patients presenting with PROMs near term taking histopathology as gold standard.

Contribution of authors

Author	Contribution
Sana Nazeef	Concept and Data collection
Jamshid Feroze	Initial Drafting
Attka Maryam	Data Analysisand final proof reading
Natasha Bushra	Data Collection and data analysis
Wajiha Rizwan	Data Analysis
Tayyiba Wasim	Discussion Writing and Final Proof reading
Shazia Haider	Discussion Writing
Sana Amin	References writing

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