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Evaluation of CRP as Predictor of Chorioamnionitis in Premature Rupture of Membranes

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Abstract

Background: Early identification of sepsis is essential as the mother has risk of chorioamnionitis. C reactive protein levels are done along with placental histopathology to detect chorioamnionitis. It is one of the most significant causes of high perinatal morbidity and mortality.

Aim and Objective: To determine c-reactive protein levels and placental histopathology in premature rupture of membranes for maternal chorioamnionitis.

Methodology: Prospective study was conducted in a tertiary care university medical college hospital and research center in western Maharashtra. A total 250 pregnant women reported with per vaginal leak during the study period and CRP levels were sent along with urine culture sensitivity and high vaginal swab, post delivery the placenta was sent for histopathology were included in the study analysis.

Results: The histopathology was done in all 250 pregnant women, chorioamnionitis was evident in 46 pregnant women. This gives the incidence of 18.4% of chorioamnionitis in the study population. The sensitivity for CRP was calculated to be 15.22%, with a specificity of 99.02%, positive and negative predictive values of 77.78% and 83.82%, respectively, with an accuracy of 83.60%.

Conclusion: Normal CRP level has good predictive values to rule out maternal chorioamnionitis. But raised single CRP level has low sensitivity to predict for histological chorioamnionitis prior to its clinical expression.

Keywords: Maternal Chorioamnionitis; Premature Rupture of Membranes; PROM; High Vaginal Swab; CRP.

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INTRODUCTION

Premature membrane rupture refers to the spontaneous rupture of the membranes at any time after 20 weeks of pregnancy but before the start of labour preterm rupture of membranes (PROM)[1] Premature rupture of membranes (PPROM) slightly varies in severity across the globe and complicates 1-4[1] percent of all pregnancies. Developing nations are particularly affected by maternal morbidities

and neonatal deaths brought on by premature births.[2,3]

PPROM frequently has an intra amniotic infection associated with it. Short cervical length, vaginal bleeding during the second or third trimester, uterine over distension, connective tissue disorders, nutritional deficiencies in copper and ascorbic acid, low body mass index, low socio economic status, smoking, and illicit drug use are the main risk factors for PPROM. Despite a wide range of aetiologies, patients who present with PROM frequently lack an obvious cause.[4]

Clinical suspicion, patient history, and easy testing can all be used to determine the diagnosis of PPROM. Patient history is 90% accurate in diagnosing PPROM and should not be disregarded.[4] Acute inflammation of the placenta's membranes and chorion, also known as chorioamnionitis or intra amniotic infection, is frequently caused by an ascending polymicrobial bacterial infection in the context of membrane rupture. Urea plasma urealyticum, Chlamydia trachomatis, Neisseria gonorrhoea, Mycoplasma hominis, group B streptococcus, and Trichomonas vaginalis are a few of these frequently found pathogens. Chorioamnionitis has also been linked to fungi, including several species of Candida (Candida albicans, Candida tropicalis, and Candida glabrata). Gram-negative anaerobes, such as Gardnerella vaginalis and Bacteroides spp., are another type of bacteria.[5]

The membranes in chorioamnionitis may appear normal or exhibit signs of infection. A fluid may be cloudy or clear. On histologic examination, the decidua shows neutrophilic infiltration, and in more serious cases, micro abscesses are visible.[5] The primary indicator of clinical chorioamnionitis is the presence of maternal fever, which is defined as a temperature of at least 100.4 F (38 degree C).

Numerous parameters have been suggested as helpful clinical and diagnostic tools. Clinical signs of chorioamnionitis include uterine tenderness or irritability, foetal or maternal tachycardia, and amniotic fluid with an unpleasant odour. Maternal leukocytosis (increased white blood cell count), the differential or band neutrophil count, and the erythrocyte sedimentation rate are the most frequently observed laboratory variables.[3] The liver produces the serum protein known as C-reactive protein (CRP). Within a few hours of an injury or the start of an inflammatory response, its rate of synthesis and secretion increases significantly.

Compared to clinical febrile morbidity, elevated C-reactive protein levels were more closely associated with histopathologic evidence of chorioamnionitis. Since intrauterine infections have been linked to elevated serum CRP levels, and since these infections have been linked to PROM, measuring CRP is helpful in predicting infection in these conditions.[6]

Preterm delivery, postpartum hemorrhage, operative delivery, severe pelvic infections, subcutaneous wound infections, and maternal sepsis are among the maternal complications of chorioamnionitis.[6]

METHODOLOGY

A prospective observational study was conducted in the department of obstetrics and gynecology at tertiary care university hospital, over a period of 2 years in antenatal females coming to OPD with per vaginal leak after 24 weeks of gestation. The study was initiated after obtaining approval from the Institutional Ethics Committee. The purpose and rationale of the study as well as their role as participants was explained to all the patients in the study. Written informed consent was obtained from all the patients. All pregnant women who fulfilled inclusion criteria coming to OPD with per vaginal leak after 24 weeks of gestation were included in the study. Detailed history of each case was taken regarding name, age and per vaginal leaking and speculum examination. Investigation sample were sent CRP levels, placental histopathology to lab. The reports of investigations were collected and CRP levels estimated were recorded. Inclusion criteria include pregnant women above 24 weeks of gestation with demonstrable per vaginal leak on examination. Exclusion criteria include women less than 24 weeks of gestational age, complications like antepartum hemorrhage. The sample size was estimated by the formula for calculation of sample size n-250.

The collected data was coded and entered in Microsoft Excel sheet. The data was analyzed using SPSS (statistical package for social sciences) version 26.0 software.

RESULTS

A total of 250 patients who came with per vaginal leak according to inclusion criteria were included in our study analysis. The most common type of

delivery was preterm LSCS, followed by full term vaginal delivery, full term LSCS, preterm vaginal delivery. All 250 were live births, no mortality was reported in the study.

Table 1: Demographic and clinical parameters assessed at the time of admission

	Mean	SD	Minimum	Maximum
Age	24.28	2.89	19.00	38.00
Pulse (BPM)	92.31	7.15	70.00	108.00
Systolic BP	113.20	5.82	110.00	150.00
Diastolic BP	75.00	5.25	70.00	100.00
Weight (Kg)	2.19	0.46	1.70	3.30
APGAR Score 1 Min	7.24	1.27	5.00	8.00
APGAR Score 5 Min	8.71	0.51	7.00	9.00
TLC (×10)	120.85	1695.90	8000.00	18500.00
CRP	1.25	0.57	0.90	5.00

Table 2: Type of delivery

	Frequency	Percent
PTLSCS	95	38.0
FTVD	62	24.8
FTLSCS	55	22.0
PTVD	37	14.8
Emergency LSCS	1	0.4
Total	250	100.0

Table 3: Comparison of CRP and TLC patients with and without mild chorioamnionitis

	Histopathology				p value
	Mild chorioamnionitis		No chorioamnionitis		
	Mean	SD	Mean	SD	
CRP (mg/L)	1.74	1.09	1.28	0.37	<0.0001
TLC (cells/mm3)	12689.13	1940.93	11948.58	1609.75	0.01

Table 4: Effectiveness of CRP for diagnosis of chorioamnionitis against histopathology

	Histopathology				p value
	Mild chorioamnionitis		No chorioamnionitis		
	Mean	SD	Mean	SD	
CRP (mg/L)	1.74	1.09	1.28	0.37	<0.0001
TLC (cells/mm3)	12689.13	1940.93	11948.58	1609.75	0.01

RESULTS

Premature rupture of membranes (PROM) is a risk for chorioamnionitis. When PROM occurs near term, immediate delivery is a straight forward obstetric decision. Preterm PROM (PPROM) becomes a dilemma for obstetric management. PPROM occurs in 5 to 10 percent of all deliveries. It is a significant contributor to perinatal mortality and preterm birth.[7]

The present study was carried out to determine the association between c-reactive protein levels and placental histopathology in premature rupture of membranes for maternal chorioamnionitis. A total of 250 pregnant women above 24 weeks of gestation who attended OPD with demonstrable vaginal leak on examination were included in the

present study.

The mean age of the patients was 24.28 ± 2.89 years, ranging between 19 to 38 years. The mean CRP level in all patients was 1.25 ± 0.57 mg/L. Among 250 women recruited, 133 gave birth preterm, and the remaining 117 were term deliveries. The most common comorbidity reported was hypothyroidism (22%), followed by Rh negative (19.6%), and there were 3 (1.2%) cases each of pre-eclampsia and previous history of LSCS. Among others are DGGT, epilepsy, HBsAg positive and previous LSCS with pre-eclampsia, all with 1 case (0.4%) each.

The histopathology was done in all 250 pregnant women: mild chorioamnionitis was evident in 46 pregnant women. This gives an incidence of 18.4% of chorioamnionitis in the current study population. There was no statistically significant difference in any of the demographic, maternal, or fetal clinical parameters between patients with and without histologically confirmed mild chorioamnionitis. We found no link between the type of birth, type of delivery, and the need for NICU admission with chorioamnionitis in this study. Similar non-significant associations were reported for comorbidities, HVS, and urine C/S findings with chorioamnionitis.

The results of the high vaginal swab showed positivity among 59 patients, of which the majority belonged to patients without chorioamnionitis, compared to 15 in patients with chorioamnionitis.

Among patients with chorioamnionitis, 12 showed culture positive results for E. coli, 2 had Candida albicans, and 1 had Hemophilus. On the other hand, 42 were positive for E. coli, and 2 were positive for Candida albicans in a group of patients without chorioamnionitis.

The most frequent organism isolated from the placental membrane, similar to the study by Sinha V *et al.*, was E. coli, with Streptococci coming in second. Chorioamnionitis is a completely unwelcome sequel. The best course of action in this circumstance can be determined with the aid of systematic vaginal and blood sampling. Although not yet fully validated for clinical use, the various serologic and amniotic fluid tests that may detect activation of the host immune and inflammatory responses as a result of the microbial invasion of the amniotic cavity are very promising.[8]

C reactive protein (CRP), leukocyte count, vaginal microbiological studies, and histological study are a few examples of these.

Although it is a marker for many inflammatory, infectious, and malignant conditions, it is not specifically for infection. Despite conflicting reports regarding its effectiveness, CRP has been widely used in obstetrics, particularly in the early diagnosis of chorioamnionitis in the absence of clinical signs of infection.[6]

Serial CRP measurements appear to have potential. However, a strong correlation between the presence of histopathological chorioamnionitis and preterm delivery has only recently been reported, indicating that occult antepartum genital tract infection is a significant contributor to preterm delivery.[7]

Obstetricians and gynecologists have used CRP for the past three decades to diagnose chorioamnionitis and other inflammatory conditions.

In the present study, we reported a significantly higher level of CRP in patients with chorioamnionitis compared to patients without chorioamnionitis.[9]

Clinical experts disagree significantly about the best method for chorioamnionitis diagnosis, whether it be histological or clinical. The reported value of CRP for the chorioamnionitis diagnosis varies widely.[6]

We compared our CRP results with histopathology. There were a total of 7 (15.2%) true positive cases by CRP, 202 (99%) true negative cases by CRP, 39 (84.8%) false negative cases by CRP, and 2 (1%) cases were false positives by CRP compared to histopathological findings for chorioamnionitis. The sensitivity for CRP was calculated to be 15.22%, with a specificity of 99.02%, positive and negative predictive values of 77.78% and 83.82%, respectively, with an accuracy of 83.60%.

Martin Stepan *et al.* from France also found 15% sensitivity of CRP in predicting HCM. Similar to the current study, the low sensitivity of 15% restricts the clinical utility of CRP in predicting histopathological chorioamnionitis.[9]

CONCLUSION

Our study has revealed that normal CRP level has good predictive values to rule out maternal chorioamnionitis. But raised single CRP level has low sensitivity to predict for histological chorioamnionitis prior to its clinical expression. So maternal serum CRP level may be used as screening test for chorioamnionitis rather than a diagnostic test.

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