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A comparative investigation to evaluate the usefulness of maternal CRP and WBC count in predicting intra-amniotic infection in preterm rupture of membranes

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Abstract
Aim: To evaluate the usefulness of maternal CRP and WBC count in diagnosing intra-amniontic infection in the preclinical stage in women with preterm rupture of membranes.
Methods: This prospective observational study was carried out in the Department of Obstetrics and Gynaecology at Sri Devaraj Urs Medical College, Kolar from November 2018 to December 2019. Intra-amniotic infection was confirmed by obtaining amniotic fluid vaginally and subjecting it for aerobic and anaerobic culture.
Results: A total of 220 antenatal women were enrolled in the study. The distribution of cases into preterm premature rupture of membranes (PPROM) and premature rupture of membranes (PROM) was 55 each group. 110 gestational age matched controls were equally distributed between PPROM and PROM. Rupture of membranes was more commonly found in women belonging to low socio-economic status in both PPROM and PROM group. The sensitivity and specificity of maternal CRP was 82.17% and 83.13% respectively. The sensitivity and specificity of WBC count in predicting intra-amniotic infection was 67.16% and 59.14% respectively.
Conclusion: CRP is a reliable diagnostic marker than WBC count for predicting intra-amniotic infection in pregnancies complicated with rupture of membranes.

Keywords: C-reactive protein, preterm premature rupture of membranes, premature rupture of membranes, white blood cell count

Introduction
Premature rupture of membranes refers to a spontaneous membrane rupture that happens before the start of labour (PROM). Preterm premature rupture of membranes (PPROM), or prelabor rupture of membranes before the 37th week of pregnancy, is a frequent obstetric problem that affects about 3-4.5 percent of all pregnancies [1]. PPROM is linked to 30% of newborn morbidity and mortality in preterm birth, and it continues to be a problem for obstetricians [2, 3]. Chorioamnionitis, an acute inflammation of the membranes (amnion and chorion), suggests a significant risk of poor newborn outcomes [4-8]. In patients with PPROM and PROM, chorioamnionitis is usually caused by microbial invasion, but it may also be caused by genital mycoplasmas such Ureaplasma and Mycoplasma hominis, or systemic infection despite intact membranes [9]. Patients with two or more of the following symptoms are identified as having clinical chorioamnionitis: high fever, maternal tachycardia, foetal tachycardia, uterine pain, foul-smelling amniotic fluid, maternal leukocytosis with bands, and positive C reactive protein (CRP) [10]. Serum from the mother The use of C-reactive protein (CRP) as an adjuvant in the identification of subclinical infection in pregnant women with preterm labour or premature rupture of membranes has been investigated. CRP is an acute-phase protein generated by the liver's hepatocytes and is typically present in trace amounts in the blood. Following injury and inflammation, there is a substantial increase in concentration [11]. CRP is linked to altered or necrotic membrane structures once released, and its biological effects include phagocytosis amplification, leukocyte motility stimulation, and opsonic effects, suggesting a role in tissue regeneration and repair [12]. The endothelium system's macrophages, endogene pyrogens, and prostaglandins are all potential humoral mediators [13]. The initiating stimulus produces maximal concentrations 24 to 48 hours later. CRP does not pass through the placenta [14]. Preclinical chorioamnionitis has been diagnosed using a variety of non-invasive indicators. Total leukocyte count (TLC), differential leukocyte count (DLC), urine culture, and vaginal culture are the most common laboratory markers used to indicate intra-amniotic infections.

The goal of this study was to evaluate maternal CRP and WBC count in predicting intra-amniotic infection in pregnancies complicated by membrane rupture.

Material and Methods

This prospective observational study was carried out in the department of Obstetrics and Gynaecology at Sri Devaraj Urs Medical College, Kolar from November 2018 to December 2019.

Inclusion Criteria

Pregnant women with gestational age > 28 weeks and with Ruptured membranes
Singleton pregnancy

Exclusion criteria

Pregnant women with congenital anomalies, antepartum haemorrhage, pre-eclampsia
Pregnant women with medical disorders like diabetes, hypertension, cardiac disease and renal disease
Intrauterine death
Pregnant women with multiple pregnancies

Methodology

This prospective study included a total of 220 women, 110 of whom had ruptured membranes and 110 of whom were gestational age matched controls with intact membranes. The individuals had a general, systemic, and obstetrical examination. On sterile per speculum inspection, a gush of fluid was detected flowing from the cervical os upon coughing, indicating a rupture of membranes. On admission, investigation like CBC & C-reactive protein levels estimation were done in both study and control group. Markers of intrauterine infection were maternal WBC count more than 15,000 cells/cu.mm with positive C-reactive protein levels. CRP determination was done using latex agglutination method with the help of CRP reagent kit. CRP values were considered abnormal (positive), when the values exceeded 6 mg/l. In subjects with leaking per vaginum on speculum examination, vaginally obtained amniotic fluid was sent for aerobic and anaerobic culture to confirm presence of intraamniotic infection.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages.

Results

Table 1: Showing distribution according to age, parity and socio-economic status

Characteristic	PPROM (55)	Gestational age - matched controls (55)	PROM (55)	Control (55)
Age in years				
Below 25	33	31	20	25
25-35	22	24	35	30
Gravidity				
Primigravida	15	29	25	13
Multigravida	40	26	30	42
Socioeconomic status				
Low	10	33	41	37
Middle	39	14	7	11
High	6	8	7	7

Table 2: Showing Parameter of intra-amniotic infection

Parameter	PPROM (55)	Gestational age - matched controls (55)	PROM (55)	Control (55)
Positive	45	7	41	9
Negative	10	48	14	46
>15,000 / cu.mm	19	14	37	10
≤15,000 / cu.mm	36	41	18	45
Growth present	33	11	25	13
Growth absent	17	44	30	42

Table 3: Amniotic fluid culture results in PPROM and controls

	PPROM (55)		Controls (55)	
	Culture(+ve)	Culture(-ve)	Culture(+ve)	Culture(-ve)
CRP				
CRP Positive	32	14	6	0
CRP Negative	4	5	7	42
WBC Count / cu.mm.				
>15,000 cells	13	7	7	7
≤15,000 cells	23	12	5	36

Table 4: Amniotic fluid culture results in PROM and controls

	PROM (55)		Controls (55)	
	Culture(+ve)	Culture(-ve)	Culture(+ve)	Culture(-ve)
CRP				
CRP Positive	19	22	5	5
CRP Negative	6	8	8	37
WBC Count / cu.mm.				
>15,000 cells	14	21	4	5
≤15,000 cells	11	9	9	37

Table 5: Comparison of maternal CRP and WBC count in present study

Marker	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Maternal CRP	82.17%	83.13%	84%	86%
WBC Count	67.16%	59.14%	53%	74%

Discussion

Chorioamnionitis, also known as intra-amniotic infection, is an acute inflammation of the placental membranes and chorion caused by an ascending polymicrobial bacterial infection following membrane rupture. Expectant management is now a well acknowledged therapeutic option for preterm premature rupture of membranes. Nonetheless, the major clinical issue remains the risk of chorioamnionitis in the mother. During the conservative therapy of preterm rupture of membranes, early identification of infection is critical (PROM).

Expectant management is now a widely acknowledged therapeutic option for preterm labour and early rupture of membranes. Nonetheless, the major clinical issue remains the risk of Chorioamnionitis in the mother. As a result, expectant management is focused on the observation of symptoms and indicators of imminent illness.

In the present study, the sensitivity of maternal CRP in predicting intra-amniotic infection in premature rupture of membranes was 82.17% and specificity 83.13%, positive predictive value was 84% and negative predictive value was 86%.

The sensitivity of WBC count in predicting intra-amniotic infection was 67.16% and specificity 59.14%, positive predictive value 53% and negative predictive value was 74% with amniotic fluid culture as the reference standard. The findings are similar to those of Saini S *et al.* [15], who reported

that CRP measurement had an 80% sensitivity and specificity as an early predictor of subclinical chorioamnionitis. In identifying asymptomatic chorioamnionitis, TLC showed a poor sensitivity of 20% and a high specificity of 60%. CRP was found to be a good early indicator of amniotic infection in a study by Ibarra V *et al.* [16], with a sensitivity of 94.12 percent, a specificity of 100 percent, a positive predictive value of 100 percent, and a negative predictive value of 98.86 percent. Our findings are consistent with those of Aggarwal A *et al*., who found that CRP was the most early and accurate diagnostic marker of clinical and histological chorioamnionitis in individuals with preterm premature rupture of membranes [17]. In their investigation, Ismail MA *et al*. found that whereas C-reactive protein levels are a highly sensitive predictor of infectious morbidity in premature membrane rupture, their specificity is low [18]. Kurki T *et al*. found that repeated CRP readings improve test performance, and that CRP's strong negative predictive value indicated that it may be used to predict the absence of chorioamnionitis [19].

Conclusion

In pregnancies complicated by rupture of membranes, CRP is a more reliable diagnostic indicator than WBC count for predicting intra-amniotic infection, according to the findings of this study. If CRP is elevated (>6 mg/l) on admission, the pregnancy should be terminated as quickly as possible to save both the mother and the baby.

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