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"EVALUATION OF THE PREDICTIVE ROLE OF C REACTIVE PROTEIN IN MATERNAL OUTCOME OF PRETERM PREMATURE RUPTURE OF MEMBRANES (PPROM)"

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ABSTRACT **AIMS AND OBJECTIVE:** To evaluate the role of maternal C-reactive protein(CRP) as a predictor of maternal outcomes- chorioamnionitis, Puerperal pyrexia, wound infection, PPH, URTI and UTI in preterm premature rupture of membranes(PPROM). **METHODS:** An institutional based prospective case control study was conducted in Gauhati Medical College and Hospital from 1st July 2019 to 31st June 2020.This study was conducted on total 280 antenatal women, 140 cases of PPROM (Group I) and 140 cases of normal term pregnancy (Group II) were used as a control. Cases were selected by sampling who fulfilled the inclusion and exclusion criteria. The data collected in the study was analysed statistically using descriptive statistics and analysis was carried out by Fischer's exact test. Results were tabulated and analysed statistically using SPSS version 21.0. **RESULTS:** A total of 280 mothers participated in this study which yields 100% response rate. Among the study groups more complications were observed in Cases group (Group I). The most common maternal complications were found to be puerperal pyrexia (6.40%) followed by wound infection (5.00%) in cases group where as in control groups puerperal pyrexia was seen in 3.60% of mothers and wound infection in 2.10% mothers of control group (Group II). Chorioamnionitis was seen only in cases group (Group I) among 4 patients (2.9%) and all of these had CRP>20mg/L. There was no maternal mortality recorded. CRP has sensitivity 100% (95% CI, 85.18% to 100.00%) and specificity 65.81% (95% CI, 56.47% to 74.33%) and PPV 36.51% (95% CI, 30.90% to 42.51%) and NPV 100%. Thus we can utilize CRP as a predictive tool for maternal complications in PPROM mothers. **CONCLUSIONS AND RECOMMENDATION:** Antenatal diagnosis of preterm PROM by identifying risk factors is an important tool in the management of PPROM. CRP is early and reliable indicator of maternal complications with high sensitivity and high negative predictive value. Maternal serum CRP at admission is the most accurate infectious marker for predicting the maternal outcome that is currently in routine use. It may serve as a non-invasive screening tool to distinguish between women with PPROM who are at high or at low risk for adverse maternal outcome.

KEYWORDS : PPROM, C Reactive Protein, Maternal Morbidity & Mortality.

INTRODUCTION

Preterm premature rupture of membranes is defined as spontaneous rupture of the fetal membranes before 37 completed weeks and before labour onset (American College of Obstetricians and Gynaecologists, 2016) [1].

Preterm premature rupture of membranes (PPROM) complicates approximately 2-4% of all pregnancies (2) (3) and intrauterine infection might be responsible for 40–50% of preterm deliveries (4) which can result in significant neonatal morbidity and mortality. (5)

PPROM possess one of the most serious dilemmas in obstetrics since it significantly increases the likelihood of prematurity and serious perinatal infection. Potential pathogens largely arise from the ascending route and the endogenous vaginal flora and may cause chorioamnionitis. (6)

Measurement of inflammatory markers can be an alternative method to detect early infection of PPROM. One of the markers in maternal serum, which indicates an increased risk of preterm delivery or chorioamnionitis, is the C-reactive protein (CRP). (7)

Measuring inflammatory markers can be a predictive method for detecting women at high risk for preterm labour. C-reactive protein (CRP) is a sensitive marker for systemic inflammation. It is produced in hepatocytes in response to infection and tissue damage. It is a sensitive marker of inflammation that remains stable in serum irrespective of gestational age.

AIMS AND OBJECTIVES

- To evaluate the role of maternal C-reactive protein(CRP) as a predictor of maternal outcomes- chorioamnionitis, Puerperal pyrexia, wound infection, PPH, URTI and UTI in preterm premature rupture of membranes(PPROM).

MATERIALS AND METHODS

- The present study was conducted in the Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, Guwahati with a study period of 12 months-From 1st July 2019 to 30th June 2020. The study group includes patients admitted with PPROM under the Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, Guwahati.
- **Study design**: Prospective case control study.
- **Sample size:** A study conducted on total 280 antenatal women, 140 cases of PPROM (Group I) and 140 cases of normal term pregnancy were used as a control (Group II)
- Considering a prevalence of 10% with power 88.9% we need 120 samples and considering 15% nonresponse rate (15/100*120=18) a total of 120+18 = 138 round off 140 sample will be required at 5% level of significance. [Sample size calculated using Medcal Software (demo version)].

Inclusion criteria

1. Women with gestational age more than 28weeks and less than 37 weeks of gestational age with preterm premature rupture of membranes (**For cases group**) (Group I).
2. Primigravida/Multi gravida
3. Singleton pregnancy

Exclusion criteria

Patients with the following conditions were excluded from study.

1. Pre- gestational diabetes, Gestational diabetes & Overt diabetes
2. Pregnancy induced hypertension, chronic hypertension
3. Fetal growth restriction.
4. Any systemic disease or severe systemic infection in the past year.

For Control Group (Group II) Antenatal women with normal Term gestation with same inclusion and exclusion criteria were analysed.

Sample specifications

Clinical samples such as blood and urine were collected from both the cases (Group I) and control groups (Group II) under the Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, Guwahati. A detailed clinical examination was performed. In all cases, routine haematological investigations (Haemoglobin, Total leucocyte count, platelet count, Random blood sugar, serum thyroid stimulating hormone, serum creatinine), urine examination, High vaginal swab (in cases group only) and obstetric ultrasound examination was performed at the time of admission.

Single estimation of Serum CRP level done by a Semi quantitative rapid CRP latex agglutination test at the time of admission.

Principle of the test: The Cortez CRP TEST is based on the latex-agglutination method. The principle of this test is based on the immunological reaction between CRP as an antigen and the corresponding antibody coated on the surface of biologically inert latex particles. CRP Latex Reagent: Contains polystyrene latex particles coated with anti-human CRP in a stabilized buffer with less than 0.1% sodium azide as preservative.

RESULTS AND OBSERVATION

Distribution of cases as per Maternal complications

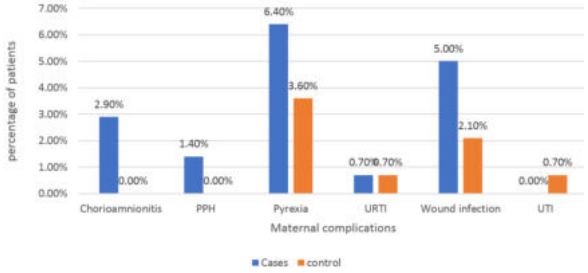

Figure 1: Maternal complications

Among the study groups more complications were observed in Group I and most common maternal complication was found to be puerperal pyrexia (6.40%) and wound infection (5.00%) in Group I where as in Group II puerperal pyrexia was seen in 3.60% of mothers and wound infection in 2.10% mothers of control group. Chorioamnionitis was seen only in cases group (Group I) among 4 patients (2.9%) and all of these had CRP>20mg/L.

There was no maternal mortality recorded.

Table 1: Distribution of study groups as per maternal complications and on the basis of CRP levels

Maternal complications		CRP(mg/L)		Total	p value
		<=5mg/L	>5mg/L		
Cases(n=140) (Group I)	No complications	55.0%	28.6%	2.9%	<0.0001
	Chorioamnionitis	0.0%	2.9%	83.6%	
	PPH	0.0%	1.4%	1.4%	
	Pyrexia	0.0%	6.4%	6.4%	
	URTI	0.0%	0.7%	0.7%	
	Wound infection	0.0%	5.0%	5.0%	
	Total	55.0%	45.0%	100.0%	
Control (n=140) (Group II)	No complications	90.7%	2.1%	92.9%	<0.0001
	Pyrexia	0.0%	3.6%	3.6%	
	URTI	0.0%	0.7%	0.7%	
	UTI	0.0%	0.7%	0.7%	
	Wound infection	0.0%	2.1%	2.1%	
	Total	90.7%	9.3%	100.0%	

In this study all the maternal complications were seen in mothers with CRP >5mg/L in both the cases and control groups. From the analysis it was observed that higher level of CRP (>5 mg/L) was statistically significantly associated with maternal complications with p<0.0001 in both cases (Group I) and control groups (Group II). Thus we can utilize CRP as a predictive tool for maternal complications in PPROM mothers.

Table 1.20: The diagnostic accuracy of CRP values in Maternal complications of PPROM cases evaluated statistically

CASE (Group I):		
Statistic	**Value**	**95% CI**
Sensitivity	100.00%	85.18% to 100.00%
Specificity	65.81%	56.47% to 74.33%
Positive Likelihood Ratio	2.92	2.27 to 3.76
Negative Likelihood Ratio	0	
Disease prevalence (*)	16.43%	10.71% to 23.62%
Positive Predictive Value (*)	36.51%	30.90% to 42.51%
Negative Predictive Value (*)	100.00%	
Accuracy (*)	71.43%	63.19% to 78.74%

Sensitivity, specificity, Positive Predictive Value, Negative Predictive Values was further evaluated Based on the cut of point obtained through ROC Curve.

Table 1.21: The diagnostic accuracy of CRP values in Maternal complications of control group evaluated statistically:

CONTROL (Group II)		
Statistic	**Value**	**95% CI**
Sensitivity	100.00%	69.15% to 100.00%
Specificity	97.69%	93.40% to 99.52%
Positive Likelihood Ratio	43.33	14.16 to 132.61
Negative Likelihood Ratio	0	
Disease prevalence (*)	7.14%	3.48% to 12.74%
Positive Predictive Value (*)	76.92%	52.14% to 91.07%
Negative Predictive Value (*)	100.00%	
Accuracy (*)	97.86%	93.87% to 99.56%

Among 280 mothers in our study groups, CRP >5mg/L could predict 33/33 cases of Maternal complications.

CRP has sensitivity 100% (95% CI, 85.18% to 100.00%) and specificity 65.81% (95% CI, 56.47% to 74.33%) and PPV 36.51% (95% CI, 30.90% to 42.51%) and NPV 100%.

Hence CRP has 100% sensitivity and 100% negative predictive value in predicting maternal complications in both cases (Group I) and control groups (Group II).

Thus we can utilize CRP as a predictive tool for maternal complications in PPROM mothers.

DISCUSSION

Among 140 cases, maternal complications were present only in 16.4% of the population of which Puerperal pyrexia was predominating (6.40%) followed by wound infection was (5.00%) and 2.9% had chorioamnionitis.

STUDY	Puerperal pyrexia	Chorioamnionitis
Artal k study[10]	13%	3%
Shweta patil study(2014)[8]	11%	3%
Shweta anant et al (2015)[9]	12%	-
Our study(2020)	6.4%	2.9%

Among 280 mothers in our study groups, CRP >5mg/L could predict 33/33 cases of Maternal complications.

CRP has sensitivity 100% (95% CI, 85.18% to 100.00%) and specificity 65.81% (95% CI, 56.47% to 74.33%) and PPV 36.51% (95% CI, 30.90% to 42.51%) and NPV 100%.

Hence CRP has 100% sensitivity and 100% negative predictive value in predicting maternal complications in PPROM mothers.

In a study conducted **by Bayar et al (2014)** who showed negative predictive value 100%. [11]

In a study conducted by **Sujata et al (2016)** [12] found CRP level to be more sensitive (100%) but less specific (36.89%) in identifying clinical chorioamnionitis. The positive predictive value was 35.7% and negative predictive value was 100%. Our results were in accordance with other studies.

Study	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Bayar et al (2014)[11]	100%	36.89%	35.7%	100%
Dr.Sujata et al (2016)[12]	100%	36.89%	35.7%	100%
Our study (2020)	100%	65.81%	36.51%	100%

Our results were comparable with other studies.
Thus we can utilize CRP as a predictive tool for diagnostic evaluation of maternal complications in PPROM mothers (Group I).

CONCLUSION

PPROM is a common cause of preterm delivery and it is responsible for increased maternal morbidity and perinatal morbidity and mortality. Strict aseptic precautions, appropriate therapy, regular antenatal follow-up are important factors in the prevention and management of PPROM. The ultimate solution lies in accurate determination of etiological factors and prevention of rupture of membranes and to predict the possibilities of maternal morbidities early and treat it. CRP is early and reliable indicator of maternal complications with high sensitivity and high negative predictive value. Maternal serum CRP at admission is the most accurate infectious

marker for predicting the maternal outcome in PPROM that is currently in routine use. It may serve as a non-invasive screening tool to distinguish between women with PPROM who are at high or at low risk for adverse maternal outcome.

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