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Original Research Article

TO DETERMINE THE ROLE OF C- REACTIVE PROTEIN IN FETOMATERNAL OUTCOME IN ANTENATAL SUBJECTS WITH PREMATURE RUPTURE OF MEMBRANE

Shraddha Mehta[1], Gita Guin[2], Ranu Jain[3], Jagmohan Singh Dhakar[4]

[1]Postgraduate Student, Department of Obstetrics and Gynecology, NSCB Medical College, Jabalpur, Madhya Pradesh, India
[2]Professor & Head, Department of Obstetrics and Gynecology, NSCB Medical College, Jabalpur, Madhya Pradesh, India
[3]Assistant Professor, Department of Obstetrics and Gynecology, NSCB Medical College, Jabalpur, Madhya Pradesh, India
[4]Assistant Professor (Statistics), Department of Community Medicine, VKS Government Medical College, Neemuch, Madhya Pradesh, India

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Corresponding Author
Shraddha Mehta
Email: mehtashraddha0gmail.com

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Abstract

Background: We conducted this study at tertiary care centre to determine the correlation of C-reactive protein (CRP) with Premature rupture of membranes (PROM) and its association with fetomaternal outcome among antenatal subjects with premature rupture of membranes. **Materials and Methods:** This study was conducted as a prospective observational study on 130 antenatal subjects admitted at Department of Obstetrics and Gynecology, Government Medical college, Jabalpur M.P. with premature rupture of membranes during the study period of 18 months i.e. from 1st August 2022 to 31st January 2024. Detailed history taking and examination was done and routine investigations were done along with CRP. Fetal and maternal outcome was assessed. **Result:** C-reactive protein was found to be positive in 39.2% subjects of PROM. We found a significant association of CRP positivity with maternal pyrexia, increased White blood cell count, foul smelling lochia, poor APGAR score and increased NICU admission ($p<0.05$). We found a significant association of positive vaginal swab culture with maternal pyrexia, increased WBC count, foul smelling lochia, poor APGAR score and NICU admission ($p<0.05$). **Conclusion:** In Obstetrics, premature rupture of membrane is associated with significant maternal and neonatal morbidity and mortality. CRP can be utilized as an early diagnostic marker for adverse feto-maternal outcome in patients with PROM. The prompt use of appropriate antibiotics, steroids for fetal lung maturity and labor induction or augmentation minimizes morbidity due to PROM and improve perinatal and maternal outcome. Hence it is the need of the hour to motivate parturient for regular antenatal check-up.

INTRODUCTION

Premature rupture of membrane, also called as prelabour rupture of membranes is a common condition with global incidence varying from 5% to 10% of all the deliveries whereas the incidence of PPROM is approximately 3%.[1] The incidence of PROM is documented to range between 18% and 20% in developing countries.[2] PROM is associated with significant maternal and perinatal morbidity as well as mortality. It not only causes physical morbidities, but also causes national economic loss due to prolonged hospitalization, drug expenses, and absence from workplace.[3]

Numerous variables, including gestational age at time of labour, the use of antibiotics and steroids, the length of labor, and the occurrence of intrapartum chorioamnionitis determine the fetal and mother outcomes. Among these, the latent period of leaking, that is, the time between the rupture of membranes and the initiation of labor, is crucial for deciding the result for both the mother and the fetus.[4] The common causes of lower genital infections include aerobic vaginitis, bacterial vaginosis and candidiasis. For diagnosis of these infections, a high vaginal swabs are collected and subjected to culture and sensitivity so as to diagnose these infections as early as possible, so that PROM can be prevented.[5]

The diagnosis of PROM is done by speculum vaginal examination of cervix and vaginal cavity. Presence of amniotic fluid in the vagina pooling from cervical canal typically confirm the diagnosis of rupture of

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membranes. The dried fluid obtained from cervical canal on speculum show ferning under microscope and Nitrazine paper suggesting alkalinity of fluid confirm the diagnosis.[6] In 30–40% of PPROM cases, microbial invasion of the amniotic cavity (MIAC) has been found, especially in the early stages of pregnancy. A shorter delay to delivery and an earlier gestational age at birth are linked to the inflammatory response that is triggered in the amniotic cavity when bacteria are present. Both the mother and the fetus are at risk from acute chorioamnionitis, especially in the early stages of pregnancy. One of the marker in the maternal serum indicating high risk of chorioamniotis in women undergoing preterm delivery is C reactive protein, which may be early predictor of chorioamnionitis.[7] According to American College of Obstetrics and Gynaecology guidelines, induction of labour must be performed immediately to reduce the risk of chorioamnionitis and other complications, regardless of gestational age.[8] Based upon the intrapartum risk factors and previous culture reports, Group B streptococcal prophylaxis is recommended.[9] With the above background, we conducted this study at tertiary care centre to determine the correlation of C-reactive protein and vaginal swab culture with premature rupture of membranes and its association with fetomaternal outcome among the study population.

MATERIALS AND METHODS

The present study was conducted as a prospective observational study on 130 antenatal subjects with gestational age of 37 weeks or beyond admitted at Department of Obstetrics and Gynecology, NSCB Medical College and Hospital, Jabalpur M.P. with premature rupture of membranes during the study period of 18 months i.e. from 1st August 2022 to 31st January 2024. Antenatal subjects admitted in Department of Obstetrics and Gynecology at or beyond 37 weeks of gestation with premature rupture of membranes in NSCB medical College and Hospital, Jabalpur were included whereas all antenatal subject with gestational age less than 37 weeks presenting with premature rupture of membranes, subjects in active stage of labour and non consenting antenatal subjects were excluded from the study.

After obtaining ethical clearance from Institute's ethical committee, all the patients satisfying inclusion criteria were enrolled and written consent was obtained from all of them. Detailed history was obtained and documented in proforma. All the patients were then subjected to detailed general and systemic examination. Per-abdominally height of uterus and abdominal girth were measured and fetal heart sounds were assessed using fetal doppler. CTG was done to assess the status of fetus. Routine investigations along with high vaginal swab culture and C-reactive protein- by immunoturbidimetric analysis to confirm PROM. After assessing the condition of patients, delivery was conducted either vaginally or by LSCS. For induction, patients were selected randomly for induction with PGE1/PGE2 as induction agent and their process of labour was recorded. After induction, the subjects who underwent NVD and who required LSCS were recorded along with indication of LSCS. Timing from induction to delivery was recorded in all the cases and documented in proforma. Fetal and maternal outcome was assessed and noted in proforma.

Statistical Analysis: Data was compiled using MsExcel and analysis was done with the help of IBM SPSS software version 20. Categorical variables were expressed as frequency and proportion whereas continuous variables were presented as mean and standard deviation. Association of fetomaternal outcome with CRP and mode of delivery with induction was done using chi square test. P value of less than 0.05 was considered statistically significant.

RESULTS

The present study was conducted on a total of 130 subjects presenting with PROM at our study area during the study period. Mean age of patients presenting with PROM was 26.01±3.193 years and majority i.e. 42.3% subjects belonged to 20 to 24 years of age. Majority of subjects with PROM belonged to lower socioeconomic status (46.2%), and about 50% of the subjects with PROM were booked whereas 40.8% of the subjects were unbooked. Majority of patients with PROM were primigravida (36.9%) with mean gravidity of 2.22±1.09. Mean gestational age of patients presenting with PROM was 38.17±1.08 weeks and majority i.e. 34.6% subjects belonged to gestational age of 37 to 38 weeks (34.6%). Duration of leaking ranged from 6 to 12 hours in majority of subjects (39.2%) [Table 1].

Table 1: Distribution of subjects with PROM according to baseline variables.

Baseline variables		Frequency (n=130)	Percentage
Age (years)	20-24	55	42.3
	25-29	51	39.2
	30-34	24	18.5
Socioeconomic status	Upper	4	3.1
	Upper middle	12	9.2
	Middle	30	23.1
	Lower middle	24	18.5
	Lower	60	46.2
Booking status	Booked	65	50.0

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	Partially booked	12	9.2
	Unbooked	53	40.8
Gravida	1	48	36.9
	2	24	18.5
	3	40	30.8
	4	18	13.8
Gestational age (weeks)	37	42	32.3
	37-38	45	34.6
	38-39	25	19.2
	39-40	15	11.5
	>40	3	2.3
Duration of leaking (hours)	<6	40	30.8
	6-12	51	39.2
	12-18	33	25.4
	>18	6	4.6

Mean induction to delivery time was 11±3.42 hours (range- 0 to 14 hours).
We found C-reactive protein to be positive (>6 mg/L) in 39.2% subjects of PROM. Vaginal culture was positive for E.coli in 16.2% subjects, candidal species in 2.3% subjects, enterococcus in 1.5% subjects and coagulase negative streptococci in 0.8% cases.

Table 2: Association of CRP with fetomaternal outcome

Outcome			**CRP**				**P value**
			Negative		**Positive**		
			n	**%**	**n**	**%**	
Maternal	Maternal pyrexia	Absent	48	60.8	9	17.6	0.001
		Present	31	39.2	42	82.4	
	Maternal WBC count	<10000	27	34.2	9	17.6	0.001
		10000-20000	40	50.6	12	23.5	
		20000-25000	12	15.2	18	35.3	
		>25000	0	0	12	23.5	
	Foul smelling lochia	Absent	76	96.2	30	58.8	0.001
		Present	3	3.8	21	41.2	
Fetal	Condition	Alive	75	94.9	48	94.1	0.84
		Death	4	5.1	3	5.9	
	Birth weight (kg)	<2.5	30	38	27	52.9	0.093
		>2.5	49	62	24	47.1	
		Mean±SD	2.62±0.48		2.51±0.22		
	APGAR score	<3	3	3.8	21	41.2	0.001
		3-7	21	26.6	21	41.2	
		>7	55	69.6	9	17.6	
	NICU admission (days)	No	58	73.4	12	23.5	0.001
		Yes	21	26.6	37	76.5	
		Mean±SD	0.61±0.34		2.65±1.44		

We found a significant association of CRP positivity with maternal pyrexia, increased WBC count, foul smelling lochia, poor APGAR score and increased NICU admission ($p<0.05$) (Table 2).

Table 3: Association of vaginal swab with fetomaternal outcome

Outcome			**Vaginal swab culture**										**P value**
			Sterile		**E.coli**		**CONS**		**Candida**		**Enterococcus**		
			n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	
Maternal	Maternal pyrexia	Absent	54	52.4	3	14.3	0	0	0	0	0	0	0.004
		Present	49	47.6	18	85.7	1	100	3	100	2	100	
	WBC count	<10000	33	32	3	14.3	0	0	0	0	0	0	0.001
		10000-20000	49	47.6	1	4.8	0	0	1	33.3	1	50	
		20000-25000	21	20.4	7	33.3	0	0	1	33.3	1	50	
		>25000	0	0	10	47.6	1	100	1	33.3	0	0	
	Foul smelling lochia	Absent	100	97.1	4	19	0	0	1	33.3	1	50	0.001
		Present	3	2.9	17	81	1	100	2	66.7	1	50	
Neonatal	Condition	Alive	96	93.2	21	10	1	100	3	100	2	100	0.523
		Death	7	6.8	0	0	0	0	0	0	0	0	
	Birth weight (kg)	<2.5	42	40.8	11	52.4	1	100	2	66.7	1	50	0.56
		>2.5	61	59.2	10	47.6	0	0	1	33.3	1	50	
		Mean±SD	2.61±0.44		2.47±0.16		2.3±0		2.5±0.2		2.6±0.2		
	APGAR score	<3	3	2.9	17	81	1	100	2	66.7	1	50	0.001
		3-7	36	35	4	19	0	0	1	33.3	1	50	

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		>7	64	62.1	0	0	0	0	0	0	0	0	
	NICU admission (days)	No	67	65	3	14.3	0	0	0	0	0	0	0.001
		Yes	36	35	18	25.7	1	100	3	100	2	100	
		Mean±SD	0.76±0.33		4.1±2.4		5±0		3.3±1.1		2.5±1.2		

We found a significant association of positive vaginal swab culture with maternal pyrexia, increased WBC count, foul smelling lochia, poor APGAR score and NICU admission ($p<0.05$) (Table 3).

Table 4: Correlation of vaginal culture and CRP in patients with PROM

Vaginal culture	CRP Negative (n=79)		CRP Positive (n=51)	
	n	%	n	%
Sterile	79	100	24	47.1
E. coli	0	0	21	41.2
Coagulase negative streptococci	0	0	1	2
Candidal species	0	0	3	5.9
Enterococcus	0	0	2	3.9
P value	0.001			

Vaginal culture was found to sterile in 100% CRP negative subjects with PROM whereas it was sterile in 47.1% subjects with positive CRP. More than half of the subjects with positive CRP showed positive culture. The observed correlation of vaginal culture with CRP statistically significant ($p<0.05$) [Table 4].

DISCUSSION

Premature rupture of membranes also called prelabour rupture of membranes is one of the common obstetric complication associated with preterm labour, low birth weight and high perinatal morbidity and mortality.[1] PROM is associated with various risk factors such as inadequate care during pregnancy, low socioeconomic status, intrauterine infection during early gestational period, sexually transmitted infections etc. Vaginal infections are one of the most common causes associated with PROM and thus early diagnosis and treatment of these infection may help in reducing the risk of PROM and thus reducing perinatal morbidity and mortality.[10] The present study was conducted on a total of 130 subjects presenting with PROM at our hospital to determine the correlation of C-reactive protein with PROM. We also aimed to determine the fetomaternal outcome among antenatal subjects with premature rupture of membranes. We included 130 subjects with term pregnancy (>37 weeks) and mean gestational age of patients with PROM was 38.17±1.08 weeks.

We aimed to study correlation of CRP and vaginal culture in patients with PROM. We found CRP to be positive in 39.2% subjects with PROM and vaginal culture revealed growth of micro-organisms in 20.8% subjects (E.coli in 16.2% subjects, candidal species in 2.3% subjects, enterococcus in 1.5% subjects and coagulase negative streptococci in 0.8% subjects). In present study, we found a significant association of vaginal culture with CRP i.e. all the CRP negative subjects had sterile vaginal culture whereas 52.9% CRP positive subjects showed growth of either E.coli or other gram negative bacteria on vaginal culture ($p<0.05$). Further, we stratified patients based upon duration of leaking and documented that duration of leaking of less than 6 hours was associated with sterile culture in 100% subjects irrespective of CRP levels, however, as the duration of leaking increased, we found significant increase in growth in vaginal cultures, which correlated with increased CRP levels ($p<0.05$). All the subjects with duration of leaking of more than 18 hours had positive CRP and showed growth in culture.

Singh et al reported higher positivity rate in culture (84%), most common being Staphylococcus aureus (12.6%), followed by E.coli (12%). Raised CRP was documented in 44% subjects whereas raised TLC were found in 29.33% subjects, however, correlation between CRP and vaginal culture was not assessed.[11] In a study of Chandra et al, CRP was found to be positive in 44% subjects and growth on cervical swab was documented in 38% subjects, most common being E.coli (35.1%), followed by Klebsiella (20.3%) and Group B Streptococcus (13.5%). however, no such association was observed with positive culture ($p>0.05$).[12] In another study by Jaiswal et al, CRP was positive in 20.5% subjects and 6.7% subjects had positive blood culture.[13]

Amongst maternal risk factors, maternal pyrexia was present in 56.2% subjects with PROM and WBC counts were raised in 72.3% subjects with 9.2% subjects having WBC count above 25000. History of foul smelling vaginal discharge was present in 18.5% subjects.

We documented maternal pyrexia, WBC counts and foul smelling lochia to be significantly linked with higher rate of CRP positivity as well as positive growth on culture ($p<0.05$). The findings of our study were supported by the findings of Chandra et al, in which positive CRP was associated with unfavourable maternal outcome ($p<0.05$).[12] Similar findings were documented by Patel et al, in which the authors found a significant association of CRP with chorioamnionitis ($p<0.05$). In this study, out of 57 CRP positive patients, chorioamnionitis was found in 47.36% cases whereas 2.32% cases with CRP negative status developed chorioamnionitis ($p<0.05$).[14] Fathey et al also documented a significant association of maternal CRP with raised ESR, TLC and offensive discharge PV ($p<0.05$).[15]

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Neonatal outcome was assessed in terms of condition of neonate, birth weight, APGAR score, and need for NICU admission. We found a significant association of CRP positivity and vaginal culture growth with poor APGAR score in neonates as well as higher risk of NICU admissions ($p<0.05$). The findings of our study were supported by the findings of Chandra et al, in which positive CRP was associated with unfavourable neonatal outcome ($p<0.05$).[12] Similarly Patel et al found CRP positivity to be significantly associated with adverse neonatal outcome ($p<0.05$).[14] Fathey et al also documented a significant association of maternal CRP with poor APGAR score, need of fetal hospitalization as well as low birth weight ($p<0.05$).[15]

Small sample size was the obvious limitation of the study. Secondly, due to lack of control group, association and causality of various risk factors with PROM could not be established.

CONCLUSION

In Obstetrics, premature rupture of membrane is associated with significant maternal and neonatal morbidity and mortality. It has detrimental implications on the health of both the mother and the fetus, and presents a difficult situation for obstetricians who are caught in this situation. CRP can be utilized as an early diagnostic marker for adverse feto-maternal outcome in patients with PROM. CRP correlate well with positive growth on culture reports. The prompt use of appropriate antibiotics, steroids for fetal lung maturity and labor induction or augmentation minimizes morbidity due to PROM and improve perinatal and maternal outcome. Hence it is the need of the hour to motivate parturient for regular antenatal check-up. Proper education, counselling through antenatal checkups will give them a safe motherhood opportunity thereby decreasing burden and the fear of pregnancy related complications.

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