Original research article

Role of maternal CRP with WBC count in predicting intra-amniotic infection in premature rupture of membranes: a comparative study

Anupama Sinha[1], Krishna Sinha[2*]

[1]Associate Professor,Department of Obstetrics & Gynaecology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India.

[2]Associate Professor,Department of Obstetrics & Gynaecology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India.

Received: 03-08-2020 / Revised: 08-10-2020 / Accepted: 27-10-2020

Abstract

Aim: To evaluate the usefulness of maternal CRP and WBC count in diagnosing intra-amniontic infection in the preclinical stage in women with prelabor rupture of membranes.

Methods: This prospective observational study was carried out in the Department of Obstetrics and Gynecology at Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India from feb 2019 to November 2019. Intra-amniotic infection was confirmed by obtaining amniotic fluid vaginally and subjecting it for aerobic and anaerobic culture.**Results:** A total of 200 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 50 each group. 100 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. In PPROM, 43 cases were positive for maternal CRP while 38 out of 50 were positive in PROM group. 17 PPROM cases out of 50 indicated presence of infection. Among PROM group, 34 cases had maternal WBC count > 15,000 cells/cu.mm. The sensitivity and specificity of maternal CRP was 80.67% and 81.33% respectively. The sensitivity and specificity of WBC count in predicting intra-amniotic infection was 65.66% and 59.84% respectively.

Conclusion: Present study concluded that 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

Spontaneous membrane rupture that occurs before the onset of labor is termed as premature rupture of membranes (PROM). Prelabor rupture of membranes before the 37th week of gestation, termed preterm premature rupture of membranes (PPROM), is a common obstetric complication which occurs in approximately 3-4.5% of all pregnancies.[1]

**Correspondence*

Dr. Krishna Sinha

Associate Professor,Department of Obstetrics & Gynaecology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India.

E-mail: drkrishnabgp@gmail.com

PPROM is associated with 30% of neonatal morbidities and mortalities in preterm delivery and remains a challenge for the obstetrician.[2,3] Acute inflammation of the membranes (amnion and chorion), chorioamnionitis, indicates high risk of adverse neonatal outcomes.[4-8] Chorioamnionitis is typically the result of microbial invasion in patients with PPROM and PROM, but can also be caused by genital mycoplasmas, such as Ureaplasma and Mycoplasma hominis or systemic infection inspite of intact membranes.[9] Clinical chorioamnionitis is diagnosed in patients presenting with two or more of the following criteria: high temperature, maternal tachycardia, fetal tachycardia, uterine tenderness, foul smelling amniotic fluid, maternal leukocytosis with bands, and

positive C reactive protein (CRP).[10] Maternal serum C-reactive protein (CRP) has been studied as an adjunct in the diagnosis of subclinical infection among pregnant women with preterm labor or preterm rupture of membranes. CRP is an acute-phase protein produced in the hepatocytes of the liver, and is normally present as a trace constituent in the serum. A significant rise in the concentration is seen following injury and inflammation.[11] Once released, CRP is bound to altered or necrotic membrane structures, and its biological effects include enhancement of phagocytosis, stimulation of leukocyte motility and opsonic effects, suggesting a specific role in tissue regeneration and repair.[12] Possible humoral mediators are the macrophages of the endothelial system, the endogene pyrogens and the prostaglandins.[13] Maximal concentrations are seen 24- 48 h after the inducing stimulus. CRP is not transferred across the placenta.[14] Various non-invasive markers have been studied to diagnose chorioamnionitis in the preclinical stage. The laboratory indicators most often used to predict intra-amniotic infections are total leucocyte count (TLC), differential leukocyte count (DLC), urine culture, and vaginal culture. The present study was conducted with the aim to compare maternal CRP and WBC count in predicting intra- amniotic infection in pregnancies complicated with rupture of membranes.

Material & Methods

This prospective observational study was carried out in the department of Obstetrics and Gynaecology at Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India from feb 2019 to November 2019.

The study protocol was reviewed by the Ethical Committee of the Hospital and granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained.

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

Total 200 women were included as subjects in this prospective study, out of which 100 had ruptured membranes and 100 were gestational age matched controls with intact membranes. History taking, general, systemic and obstetrical examination of subjects was done.

Diagnosis of rupture of membranes was made by gush of fluid seen coming through the cervical os on coughing on sterile per speculum examination.

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 (50)	Gestational age - matched controls (50)	PROM (50)	Control (50)	n=200
Age in years					
Below 25	30	28	18	23	99
25-35	20	22	32	27	101
Gravidity					
Primigravida	13	27	23	10	73
Multigravida	37	23	27	40	127

Socioeconomic status					
Low	9	31	39	35	114
Middle	37	12	6	10	65
High	4	7	5	5	21

Table 2: Showing Parameter of intra-amniotic infection

Parameter	PPROM (50)	Gestational age - matched controls (50)	PROM (50)	Control (50)	n=200
Maternal CRP					
Positive	43	5	38	7	93
Negative	7	45	12	43	107
WBC count					
>15,000 / cu.mm	17	12	34	8	71
≤15,000 / cu.mm	33	38	16	42	129
Amniotic fluid culture					
Growth present	33	10	23	11	77
Growth absent	17	40	27	39	123

Table 3: Amniotic fluid culture results in PPROM and controls

	PPROM (50)		Controls (50)	
	Culture(+ve)	Culture(-ve)	Culture(+ve)	Culture(-ve)
CRP				
CRP Positive	30	13	5	0
CRP Negative	3	4	5	40
WBC Count / cu.mm.				
>15,000 cells	11	6	6	6
≤15,000 cells	22	11	4	34

Table 4: Amniotic fluid culture results in PROM and controls

	PROM (50)		Controls (50)	
	Culture(+ve)	Culture(-ve)	Culture(+ve)	Culture(-ve)
CRP				
CRP Positive	18	20	4	3
CRP Negative	5	7	7	36
WBC Count / cu.mm.				
>15,000 cells	13	20	3	4
≤15,000 cells	10	7	8	35

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

Marker	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Maternal CRP	80.67%	81.33%	82%	83%
WBC Count	65.66%	59.84%	51%	72%

Discussion

Chorioamnionitis or intra-amniotic infection is an acute inflammation of the membranes and chorion of the placenta, typically due to ascending polymicrobial bacterial infection in the setting of membrane rupture. Expectant management for preterm premature rupture of membranes is now an accepted modality of treatment. Nevertheless, the main clinical concern is still the danger to the mother of acquiring chorioamnionitis. Early detection of infection is of utmost importance during the conservative

management of premature rupture of membranes (PROM).

Expectant management for preterm labour and preterm premature rupture of membranes is now an accepted modality of treatment. Nevertheless, the main clinical concern is still the danger to the mother of acquiring Chorioamnionitis. Therefore, an approach to expectant management is based on monitoring for symptoms and signs of impending infection.

In the present study, the sensitivity of maternal CRP in predicting intra-amniotic infection in premature rupture of membranes was 80.67% and specificity 81.33%, positive predictive value was 82% and negative predictive value was 83%. The sensitivity of WBC count in predicting intra-amniotic infection was 65.66% and specificity 59.84%, positive predictive value 51% and negative predictive value was 72% with amniotic fluid culture as the reference standard. The study is comparable to study done by Saini S *et al*., in which sensitivity and specificity of CRP determination was found to be 80% each as an early predictor of subclinical chorioamnionitis.[15] TLC had a low sensitivity of 20% and specificity of 60% in detecting subclinical chorioamnionitis. Study done by Ibarra V *et al*. showed CRP as an early detector of amniotic infection with a sensitivity of 94.12% and a specificity of 100%, positive predictive value of 100% and a negative predictive value of 98.86%.[16] Our study also co-relates with study done by Aggarwal A *et al*., wherein they concluded that CRP was the earliest and most reliable diagnostic marker of clinical as well as histological chorioamnionitis in patients with preterm premature rupture of membranes.[17] Ismail MA *et al*. in their study concluded that C-reactive protein level is a very sensitive predictor of infectious morbidity in premature rupture of membranes, its specificity is not high.[18] In study done by Kurki T *et al*. concluded that use of serial CRP measurements increases the test performance and the high negative predictive value suggested that CRP was useful in predicting the absence of chorioamnionitis.[19]

Conclusion

The present study concluded that CRP is a reliable diagnostic parameter than WBC count for predicting intra-amniotic infection in pregnancies complicated with rupture of membranes. If CRP is found positive (>6 mg/l) on admission, pregnancy should be terminated as soon as possible to salvage the baby as well as the mother.

Reference

1. Lee T, Silver H. Etiology and epidemiology of preterm premature rupture of the membranes. Clin Perinatol. 2001; 28:721-34
2. Gopalani S, Krohn M, Meyn L et al.: Contemporary management of preterm premature rupture of membranes: determinants of latency and neonatal outcome. Am J Perinatol. 2004; 21:183-90.
3. Garite TJ. Management of premature rupture of membranes. Clin Perinatol. 2001; 28:837-47.
4. Ecevit A, Anuk-Ince D, Yapakci E et al.: Association of respiratory distress syndrome and perinatal hypoxia with histologic chorioamnionitis in preterm infants. Turk J Pediatr. 2014; 56:56-61.
5. Dempsey E, Chen MF, Kokottis T et al. Outcome of neonates less than 30 weeks gestation with histologic chorioamnionitis. Am J Perinatol. 2005; 22:155-59.
6. De Felice C, Toti P, Laurini RN et al.: Early neonatal brain injury in histologic chorioamnionitis. J Pediatr. 2001; 138:101-4.
7. Wu YW. Systematic review of chorioamnionitis and cerebral palsy. Ment Retard Dev Disabil Res Rev. 2002; 8:25-29.
8. Nelson KB, Grether JK, Dambrosia JM et al. Neonatal cytokines and cerebral palsy in very preterm infants. Pediatr Res. 2003; 53:600-7.
9. Edwards RK. Chorioamnionitis and labor. Obstet Gynecol Clin North Am. 2005; 32:287-96.
10. Gibbs RS, Blanco JD, St Clair PJ, Castaneda YS. Quantitative bacteriology of amniotic fluid from women with clinical intraamniotic infection at term. J Infect Dis. 1982; 145:1-8.
11. Morley JJ, Kushner I. Serum C-reactive protein levels in disease. Ann NY Acad Sci. 1982; 389:406-17.
12. Gewurz H, Mold C, Siegel J, Fiedel B. C-reactive protein and the acute-phase response. Year Book Medical Publishers, 1982, 345-371.
13. Macintyre SS, Schultz D, Kushner I. Biosynthesis of Creactive protein. Ann NY Acad Sci. 1982; 389:76-87.
14. Shine B, Gould J, Campbell C, Hindocha P, Wilmot RP, Wood CBS. Serum C-reactive protein in normal and infected neonates. Clin Chim Acta. 1985; 148:97-103.
15. Saini S, God N, Sharma M, Arora B, Garg N. C-reactive proteins as an indicator of sub-clinical

infection in cases of premature rupture of membranes. Indian J Pathol Microbiol. 2003; 46(3):515-6.
16. Ibarra CV, Sanhueza SP, Mota GM, Del RPG, Karchmer S. CRP as early marker of chorioamnionitis in PROM (span). Gynaecologia Y Obstetrica de Mexico. 1989; 57:203-8.
17. Aggarwal A, Pahwa S. Evaluation of the role of CRP as an early predictor of chorioamnionitis in PPROM. Int J Reprod Contracept Obstet Gynecol, 2018; 7:1351-6.
18. Ismail MA, Zinaman MJ, Lowensohn RI, Moawad AH. The significance of C-Reactive protein levels in women with premature rupture of membranes. Am J Obstet Gynecol. 1985; 151(4):541-44.
19. Kurki T, Teramo K, Ylikorkala O et al. C-reactive protein in preterm premature rupture of the membranes. Arch Gynecol Obstet. 1990; 247:31-7.

Conflict of Interest: Nil
Source of support:Nil