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A retrospective study to determine the role of vaginal infection in spontaneous preterm premature rupture of membranes

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Abstract

Introduction: Premature rupture of membranes (PROM) refers to a patient who is beyond 37 weeks POG and has presented with rupture of membranes (ROM) prior to the onset of labour. Preterm premature rupture of membranes (PPROM) is ROM prior to 37 weeks POG[1]. The incidence of PROM in preterm labour is 30% and PPROM is 10% and prematurity from these births is a leading cause of deaths in neonates[2]. Ascending uterine infection from the lower genital tract has been found to be associated with adverse gynaecological and pregnancy outcomes[3], including PROM, preterm delivery, chorioamnionitis and endometritis[4]. Despite these problems, vaginal infection is often asymptomatic and may go undetected with potentially serious consequences. Since preventive measures can prevent these complications, the present study was undertaken to study the role of vaginal infection in PPROM.

Methodology: A retrospective study was done at Rajarajeswari Medical College and Hospital, Bangalore, Karnataka. In this study, we determine the prevalence of vaginal infection in 20 cases with spontaneous PPROM. The diagnosis of vaginal infection was made by high vaginal swab culture and sensitivity.

Results: High vaginal swab had growth in 14 (70%) out of 20 women with PPROM. Out of the 14 cases with PPROM and vaginal infection, 10 (71.42%) were unbooked while 4 (28.57%) were booked, 1 (7.14%) was of Upper Class, 5 (35.71%) were of Middle Class, 8 (57.14%) were of Lower Class. E. Coli (28.57%) was the commonest isolated organism grown followed by

Enterococci (21.42%). Most of pathological isolates were sensitive to cefixime, ampicillin and gentamicin.

Conclusion: The results of this study add to the existing evidence that vaginal infection is an important causative factor for PPROM. This study provides important data about lower genital tract micro biodata of PPROM in pregnant women and most of pathological isolates were sensitive to cefixime, ampicillin and gentamicin. Preventive measures can prevent vaginal infection. Vaginal infection was seen more in unbooked patients of lower socio economic class than in booked patients or patients of middle or upper socioeconomic class. Therefore, timely detection and treatment, education of masses and awareness about importance of regular antenatal visits is important to avoid infections, preterm labour, prematurity, associated neonatal morbidity and mortality.

Keywords: Antibiotics, Preterm premature rupture of membranes, Prematurity, Vaginal infection

Introduction

Preterm birth is the most common cause of neonatal morbidity and mortality worldwide. It is seen in 85% of infant deaths[5]. Preterm labour is defined as occurrence of regular uterine contractions and associated cervical changes in women with intact foetal membranes with gestational age more than 20 weeks and less than 37 weeks[6]. Premature rupture of membranes (PROM) refers to a patient who is beyond 37 weeks POG and has presented with rupture of membranes (ROM) prior to the onset of labour. Preterm premature rupture of membranes (PPROM) is ROM prior to 37 weeks POG[1]. The incidence of PROM in preterm labour is 30% and PPROM is 10% and prematurity from these births is a leading cause of deaths in neonates[2]. The associated complications include respiratory distress syndrome, hypothermia, hypoglycaemia, necrotising enterocolitis, and intra-ventricular haemorrhage. Risk of foetal death is 1-2% in PPROM[2]. Once the membranes rupture, delivery is recommended when the risk of ascending infection outweighs the risk of prematurity. In other cases, expectant management can be done by administering corticosteroids and antibiotics, and under careful monitoring for the signs of worsening infection.

The aetiology of most cases of preterm labour, PPROM, PROM is unknown, but a vast number of conditions have been found to be associated with an increased risk of preterm delivery. One of the most important causes being vaginal infection, commonly seen in women of reproductive age. It has been associated with increased risks for prematurity and PROM. 33% of patients with PPROM show a positive microbial culture from the amniotic fluid[7-11].

Vaginal infection is associated with symptoms of abnormal vaginal discharge, odour and irritation, itching, or burning. About 50% of women with vaginal infection have no symptoms to alert the physician or patient[12]. The most common causes are vulvovaginal candidiasis, bacterial vaginosis and trichomoniasis. In developing countries, the prevalence of vaginal infection was as high as 52% whereas European studies of asymptomatic pregnant women show the prevalence to be in the range of 4.9% to 21.9%[13-15]. This variation could be attributed to differences in socio-cultural practices in different communities[16].

Intrauterine infection has been a contributing factor in up to 60 % of cases of PPROM[18,19]. Ascending infection from vagina is the most common cause of infection. However, infection caused by ascending microorganisms may also occur secondary to PPROM[18,19]. It has been suggested that many organisms that are present in the

vaginal flora, including E. Coli, group B streptococcus, Staphylococcus aureus, Mycoplasma, Chlamydia, Yeast, Neisseria gonorrhoeae and organisms causing bacterial vaginosis secrete phospholipase that degrades collagen and weaken the foetal membranes leading to PROM[20,21]. Main cause for rupture of membranes is decrease or loss of tensile power of the membranes. The collagens contribute to the tensile strength of the membranes. The pathophysiology of infection (intrauterine/cervical/choriodecidual) causing PPROM is due to an innate immune system response to infection when microorganisms bind to pattern-recognition receptors (e.g. toll-like receptors). This is followed by release of inflammatory chemokines and cytokines like IL-8, IL1β, TNFα. Apart from this, microbial endotoxins produce prostaglandins and matrix-degrading enzymes[17]. Prostaglandins are responsible for uterine contractions. Meanwhile, matrix-degrading enzymes lead to increase in metalloproteinase, which is responsible for collagen degradation. Collectively, uterine contractions and degradation of extracellular matrix in the foetal membranes predisposes PROM as there is decrease in the tensile power of the membranes.

Urinary tract infections are also found to be the cause of PPROM in 5-10% cases. Recent data suggests that some microbes invade the amniotic cavity from the bloodstream after dissemination from remote sites as well, e.g. from the gastrointestinal tract[22].

The present study determines the prevalence of vaginal infection in patients with spontaneous PPROM. Two other important factors leading to vaginal infection and PPROM include lower socioeconomic status and lack of education. Hence, this study also compares the incidence of vaginal infection and PPROM in women regularly visiting health care facility for antenatal care with unbooked patients, presenting for the first time to the facility with the complication of PPROM or at term. Lastly, women of different socioeconomic strata have also been compared. Pathological isolates obtained from the vaginal micro biodata have been studied and evaluated for antimicrobial susceptibility and sensitivity as well.

Aims and Objectives

A. To study the relation of vaginal infection with spontaneous preterm premature rupture of membranes.
B. To compare the incidence of vaginal infection and PPROM amongst women of different socioeconomic classes and antenatal care status.
C. To evaluate for antimicrobial susceptibility of the pathogens isolated using commonly used antibiotics.

Methodology

Design: This study is a retrospective study.

Setting: The study has been conducted at the Labour Ward in the Department of Obstetrics and Gynaecology, Rajarajeswari Medical College and Hospital, Bangalore, Karnataka.

Study Population: All pregnant women admitted to the labour ward for delivery were eligible for the study if they have started draining liquor between 28 weeks and 36 weeks and 6 days POG.

Inclusion Criteria

- Booked and unbooked cases
- Both primigravida and multigravida irrespective of socioeconomic status

Exclusion Criteria

- POG< 28weeks
- Multiple pregnancy
- Malpresentation
- Placenta previa / APH

- Cervical incompetence treated with cervical encerclage
- Polyhydramnios
- Hypertensive disorder of pregnancy
- Fever, UTI, Acute Gastroenteritis, Respiratory tract infection
- Anaemia, Heart disease, Gestational Diabetes Mellitus, Overt Diabetes Mellitus
- Antibiotic therapy within last 30 days
- Intra uterine growth retardation
- Intra uterine death

A total number of 20 women have been studied.

Clinical Study: A comprehensive history was taken, including menstrual and obstetric history. The period of gestation was confirmed from last menstrual period and was correlated with clinical examinations and ultrasonographic gestational age. In the current pregnancy a detailed history of complication associated with pregnancy was taken. General physical and obstetrical examinations were done. Enrolled women were evaluated using a sterile speculum examination. The diagnosis of spontaneous rupture of the membranes was confirmed by inspection of the cervix for flow of amniotic fluid by asking the patient to cough and/or gushing of the fluid on applying fundal pressure. Presence of ferning was noted. Nitrazine paper test was done. Swab from the posterior fornix of the vagina was taken and sent for Gram's staining and culture sensitivity.

Microbiological Analysis: The specimen was collected by putting the patient in dorsal supine position. Under all aseptic conditions the posterior vaginal wall was retracted with Sims' speculum and vaginal swab was taken from posterior fornix by sterile cotton swab and sent to the Department of Microbiology. The Gram's staining was done followed by inoculation on Blood and MacConkey agar as per standard protocols. After 48 hours of incubation, plates were checked for growth. Identification of pathogen was done, and the significant pathogen was then evaluated for antimicrobial susceptibility testing using the following antibiotics: ampicillin, cefixime, ceftazidime, gentamicin.

Results

Out of the total 20 swabs studied for vaginal infection, 14 (70%) swabs were positive & 3 (30%) swabs were sterile.

Table 1: Baseline characteristics of study population.

High Vaginal Swab Growth	PPROM
Positive	14 (70%)
Negative	6 (30%)

Out of the 14 patients that tested positive for vaginal infection, 4 (28.57%) were booked for antenatal care at a health care facility, while 10 (71.42%) were unbooked patients, presenting for the first time to the facility with the complication of PPROM (Table 2).

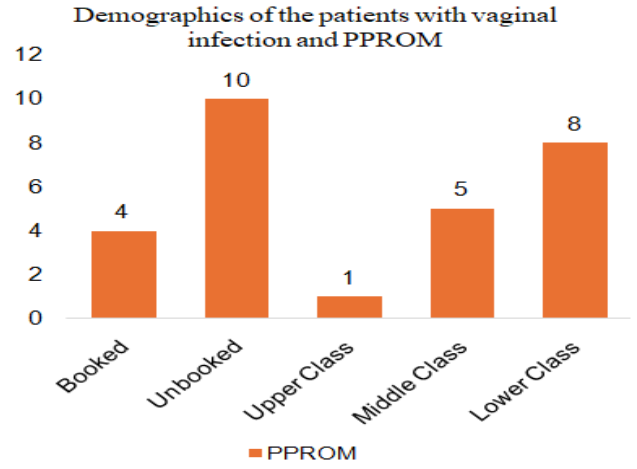
Table 2: ANC status with vaginal infection and PPROM

ANC Status	Vaginal infection + PPROM
Booked	4 (28.57%)
Unbooked	10 (71.42%)

Out of the 14 patients that tested positive for vaginal infection, 1 (7.14%) was of Upper Class, 5 (35.71%) were of Middle Class, and 8 (57.14%) were of Lower Class (Table 3).

Table 3: Socio-economic Class with vaginal infection and PPROM

SEC(Modified Kuppuswamy Classification)		PPROM
Upper Class (7.14%)	Class I	1 (7.14%)
Middle Class (35.71%)	Class II	2 (14.28%)
	Class III	3 (21.42%)
Lower Class (57.14%)	Class IV	5 (35.71%)
	Class V	3 (21.42%)



Graph 1

Table 4: Duration of leak (hours) of cases studied (PPROM)

Duration of leak (hours) to delivery interval	Number
1 to 5	5 (35.71%)
6 to 10	9 (64.28%)
11 to 20	5 (35.71%)
>20	1 (7.14%)

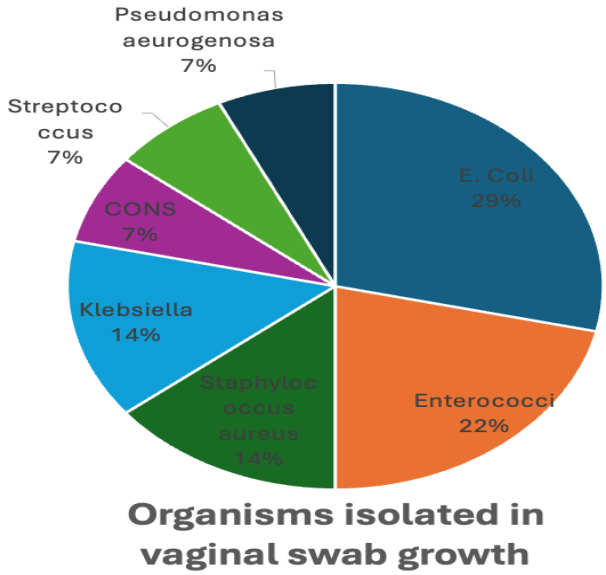
Most common organism isolated in the positive cultures was E. Coli 4 (28.57%). Enterococci 3 (21.42%) formed the second largest group of positive culture study. The other organisms isolated were Staphylococcus aureus, Klebsiella, CONS (coagulase negative staphylococcus aureus), Streptococcus and Pseudomonas aeruginosa (Table 5). Most of the organisms were found to be sensitive to Cefixime (50%), Ampicillin (28.57%) and Gentamicin (14.28%) especially, E. coli and Enterococci (Table 6).

Table 5: High vaginal swabs growth in patients studied

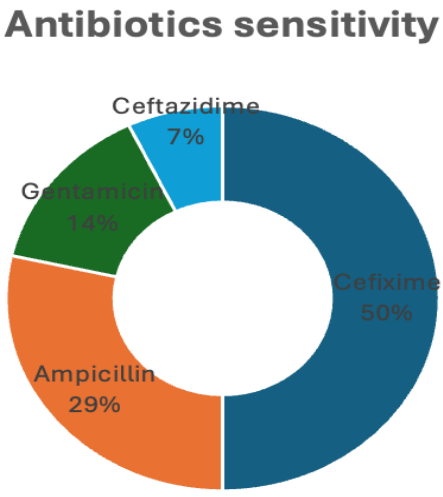
Organism isolated in vaginal swab growth	Number
E. Coli	4 (28.57%)
Enterococci	3 (21.42%)
Staphylococcus aureus	2 (14.28%)
Klebsiella	2 (14.28%)
CONS	1 (7.14%)
Streptococcus	1 (7.14%)
Pseudomonas aeruginosa	1 (7.14%)

Table 6: Antibiotics sensitivity

Antibiotics	Sensitivity
Cefixime	7 (50%)
Ampicillin	4 (28.57%)
Gentamicin	2 (14.28%)
Ceftazidime	1 (7.14%)



Graph 2



Graph 3

Summary Table

No.	Age	SES	Parity	POG (weeks)	Booked	Duration of leak (hours)	High vaginal swab growth	Organism	Sensitivity
1	33	IV	G3P1L1A1	32+1	NO	8	(+)	Enterococci	Ampicillin
2	20	III	PRIMI	33+5	YES	3	(-)	x	x
3	31	I	PRIMI	35+1	YES	5	(-)	x	x
4	22	IV	G3P1L1A1	29+4	NO	15	(+)	E. Coli	Cefixime
5	20	III	PRIMI	33+3	NO	13	(+)	E. Coli	Cefixime
6	21	II	PRIMI	36+1	YES	6	(-)	x	x
7	22	I	PRIMI	30+6	YES	7	(+)	E. Coli	Cefixime
8	28	III	G2A1	34+5	NO	4	(-)	x	x
9	25	V	G2P1L1	32+1	NO	18	(+)	Enterococci	Ampicillin
10	22	II	PRIMI	36+0	NO	7	(-)	x	x
11	40	IV	G2P1L1	33+4	NO	16	(+)	Enterococci	Ampicillin
12	28	V	PRIMI	36+4	NO	24	(+)	CONS	Gentamicin
13	20	V	G2A1	36+4	NO	17	(+)	Pseudomonas aeruginosa	Ceftazidime
14	21	IV	PRIMI	36+1	YES	9	(-)	x	x
15	24	III	PRIMI	31+5	YES	10	(+)	Staphylococcus aureus	Gentamicin
16	23	IV	G3P2L1	36+3	NO	5	(+)	Streptococcus	Ampicillin
17	23	IV	PRIMI	36+3	YES	8	(+)	Klebsiella	Cefixime
18	24	II	G2P1L1	36+6	NO	7	(+)	Staphylococcus aureus	Cefixime
19	22	III	PRIMI	35+6	NO	2	(+)	Klebsiella	Cefixime
20	22	II	PRIMI	36+5	YES	8	(+)	E. Coli	Cefixime

Discussion

In this case-control study, lower genital tract culture in pregnant women with PPROM was performed and the vaginal infection and their antibiotic sensitivity were studied with controls as women with term gestation without any complications. Most common isolated bacteria were E. Coli followed by Enterococci. In low-resource settings where microbiological evaluation of amniotic fluid is not feasible, identification of bacteria in high vaginal swab can guide antibiotic therapy in women with PPROM. Previous studies have shown good correlation between genital tract flora and organism grown in amniotic fluid. Studies by Naeye et al[23], McDonald et al[24], Das et al[25] showed that infection was 2 -3 times more common inpatients with ROM before 37 weeks POG than when foetal membranes ruptured at term. In this study 14 (70%) cases out of 20 cases of PPROM were culture positive.

In a study done by Dr. Samay Singh Meena, Dr. Badrilal Patidar, Dr. Girdhar Gopal Nagar and Dr. Sanjana Jourwal at Government Medical College, Kota, Rajasthan[26], it was found that the occurrence of PROM is more in unbooked cases compared to booked cases. This study adds to this evidence as out of the 14 cases with PPROM and vaginal infection, 10 (71.42%) were unbooked while 4 (28.57%) were booked.

In this study, out of the 14 cases with PPROM and vaginal infection, 8 (57.14%) were of lower

socioeconomic class. This corresponds to a review of pregnancies complicated by PPROM in 149 women of low socioeconomic status in Nigeria done by F E Okonofua, U Onwudiegwu, O A Odunsi et al[27].

CONS (coagulase negative staphylococcus aureus) was the commonest (23.4%) organism isolated in the study done by Pradeep Shivaraju, Pallavi Purra, Navatha Bheemagani, Krishna Lingegowda et al[28]. E. Coli was the commonest organism isolated in the study done by Sharma[29], Das et al[25] (44%), Raunt et al[30], Agarwal et al[31]. In this study, the commonest bacteria isolated was E. Coli 5 (28.57%). The next common organism isolated was Enterococci 3 (21.42%).

Antibiotic therapy in PPROM improves outcomes in two ways. One, they delay the progression to labour by controlling the infectious status and modulating the subsequent inflammatory process. Second, by reducing foetal infection can directly improve neonatal outcome. Due to difficulty in obtaining amniotic fluid samples and various reports indicating mixed bacterial growth in amniotic fluid cultures, broad spectrum antibiotics are prescribed during expectant management of PPROM[32]. The regimen studied by the National Institute of Child Health and Human Development trial[33] uses an intravenous combination of 2g of ampicillin and 250mg of erythromycin every 6 hours for 48 hours, followed by 250mg of amoxicillin and 333mg of erythromycin every 8 hours for 5 days. ACOG also recommends a 7-day course parenteral and oral therapy with ampicillin or amoxicillin and erythromycin in pregnant women with PPROM who are remote from term (expectant management)[34]. Prophylaxis to B Streptococcus is required during labour. This approach although simplistic can lead to inadequate treatment if causative organisms are resistant or not sensitive to these antibiotics. Also, wide spectrum resistance to penicillin group of antibiotics has been reported previously from India and other developing countries[34,35].

Conclusion

Prematurity is an important problem in obstetrics. The results of this study add to the existing evidence that vaginal infection is an important causative factor for PPROM. Vaginal infection and PPROM was seen more in unbooked patients of lower socio economic class than in booked patients or patients of middle or upper socioeconomic class. Therefore, education of masses and awareness about importance of regular antenatal visits is important to avoid infections, preterm labour, prematurity, and associated neonatal morbidity and mortality. Since preventive measures can prevent vaginal infection and hence PPROM, and the associated maternal and neonatal complications, timely detection and treatment is important. This study provides important data about lower genital tract micro biodata of PPROM in pregnant women and most of pathological isolates were sensitive to cefixime, ampicillin and gentamicin.

References

1. Premature rupture of membranes: medscape Updated: Feb 24, 2023, Author: Allahyar Jazayeri,, Chief Editor: Carl V Smith, MD
2. Prevalence of PPROM and its outcome: Shehla Noor, Ali fawwad Nazar, Journal of Ayub Medical College, Abbottabad: JAMC 19(4):14-7, October 2007.
3. Sherrard J, Wilson J, Donders G, et al. 2018 European (IUSTI/WHO) International Union against sexually transmitted infections (IUSTI) World Health Organisation (WHO) guideline on the

management of vaginal discharge. International Journal of STD & AIDS 2018; 29(13): 1258–272.

4. Gille C, Boer B, Marschal M, et al. Effect of probiotics on vaginal health in pregnancy. EFFPRO, a randomized controlled trial. Am J Obstet Gynecol 2016;215:608.e1-7.
5. Chandrahan E, Arulkumaran S. Recent advances in management of preterm labour. J Obstet Gynecol India. 2005:55(2):118-24
6. Arias F, Daftary SN, Bhide AG. Textbook of practical guide to high-risk pregnancy and delivery, A South-Asian Perspective, 3rd edition. Gurugram: Elsevier (A Division of Reed Elsevier India Pvt. Ltd.); 2008. Pp. 194-261.
7. Eschenbach, D. A., M. G. Gravett, K. C. S. Chen, U. B. Hoyme et al 1984. Bacterial vaginosis during pregnancy. An association with prematurity and postpartum complications, p. 213-222. Statistics with confidence. Br. Med. J.
8. Gravett MG, Hummel D, Eschenbach DA, Holmes KK. Preterm labour associated with subclinical amniotic Fluid infection and with bacterial vaginosis. Obstet. Gynecol. 1986;67:229-37.
9. Gravett MG, Nelson HP, DeRouen T, Critchlow CC, et al. Independent association of bacterial vaginosis and Chlamydia trachomatis infection with adverse pregnancy outcome. Jama. 1986;256:1899-903.
10. Martius J, Krohn MA, Hillier SL, Stamm WE, et al. Relationships of vaginal Lactobacillus species, cervical Chlamydia trachomatis, and bacterial vaginosis to preterm birth. Obstet Gynecol. 1988;71:89-95.
11. McGregor JA, French JI, Richter R, et al. Antenatal microbiologic and maternal risk factors associated with prematurity. Am J Obstet Gynecol. 1990;163:1465-73.
12. Mitchell H. Vaginal discharge: causes, diagnosis, and treatment. Br Med J 2004; 328: 1306-1308
13. Govender L, Hoosan AA, Moodley J, Moodley P, Sturm AW. Bacterial vaginosis and associated infections in pregnancy. Int J GynecolObstet 1996;55(1):23 –28.
14. Cristiano L, Rampello S, Noris C, Valota V. Bacterial vaginosis: prevalence in an Italian population of asymptomatic women and diagnostic aspects. Eur J Epidemiol 1996;12(4):383 –390.
15. Kurki T, Sivonen A, Renkonen OV, Savia E, Ylikorkala O. Bacterial vaginosis in early pregnancy and pregnancy outcome. ObstetGynecol 1992;80(2):173 –177.59
16. Tripathi R,Dimri S, Bhalla P, Ramji S. Bacterial vaginosis and pregnancy outcome.Int J ObstetGynecol2003;83:193-195
17. Goldenberg RL, Culhane JF, Iams JD. et al. Epidemiology and causes of preterm birth. Lancet.2008;371:75 84.
18. Mercer B M, Goldenberg R L, Das A F. et al. What we have learned regarding antibiotic therapy for the reduction of infant morbidity after preterm premature rupture of the membranes. Semin Perinatol.2003;27:217–230.
19. Mercer B M. Preterm premature rupture of the membranes. Obstet Gynecol. 2003;1101:178–193.
20. McGregor JA, French JI, Lawellin D et al Bacterial protease-induced reduction of chorioamniotic membrane strength and elasticity. Obstet Gynecol 1987; 69:167-74.
21. Draper D, Jones W, Heine RP et al. Trichomonas vaginalis weakens human amniochorion in an in

vitro model of premature membrane rupture. Infectious Disease Obstet Gynecol. 1995;2:267-74.

22. DiGiulio DB, Romero R, Kusanovic JP. et al. Prevalence and diversity of microbes in the amniotic fluid, the foetal inflammatory response, and pregnancy outcome in women with preterm pre-labour rupture of membranes. Am J Reprod Immunol. 2010;64:38–57.
23. Naeye RL, Dellinger WS, Blac WA. Foetal and maternal features of antenatal bacterial infection. Am J. Pediatrics 1978; 61:171.
24. McDonald HM, O' Loughlin JA, Jolly P, et al. Br J Obstet Gynecol. 1991;98(5):427-35.
25. Das C. R, Pattnaik PL, Sahoo PK. Prevalence of vaginal infection in preterm labour. Antiseptic 1996 April;93(4):140-43.
26. Dr. Samay Singh Meena, Dr. Badrilal Patidar, Dr. Girdhar Gopal Nagar and Dr. Sanjana. Evaluation of Feto-maternal Outcome with Prelabour Rupture of Membranes in Term Pregnancy. Int. J. Pharm. Sci. Rev. Res., 69(1), July - August 2021; Article No. 32, Pages: 220-223.
27. Okonofua FE, Onwudiegwu U, Odunsi OA. Preterm premature rupture of foetal membranes in a low socioeconomic population: results of conservative management. Int J Gynaecol Obstet. 1991 Jan;34(1):35-9.
28. Pradeep Shivaraju, Pallavi Purra, Navatha Bheemagani, Krishna Lingegowda et al. Vaginal infections and its relation to preterm labour, PPROM, PROM and its outcome. International Journal of Reproduction, Contraception, Obstetrics and Gynecology Shivaraju P et al. Int J Reprod Contracept Obstet Gynecol. 2015 Oct;4(5):1422-1426
29. Sharma JB, Prevalence of pathogenic Bacteria in Genital tract in preterm labour. J Obstet Gynecol India. 1989;229.
30. Raunt M. D, Dora H, Premature rupture of membrane – A clinical and bacteriological study. J of Obst Gyn 1988;38(1-6);184-7.
31. Agarwal SK, Rathi AK, Asha Awasthi, et al. J of Obst Gyn of India 1979:40-44.
32. Dudley J, Malcolm G and Ellwood D. Amniocentesis in the management of preterm labour J of Obst Gyn 1988;38(1-6);184-7.
33. Mercer BM, Miodovnik M, Thurnau GR, Goldenburg RL, Das AF, Ramsey RD, et al. Antibiotic therapy for reduction of infant morbidity after preterm premature rupture of the membranes. A randomized controlled trial. JAMA. 1997;278:989-95.
34. Mathew R, Kalyani J, Bibi R, Mallika M. Prevalence of bacterial vaginosis in antenatal women. Indian J Pathol Microbiol. 2001;44(2):113-6.
35. ACOG Practice Bulletin No. 80: premature rupture of membranes. Clinical management guidelines for obstetrician gynecologists. Obstet Gynecol.