MedCrave
Step into the World of Research

Obstetrics & Gynecology International Journal

Research Article

Open Access

CrossMark

Microbiological Pattern in Preterm Prelabour Rupture of the Fetal Membranes in South-Western Nigeria

Abstract

Background: Preterm prelabour rupture of the fetal membranes (PPROM) complicates 3% to 4% of all pregnancies. It is responsible for 40% of all preterm births with its attendant high perinatal morbidity and mortality.

Objective: The aim of this study was to determine the prevalence of PPROM; with profile and antibiotic susceptibility of isolated organisms.

Methodology: It was a prospective study carried out between 10th July 2011 and 22nd August 2012 among recruited pregnant women that met the inclusion criteria. Collection of samples from the endocervix and posterior vaginal fornix by sterile speculum examination was done; with same processed using standard microbiological techniques.

Results: Klessiella was the commonest organism isolated accounting for 32.1%, followed by Escherichia coli (19.6%); with highest sensitivity shown to ciprofloxacin (96.3%), and followed by amoxiclav (94.4%), ceftriazone (92.6%) and cefuroxime (90.6%).

Conclusion: Prophylactic use of antibiotics in the management of PPROM should largely be based on the demonstrated microbiological pattern and sensitivity in the environment in question.

Keywords: Microbiological pattern, Preterm PROM, Nigeria

Volume 6 Issue 4 - 2017

Adewunmi OA,[1] Olofinbiyi BA,[2] Oyekale OT,[3] Loto OM,[1] Abu SH,[4] Sotunsa John O[5]

[1]Department of Obstetrics and Gynaecology, Obafemi Awolowo University Teaching Hospitals Complex, Nigeria
[2]Department of Obstetrics and Gynaecology, Ekiti State University College of Medicine, Nigeria
[3]Department of Microbiology, Federal Teaching Hospital, Nigeria
[4]Department of Family Medicine, University of Abuja Teaching Hospital, Nigeria
[5]Department of Obstetrics and Gynaecology, Babcock University, Nigeria

Correspondence: Adewunmi OA, Department of Obstetrics and Gynaecology, Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Osun State, Nigeria, Tel 2348035298003, Email sigmaay@yahoo.com

Received: January 21, 2017 | **Published:** April 03, 2017

Introduction

Pre-labour rupture of the fetal membranes (PROM) is defined as the rupture of the fetal membranes before the onset of labour, after the age of viability. Preterm pre-labour rupture of the fetal membranes (PPROM) is rupture of the fetal membranes prior to 37weeks gestation. PPROM complicates 3% to 8% of all pregnancies.[1,2] and is responsible for 20-30% of all preterm births.[1] with attendant high perinatal mortality rate of about 54%.[3]

At term, programmed cell death and activation of catabolic enzymes such as collagenase and mechanical forces result in rupture of the fetal membranes. PPROM occurs probably due to the same mechanisms and premature activation of these pathways. However, early PROM also appears to be linked to underlying pathologic processes, most likely due to inflammation and/or infection of the membranes. Risk factors associated with aetiology of PPROM include low socioeconomic status, low body mass index, tobacco use, history of preterm labour, urinary tract infection, vaginal bleeding at any time in pregnancy, cerclage and amniocentesis.[4]

In recent years, the role of infection with lower genital tract organisms in precipitating PPROM and preterm labour has come under considerable scrutiny. Although, the aetiology of PPROM is multifactorial.[5] increasing evidence regarding clinical risk factors, membrane histology and amniotic fluid microbiology shows a strong association with infection.[5] leading to amniorhexis. There is evidence that microorganisms can penetrate intact fetal membranes.[6] Several studies have shown that women with low socio-economic status are at higher risk of PPROM and are more likely to develop chorioamnionitis as a complication of PPROM.[7]

When PPROM occurs before 34weeks gestation, conservative management is advocated to ensure fetal lung maturity. It is possible to successfully prolong the latency from membrane rupture to delivery.[8] but it is associated with development of maternal and foetal infection.[9] Recommended management strategy includes the use of corticosteroids, tocolytics and antibiotics.[10,11] Early studies suggested that prophylactic antibiotics could be beneficial in cases of idiopathic PPROM and preterm labour. There is prolongation of latency period, reduction in chorioamnionitis and possible reduction in gestational age- dependent morbidity and neonatal infections in PPROM when antibiotics are used.[8,10] Appropriate antibiotic therapy is instituted following culture and sensitivity results of amniotic fluid and/or endocervical swabs.

The purpose of this study is to determine the association and the pattern of bacteria if any in the aetiology of PPROM in this centre where the result so obtained will also be of help in the management of PPROM. To the best of our knowledge, no such study has been carried out in the centre.

Materials and methods

Study design

A prospective study design was used.

Study period

The study was done between 10th July 2011 and 22nd of August 2012.

Study location

This study was conducted at the obstetric unit of Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, South-western Nigeria. The maternity wing of the teaching hospital receives referrals from Osun, Ekiti, Oyo, Ondo, Kwara and Kogi States; all in

the same geopolitical zone. The hospital has an annual booking rate of 2,500 and delivery rate of about 2100.

Study population

This is a prospective case control study carried out at the obstetrics, gynaecology and perinatology department of Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, Nigeria, between 10th July 2011 and 22nd August 2012. Cases comprised patients presenting with PPROM while controls were patients with ongoing pregnancy without rupture of fetal membranes picked from antenatal clinic matched for age, parity and gestational age. Inclusion criteria included patients with rupture of fetal membranes before 37weeks gestation and less than 24hours duration, patients with an ongoing pregnancy without ruptured membranes matched for parity (+ or -2), age (+ or -2years) and gestational age (+ or -2weeks). Exclusion criteria included cases with rupture of membranes less than 24weeks or after/at 37 completed weeks, PPROM more than 24hours, PPROM and pyrexia-temperature of 380C and above. Also, cases with PPROM who have taken antibiotics within the last 7days, cases with malpresentation, congenital abnormalities, polyhydraminos or cervical incompetence and patients who did not have early ultrasonography and could not remember their last menstrual period. All cases with previous digital examination before presentation and a history of sexual intercourse in the last 24 hours were also excluded. A total of 56 patients met the inclusion criteria and 54 controls were studied.

Sample collection

Demographic and clinical information required such as age, parity, social class, estimated gestational age were obtained and recorded on prepared data collection form. The attending obstetrician examined and conducted sterile speculum examination which aided in diagnosis and collection of samples from the endocervix and posterior fornix. The sample were labeled with the identification number for each patient; with the labeling similar with the one on the data collection form. Samples were transported to the laboratory for analysis.

Isolation and identification of isolates and antimicrobial susceptibility testing

Each sample from cases and controls was inoculated into blood agar, Maconkay agar, chocolate agar, sabourauds dextrose agar and gentamicin blood agar. All the inoculated agars were incubated for 24hours at 370c, except for gentamycin blood agar plates which were inoculated in candle extinction. Wet mount was done with both high vaginal and endocervical swabs of both cases and controls, smeared on a slide and examined microscopically for fungal elements, *Trichomonas* and *Gardnerella vaginalis*. Gram staining of all specimens was done and examined for intracellular Gram-negative diplococci. Three drops of 10% potassium hydroxide (KOH) were also added separately for whiff test as part of criteria to diagnose of bacteria vaginosis.

Statistical analysis

This was done using Statistical Package for Social Sciences (SPSS) version 20. Frequency tables were made and results tested using the student t-test for continuous variables and chi-square for categorical variables with the level of significance set at 0.05.

Ethical consideration

Ethical clearance for the study was obtained from ethics and research committee of Obafemi Awolowo University Teaching Hospital, Ile-Ife. Informed consents were also obtained from all the patients.

Result

A total of 56 patients with PPROM were matched with 56 pregnant women without PPROM. Table 1 shows the socio demographic data of the studied population. The overall incidence of PPROM was 5.7% (88 of 1,540 pregnant women). The age distributions in the case and control groups were homogenous (p=0.35). The study population consisted mainly of those with parous experience (78.6% and 85.7%) for cases and control. No statistical significant difference was found in age and parity between cases and control (P = 0.35 and 0.17 respectively).

Table 1 Sociodemographic Characteristics of the Study Population

Characteristics	Cases n=56 (%)	Controls n=56 (%)	P value
Age (Years)			
<20	1 (1.8)	0 (0)	
20 – 24	8 (14.3)	4 (7.1)	
25 – 29	18 (32.1)	26 (46.4)	
30 – 34	26 (46.4)	21 (37.5)	0.35
35 and above	3 (5.4)	5 (9)	
Mean age in years	29.11±4.11	29.45±4.07	0.66
Parity			
0	12 (21.4)	8 (14.3)	
1-2	24 (42.9)	34 (60.7)	
3-4	20 (35.7)	13 (23.2)	0.17
5 and above	0 (0)	1 (1.8)	
Mean parity	1.82±1.29	1.77±1.17	0.82
Social class			
Low (4-5)	37 (66.1)	13 (23.2)	
Middle (3)	11 (19.6)	33 (58.9)	0.001
High (1-2)	8 (14.3)	10 (17.9)	
Mean social class	4.05±0.86	3.02±0.92	0.001
Estimated gestational age(wks)			
24-27	3 (5.3)	3 (5.3)	
28-30	14 (25)	20 (35.7)	
31-33	29 (51.8)	16 (28.6)	0.086
34-36	10 (17.9)	17 (30.4)	
Mean EGA(wks)	31±2.32	31±2.67	0.99

Wks: Weeks; < = Less than; EGA: Estimated Gestational Age.

Citation: Adewunmi OA, Olofinbiyi BA, Oyekale OT, et al. Microbiological Pattern in Preterm Prelabour Rupture of the Fetal Membranes in South-Western Nigeria. *Obstet Gynecol Int J.* 2017;6(4):101–105. DOI: 10.15406/ogij.2017.06.00215

A high percentage of the cases of PPROM (51.8%) occurred at estimated gestational age of 31-33 weeks followed by cases that occurred between 28-30 weeks gestation with 25% occurrence. The occurrence of PPROM at estimated gestational age of 34-36weeks was 17.9% while only 5.3% of cases occurred between 24-27 weeks of gestation. There is however no statistical difference in the estimated gestational age at which PPROM occurred (P = 0.087). It was found that about two thirds of the cases of PPROM occurred in patients with low socio-economic status.

Gardnerella vaginalis was demonstrated microscopically and whiff test positive in 3(5.3%) of PPROM but 1(1.8%) in the control group. *Trichomonas vaginalis* was seen microscopically in 3(5.3%) of PPROM but 2(3.6%) in the control group. Candida albicans was seen in 2(3.6%) of the cases but 7(12.5%) in the control group. These three occurred mixed with some of the positive bacterial cultures. A total of fifty four pathogens were isolated from forty seven patients out of the fifty six cases of PPROM while only five pathogens were isolated from the controls.

The occurrence of various organisms isolated from both HVS and ECS of cases and controls were as shown in Table 2; while no organism was isolated from the ECS of the controls, five of the controls had positive culture from HVS. There was substantial positive culture from both the ECS (71.3%) and HVS (73.2%) of the cases. Gardnerella vaginalis, *Trichomonas vaginalis* and Candida albicans occurred with some positive bacterial cultures in a mixed fashion.

The prevalence of various organisms isolated is shown in Table 3. There were fifty four (54) bacteriological isolates from the HVS and ECS of the cases. *Klebsiela* was the commonest organism isolated accounting for 32.1%, the other organisms isolated include *Escherichia coli* (19.6%), Proteus(14.3%), *Staphylococcus aureus* (10.7%), *Streptococus pyogenes* (7.1%), Bacteroides (5.4%), *Coagulase negative staphylococcus* (3.6%) and β haemolytic Streptococus (3.6%). Total positive cultures were 83.9% and 8.9% for case and control respectively giving a P value of 0.001.

Table 2 Isolates from cases and controls

Isolates	Cases (n=56)				Controls (n=56)			
	HVS		ECS		HVS		ECS	
	n	%	N	%	N	%	N	%
Klebsiella	12	21.4	18	32.1	-	0.0	-	0.0
E. coli	9	16.1	11	19.6	-	0.0	-	0.0
Proteus	3	5.3	8	14.3	-	0.0	-	0.0
Staph. Aureus	6	10.7	3	5.3	-	0.0	-	0.0
Strept. pyogenes	4	7.1	-	0.0	2	3.6	-	0.0
CONS	2	3.6	-	0.0	1	1.8	-	0.0
Bacteroides	3	5.4	-	0.0	1	1.8	-	0.0
β haemolytic strept.	2	3.6	-	0.0	1	1.8	-	0.0

E. coli: *Escherichia coli;* Strept. Pyogenase: *Streptococcus Pyogenase*, β *Haemolytic Strept:* β haemolytic streptococcus; HVS: High Vaginal Swab; ECS: Endocervical Swab; CONS: Coagulase negative staphylococcus

Table 3 Frequency of isolates of various organisms

Isolates	Cases (n=56)		Controls (n=56)		P value
	N	%	N	%	
Klebsiella	18	32.1	-	0.0	
E. coli	11	19.6	-	0.0	
Proteus	8	14.3	-	0.0	
Staph. Aureus	6	10.7	-	0.0	
Strept. Pyogenas	4	7.1	2	3.6	
CONS	2	3.6	1	1.8	0.001
Bacteroides	3	5.4	1	1.8	
β haemolytic strept.	2	3.6	1	1.8	
Total pathogens Isolated	54	96.4	5	8.9	

E. coli: *Escherichia coli*; *Strept. Pyogenase: Streptococcus Pyogenase*; *β haemolytic strept*: β *haemolytic streptococcus*; CONS: Coagulase Negative Staphylococcus; *Staph. Aureus*: *Staphyloccus aureus*

Table 4 shows the antibiotic sensitivity pattern of the organisms isolated; the drug that showed the highest sensitivity was Ciprofloxacin (96.3%). This was followed by amoxiclav (94.4%), ceftriaxone (92.6%) and cefuroxime (90.6%), others that showed good sensitivity were erythromycin (88.9%) gentamycin(70.4%) and Chloramphenicol (63%). Fair sensitivity was shown by cloxacillin (50%) while amoxicillin (40.7%), Co-trimoxazole (33.3%) and ampicillin (27.8%) all showed low effectiveness; with sensitivity less than (50%). The common pathogens isolated in this study were *Klebsiela*, *E. coli*, *Proteus*, *Staphylococcus aureus* and *Strptococcus pyogenase*. They showed good sensitivity to Ciprofloxacin, amoxiclav, ceftriaxone, cefuroxime, erythromycin and gentamycin.

Discussion

This study demonstrated an overall incidence of 5.7%which is higher than 2.5% obtained in a study done by -Obi et al.[12] This could be partly due to the fact that this study was a prospective study with proper record keeping and documentation, unlike the Obi's study which was a retrospective study. In this study, fifty six (56) cases of PPROM matched with fifty six (56) controls without PPROM revealed a positive culture rate of 83.9%. There was statistically significant difference between the cases and controls which suggests a strong link of genital tract infections with the occurrence of PPROM. There was no statistically significant difference in the socio-

Citation: Adewunmi OA, Olofinbiyi BA, Oyekale OT, et al. Microbiological Pattern in Preterm Prelabour Rupture of the Fetal Membranes in South-Western Nigeria. *Obstet Gynecol Int J.* 2017;6(4):101–105. DOI: 10.15406/ogij.2017.06.00215

demographic characteristics (mean age, mean gestational age, mean parity), except for mean social class (P = 0.001). It can therefore be said that the occurrence of PPROM is strongly associated with low socio–economic status. This agrees with a previous study conducted by Arnildo et al.[7] Association of PPROM with low socio–economic class could be a reflection of the personal hygiene of women in this group.

Table 4 Antimicrobial Sensitivity Pattern of Isolates

Drugs	Number Sensitive and Percentage								
	E. coli n=11 (%)	*Klebsiela* n=18 (%)	*S. pyogenes* n=4 (%)	*Proteus* n=8 (%)	CONS n=2 (%)	*S. aureus* n=6 (%)	*β. H. strept* n=2 (%)	*Bacteriodes* n=3 (%)	Total number 54 (100%)
Chloramphenicol	6 (54.5)	12 (66.7)	3 (75)	4 (50)	1 (50)	6 (100)	1 (50)	1 (33.3)	34 (63%)
Gentamicin	8 (72.7)	16 (88.9)	3(75)	4 (50)	2(100)	3 (50)	1 (50)	1 (33.3)	38 (70.4)
Co-trimoxazole	3 (27.3)	5 (27.8)	2 (50)	5(62.5)	0 (0)	2(33.3)	1 (50)	0 (0)	18 (33.3)
Ampicillin	2 (18.2)	4 (31.3)	0 (0)	4 (50)	1 (50)	3 (50)	1 (50)	0 (0)	15 (27.8)
Cloxacillin	6 (54.5)	9 (50)	3 (75)	4 (50)	1 (50)	2 (33.3)	1 (50)	1 (33.3)	27 (50)
Erythromycin	10(90.9)	16(88.9)	4 (100)	6 (75)	2(100)	5 (83.3)	2 (100)	2 (66.6)	47 (88.9)
Ciprofloxacin	11 (100)	18 (100)	4 (100)	8(100)	2(100)	6(100)	2 (100)	1 (33.3)	52 (96.3)
Amoxiclav	11(100)	16 (88.9)	4 (100)	8 (100)	2(100)	6 (100)	2 (100)	2 (66.6)	51 (94.4)
Ceftriaxone	10(90.9)	17 (94.4)	4 (100)	8 (100)	2(100)	6 (100)	2 (100)	1 (33.3)	50 (92.6)
Cefuroxime	11(100)	17(94.4)	3 (75)	8 (100)	2(100)	5 (83.3)	2 (100)	1(33.3)	49 (90.7)
Amoxicillin	5 (45.5)	7 (38.9)	2 (50)	3 (37.5)	0 (0)	3 (50)	1 (50)	1 (33.3)	22 (40.7)

E. coli: *Escherichia coli; Strept. Pyogenase*: *Streptococcus Pyogenase*; *β haemolytic strept*: *β haemolytic streptococcus;* CONS: Coagulase Negative Staphylococcus; *Staph. Aureus*: *Staphyloccus aureus*

Klebsiella spp. was the commonest organism isolated (32.1%). This is however in sharp contrast with a similar study conducted in Nigeria by Aboyeji et al.[13] However, the significance of this finding is more pronounced when consideration is given to the fact that no *klebsiella spp* was isolated among the 56 controls. *Escherischia coli* accounted for 19.6% of the organism isolated from cases and non in the control group. This gram negative aerobic organism has been found in previous studies to penetrate intact fetal membranes, cause intra- amniotic infection and subsequent amniorhexis. Proteus is a gram negative aerobe while Staphylococcus aureus is a gram positive aerobe with prevalence of 14.3% and 10.7% respectively in this study. Bahar et al.[14] reported Proteus as part of wide variety of microbes that was implicated in PPROM while isolation of *Saphylococcus aureus* in this study is also similar to the findings of Silva et al.[15] who found a wide diversity of aerobic and anaerobic organisms.[15]

Streptococcus Pyogenase (7.1%), *Coagulase negative Staphylococcus* (3.6%) and Bacteriodes (5.4%) were both isolated in cases and controls in this study. These organisms may be part of a wide variety of microbes associated with prelabour rupture of membranes as demonstrated by Aboyeji et al.[13] in their study in 2000. *β haemolytic streptococcus* has also been implicated in some studies.[15,16] as part of organisms involved in PPROM though the prevalence was low in this study.

Gardnerella vaginalis was demonstrated in 3 cases (5.3%) and 1 (1.8%) in the control group, all occurred in cases where *Bacteriodes spp* was isolated. This is worthy of note as this organism which is part of the bacterial vaginosis complex is often associated with anaerobic bacteria such as Bacteroides as demonstrated in this study and their role in the aetiology of PPROM is already well documented.[18] Microscopic isolation of *candida spp* in 7 out of the 56 controls (12.5%) as against 2 in the cases (3.5%) in this study is worthy of note. There appears to be an inverse relationship between the presence of *candida spp* and the occurrence of PPROM, reason for this is not known. This finding is at variance with that previously documented by.

The sensitivity pattern in this study revealed that ciprofloxacin had the highest sensitivity (96.3%) with almost all the isolated organisms sensitive to it. However, this drug which is a quinolone is not safe in pregnancy; other drugs that showed excellent sensitivity include amoxiclav (94.4%), ceftriaxone (92.6%), cefuroxime (90.7%) erythromycin (88.9%) and gentamicin (70.4%). All these drugs are relatively safe in pregnancy except gentamicin. *Bacteroides spp*, a gram negative anaerobic organism was found in association with *Gardnerella vaginalis* (one of the organisms implicated in bacterial vagnosis complex) in this study. This had poor sensitivity to almost all the antimicrobial agents except erythromycin and amoxiclav that had 66.6% sensitivity each.

Metronidazole sensitivity was not tested in this study as the disc was not available. Amoxiclav has been associated with neonatal necrotising enterocolitis as seen in Kenyon et al.[19] study. Chloramphenicol showed good sensitivity but is contra-indicated in pregnancy. The common antibiotics used in our general practice; ampicillin, co-trimoxacole and amoxicillin all showed low sensitivity to the bacterial isolates in this study.

Various studies had looked into the use of antibiotics in PPROM. Two of the largest studies that looked at the effectiveness of antibiotics use in PPROM are the national institute of child health and human development maternal-fetal medicine unit (NICID-MFMU) study on PPROM.[20] In the NICID-MFMU study, intravenous antibiotics; ampicillin 2gms 6 hourly and erythromycin 250mg 6 hourly were used for 48 hours. The patients were then placed on oral amoxicillin 250mg 8hourly and enteric coated Erythromycin- base 333mg every 8 hours to complete the course of antibiotic therapy for seven days. In this trial, the antibiotic group had a significantly longer duration of pregnancy than the control group.

The antibiotic group was twice as likely to remain undelivered after 7 days of treatment with increased latency period which continued up to 3 weeks after discontinuation of antibiotics. Composite primary outcome and morbidities for the neonates were lower in the antibiotic group. Incidence of chorioamnionitis and neonatal sepsis, including group B streptococcal sepsis was decreased. In the ORACLE trial; where amoxiclav was used either alone or in combination with erythromycin, an increased risk of necrotising enterocolitis occurred and there was no significant difference in latency and morbidity between the antibiotic group and controls.

Based on current evidence, seven days of antibiotics as proposed by the NICID-MFMU is being recommended for PPROM cases that are being managed conservatively. In this study conducted at Obafemi Awolowo University Teaching Hospitals Complex, Ile Ife, the sensitivity of most of the bacterial isolates to ampicillin was very poor (27.8%). The sensitivity to ceftriaxone (92.6%), cefuroxime (90.7%) and erythromycin (88.9%) were excellent and any of these can be substituted for ampicillin. The sensitivity of amoxicillin was also poor (40.7%). Cephalosporins were found to be very sensitive to isolated organisms in this study; ceftriaxone and Cefuroxime are readily available in parenteral and oral formulation and either can be used to replace ampicillin and amoxicillin.

The regimen suggested based on findings in this study is intravenous ceftriaxone 1gram daily and intravenous erythromycin 250mg 8hourly for 48hrs; then, oral ceftriaxone 400mg daily and erythromycin 500mg 8hourly to complete a 7 day course. Oral erythromycin could be started for the first 48hours with parenteral ceftriaxone and then continue to complete 7 days course in environment where parenteral erythromycin is not available.[21-14]

Conclusion

Low socio-economic status is a significant risk factor demonstrated in this study. Genital tract infection is found to be related to the occurrence of preterm premature rupture of fetal membranes (PPROM) and it is one of the major aetiologic factors in our environment with *Klebsiella* being the commonest organism isolated. Antibiotics of choice in the expectant management of PPROM include ceftriaxone, cefuroxime, amoxiclav and erythromycin. Based on the findings of the present study, it is recommended that improvement in general socio-economic condition of women is likely to have a significant impact in reducing PPROM/preterm birth with subsequent reduction in maternal and perinatal morbidity and mortality. In addition, prophylactic use of antibiotics in the management of PPROM should be based on the demonstrated microbiological pattern and their sensitivity in this centre.

Acknowledgments

None.

Conflicts of interest

None.

References

1. Tavassoli F, Ghasemi M, Mohamadzade A, et al. urvey of pregnancy outcome in preterm premature rupture of membranes with amniotic fluid index<5 and=5. *Oman Med J*. 2010;25(2):118–123.
2. Okeke TC, Enwereji JO, Adiri CO, et al. Morbidities, concordance, and predictors of preterm premature rupture of membranes among pregnant women at the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria. *Niger J Clin* . 2016;19(6):737–741.
3. Esteves JS, de Sá RA, de Carvalho PR, et al. Neonatal outcome in women with preterm premature rupture of membranes (PPROM) between 18 and 26 weeks. *J Matern Fetal Neonatal Med*. 2015;29(7):1108–1112.
4. England MC, Benjamin A, Abenhaim HA. Increased Risk of Preterm Premature Rupture of Membranes at Early Gestational Ages among Maternal Cigarette Smokers. *Am J Perinatol*. 2013;30(10):821–826.
5. Mercer BM, Creasy RK, Resnick R, et al. Premature rupture of the membranes. Creasy and Resnik's Maternal–Fetal Medicine: *Principles and Practice*. (7th edn), Elsevier Saunders, Philadelphia, PA, USA. 2014;pp.600–612.
6. Canzoneri BJ, Feng L, Grotegut CA, et al. The chorion layer of fetal membranes is prematurely destroyed in women with preterm premature rupture of the membranes. *Reprod Sci*. 2013;20(10):1246–1254.
7. Hackenhaar AA, Albernaz EP, da Fonseca TM. Preterm premature rupture of the fetal membranes: association with sociodemographic factors and maternal genitourinary infections. *J Pediatr (Rio J)*. 2014;90(2):197–202.
8. Sharp GC, Stock SJ, Norman JE. Fetal assessment methods for improving neonatal and maternal outcomes in preterm prelabour rupture of membranes. *Cochrane Database Syst Rev*. 2014;10:CD010209.
9. Medina TM, Hill DA. Florida Hospital Family Practice Residency Program, Orlando, Florida. *Am Fam Physician*. 2016;73(4):659–664.
10. Morris JM, Roberts CL, Bowen JR, et al. Immediate delivery compared with expectant management after preterm pre–labour rupture of the membranes close to term (PPROMT trial): a randomised controlled trial. *Lancet*. 2016;387(10017):444–452.
11. van der Ham DP, van der Heyden JL, Opmeer BC, et al. Management of late–preterm premature rupture of membranes: the PPROMEXIL–2 trial. *Am J Obstet Gynecol*. 2012;207(4):276.e1–276.e10.
12. Obi SN, Ozumba BC. Pre–term premature rupture of fetal membranes: the dilemma of management in developing nation. *J Obstet Gynaecol*. 2007;27(1):37–40.
13. Aboyeji AO, Abdul IF, Ijaiya MA, et al. The bacteriology of pre–labour rupture of membranes in a Nigerian Teaching Hospital. *J Obstet Gynaecol*. 2005;25(8):761–764.
14. Bahar AM, Bilal N, Eskander MA. High vaginal swab cultures in normal and preterm labour *Int J Gynaecol Obstet*. 2004;87(2):145–146.
15. Silva MG, Peracoli JC, Sadatsun T, et al. Cervical lactobacillus and leukocyte infiltration in preterm premature rupture of membranes. *Int J Gynaecol Obstet*. 2003;81(2):175–182.
16. Yan JJ, Gong M, Zhang J, et al. The relationship between group B streptococcus genital infection and premature rupture of membrane. *Zhonghua Yi Xue Za Zhi*. 2016;96(23):1847–1849.
17. Shaarawy M, El–Minawi AM. Prolactin and Calcitropic hormones in preterm premature rupture of membranes. *International Journal of Gynaecology and Obstetrics*. 2004;84(3):200–207.
18. Kinglsey CA, Emmanuel OO, Ijeoma A, et al. Association between absence of vaginal lactobacillin PCR product and nugent scores interpreted as bacterial vaginosis. *Tropical J Obstet Gynecol*. 2005;22(2):103–107.
19. Kenyon S, Boulvain M, Neilson J. Antibiotics for preterm rupture of membranes. *Cochrane Database Syst Rev*. 2013;(2):CD001058.
20. Simhan HN, Canavan TP. Preterm premature rupture of membranes: diagnosis, evaluation and management strategies. *BJOG*. 2005;112(Suppl 1):32–37.
21. Alexander JM, Cox SM. Clinical Course of premature rupture of the membranes. *Semin Perinatol*. 1996;20(5):369–374.
22. Asindi AA, Archibong EI, Mannah NB. Infant colonization and neonatal sepsis in prelabour rupture of membranes. *Saudi Med J*. 2002;23(10):1270–1274.
23. Beazley D, Lewis R. The evaluation of infection and pulmonary maturity in women with premature rupture of membranes. *Semin Perinatol*. 1996;20(5):409–417.
24. Kenyon SL, Taylor DJ, Tarnow–Mordi W. Broad–spectrum antibiotics for preterm, prelabour rupture of fetal membranes: the ORACLE I randomised trial. ORACLE Collaborative Group. *Lancet*. 2001;357(9261):979–988.
25. American College of Obstetricians and Gynecologists, Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 172: Premature Rupture of Membranes. *Obstet Gynecol*. 2016;128(4):e165–e177.