Microbial isolates and antibiotic sensitivity pattern among women with early preterm spontaneous prelabor rupture of fetal membranes in a Nigerian teaching hospital

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ABSTRACT

Background: Preterm prelabor rupture of membranes (PPROM) is a significant risk factor for prematurity, maternal, and early-onset neonatal sepsis. A study of the microbial isolates and antibiotic sensitivity pattern is needed in a resource poor country.

Objectives: To identify the microbial isolates and antibiotic sensitivity pattern of patients with early PPROM.

Materials and Methods: It was a comparative study between 60 pregnant women who had PPROM and 60 matched controls without PPROM. Study variables of interest were sociodemographic characteristics and gestational age at recruitment, microbial isolates, and antibiotic sensitivity pattern. Data obtained were presented in tabular forms and recorded as frequencies and percentages. χ² and students’ t– tests were used to compare qualitative and quantitative variables, respectively. Statistical significance was considered at P value < 0.05.

Results: Sociodemographic characteristics did not show any significant association between the two groups except for social class (χ² = 11.659, P = 0.003) and booking status (χ² = 53.494, P < 0.001). Positive culture rate of 51 (85.0%) and 9 (15.0%) were found in the PPROM and non-PPROM groups, respectively. Escherichia coli 18 (30.0%) was the most frequently isolated organism in the PPROM group. Chlamydia trachomatis antigen was detected in six cases (10.0%) among the PPROM group. Antibiotics that had excellent sensitivity to the isolated organisms were meropenem, ceftazidime, and piperacillin.

Conclusion: Genital tract infection was significantly related to the occurrence of PPROM and E. coli was the commonest microbial organism isolated. Intravenous ceftriaxone followed by oral cefixime met national institute of child health and human development, maternal-fetal medicine units (NICHD-MFMU) criteria for selection as prophylactic antibiotic in PPROM.

Key words: Antibiotic sensitivity pattern; microbial isolates; preterm prelabor rupture of membranes; socioeconomic status.

Introduction

Premature rupture of membranes (PROM) also known as prelabor rupture of membranes refers to rupture of fetal membranes before the onset of labor, after the age of viability.[1][3] It’s occurrence before 37 completed weeks is referred to as preterm prelabor rupture of membranes (PPROM).[4][6] PROM is a significant risk factor for both preterm...
borns and maternal and early neonatal sepsis. Many studies have determined that besides prematurity being the most common problem, infection was the most serious event and potential complication following PPROM. This becomes even more serious if both were combined.\textsuperscript{[4]}

The incidence of PPROM varies for different countries and population. Worldwide, it ranges between 3 and 8\% of all births.\textsuperscript{[5,6]}

Risk factors of PPROM include cervical insufficiency, smoking, low socioeconomic status, history of PROM, and multiple pregnancy. Others include cervical cerclage insertion, amniocentesis, and genital tract infection.\textsuperscript{[1,2,7,8]}

Microbial organisms implicated in PPROM are usually polymicrobial and include \textit{Neisseria gonorrhoea}, \textit{Chlamydia trachomatis}, \textit{Escherichia coli}, group B Streptococci, \textit{Candida albicans}, and \textit{ureaplasma urealyticum}, and other organisms.\textsuperscript{[2,9]}

These microbial agents are known to elaborate proteases, collagenases, elastases, and metalloproteinase, thus weakening the fetal membranes and resulting in PROM.\textsuperscript{[10,11]}

PPROM is associated with 30–40\% of all preterm births and prognosis is related primarily to gestational age at presentation and delivery.\textsuperscript{[2,12]} If rupture of membranes occurs between 37 completed weeks and 42 weeks of gestation, it is called term prelabor rupture of membranes while that occurring between 24 weeks to less than 37 completed weeks is referred to as PPROM.\textsuperscript{[2,4]} If it occurs less than 24 weeks gestation, it is an inevitable miscarriage, and if it has occurred more than 24 h, it is prolonged PROM.

Late PPROM is when rupture of fetal membranes occurs between 34 and 36 weeks of gestation, early PPROM if it occurs between 28 and 33 weeks of gestation, and very early PPROM if it occurs between 24 and 27 weeks of gestation.\textsuperscript{[13]}

Studies have shown that prompt laboratory screening for sepsis and early institution of empirical antibiotics based on local data significantly improve neonatal outcome, by preventing chorioamnionitis, prolonging the latency period (period between rupture of membranes and onset of labor) and increasing the gestational age at delivery, thereby reducing the incidence of maternal and neonatal morbidity and mortality.\textsuperscript{[2,14]} Such approaches will be a safe and cost-effective strategy, especially in resource-limited countries like Nigeria.

Although studies have been conducted on microbial isolates and antibiotic sensitivity pattern in women with PROM in Ilorin,\textsuperscript{[15]} Northern Nigeria and on PPROM in Nnewi\textsuperscript{[16]} and Ile-Ife\textsuperscript{[1]} Southern Nigeria, where they all isolated different microbial flora and antibiotic sensitivity pattern, but no study was found from Nigeria in the course of literature search, on microbial isolates and antibiotic sensitivity pattern in women with early PPROM only, who are the target group for conservative management and appropriate empirical antibiotics to prolong the latency period. It is against this background that this study has been designed, to identify the sociodemographic characteristics, microbial isolates, and antibiotic sensitivity pattern among women with early PPROM at Aminu Kano Teaching Hospital (AKTH), so as to suggest appropriate antibiotics that can be chosen as empirical antibiotics, in the management of patients with early PPROM.

**Aims**

To determine the sociodemographic characteristics, microbial isolates and antibiotic sensitivity pattern, among patients with PPROM between 28 and 33 weeks of gestation and matched patients without PPROM at AKTH, Kano.

**Objectives**

1. To evaluate the sociodemographic characteristics of patients with PPROM and matched patients without PPROM, between 28 and 33 weeks gestation
2. To determine the antibiotic sensitivity pattern of the microorganisms isolated from the endocervical samples of patients with PPROM and matched pregnant women without PPROM, between 28 and 33 weeks of gestation
3. To identify the microbial organisms, present in the endocervical samples of patients with PPROM and matched pregnant women without PPROM, between 28 and 33 weeks of gestation
4. To make recommendations on appropriate antibiotics that can be chosen as empirical antibiotics, in the management of patients with early PPROM.

**Materials and Methods**

It was a comparative study between 60 consenting pregnant women, who had early PPROM from 28 to 33 weeks of gestation, admitted to antenatal and labor wards, and 60 consenting, matched pregnant women for age, parity, and gestational age without PPROM from the antenatal clinic of AKTH. Pregnant women with ruptured membranes below 28 weeks of gestation and above 33 weeks of gestation, patients with PPROM of more than 24-hour duration, patients who had taken antibiotics within the last 7 days, those with PPROM and temperature of at least 38°C, those with PPROM and other medical disorders like diabetes mellitus, sickle cell disease, and those with PPROM but unsure of gestational age were excluded from the study.
Patients with PPROM between 28 and 33 weeks of gestation were selected using convenience sampling technique in which consecutive patient that met the inclusion criteria were recruited until the sample size was obtained. In addition, the next patient without PPROM, who were matched for age (±3 years), parity (±2), and gestational age (±2 weeks), was recruited as control. The purpose of the study was explained to the women and written consent was obtained from those willing to participate in the study. Structured, interviewer-administered questions were asked to obtain information on age, parity, educational status, husband’s occupation (social class was determined using educational status and husband’s occupation), medical history, gestational age and the time of rupture of membranes, were recorded on a proforma. This was done by the principal researcher and four trained assistants.

The diagnosis of PPROM among those with complaints of drainage of fluid from the vagina was done by the researchers. Patients with history of drainage of liquor were examined and sterile speculum examination was done to confirm the diagnosis of PPROM. The diagnostic criteria included trickling of fluid from the cervix or on Valsava maneuver, pool of amniotic fluid in the posterior fornix of the vagina, and Nitrazine paper test on pool of amniotic fluid or vaginal wall for vaginal pH. In these cases, any one of them that was positive was used to confirm the diagnosis of PPROM. Gestational age was determined from the last normal menstrual period or early ultrasound of less than 24 weeks of gestation.

For this study, two endocervical swabs were collected; one for microscopy, culture, and antibiotic sensitivity and the other for C. trachomatis antigen test, from all recruited women. In order to detect recent or active C. trachomatis infection, EUGENE chlamydia antigen test kit manufactured by Shanghai Eugene Biotech Co Ltd. No. 2179, Jingshang road 99, Jinshan District, Shanghai 201500, P.R.C was used to detect Chlamydia antigen (Batch No. 1708011).

All specimens were coded and numbered consecutively before they were sent to the microbiologist.

A test of performance (control strength) was done using the American Type Culture Collection before inoculating it on the culture media.

Isolates obtained after culture from the specimens were identified to species level using conventional microbiological techniques. Samples that developed bacteria isolates were subjected to antibiotic sensitivity analysis using the disk diffusion methods.

Results of antibiotic susceptibility testing were read and interpreted using Clinical Laboratory Standard Institute chart. Zones of inhibitions were read and results representing resistance was denoted as R, whereas sensitive as S.

Approval for the study was obtained from research and ethical committee of AKTH. Written informed consent was taken from all participants in the study. Patients were informed that they were free to opt out of the study at any time. Fees for sample analysis was paid by the researchers.

Data obtained were recorded on a proforma. Study variables of interest were age, parity, educational status, husband’s occupation, medical history, gestational age, and the time of rupture of membranes. Others were pooling of fluid in the posterior vaginal fornix, trickling of fluid from the cervix, Nitrazine test result, microbial isolates, and antibiotic sensitivity pattern.

The pattern of bacteria isolated from patients with PPROM was compared with that of patients without PPROM, in order to identify the bacteria that were significantly more frequent in the PPROM group. The antibiotic sensitivity pattern among patients in PPROM group was reviewed, so as to determine the ones that the bacterial isolates among them were sensitive to and safe in pregnancy.

The antibiotics that had less than 50% of the significantly frequent organisms sensitive to them were considered to have poor effectiveness and not suitable for empirical use while those with 50-69% were considered to have good effectiveness, those with 70–89% were considered to have very good effectiveness and finally, those with 90% or more of the organisms sensitive to them were considered to have excellent effectiveness.

Data obtained were presented in tabular forms and recorded as frequencies and percentages and analyzed using statistical package for social sciences (SPSS version 20, USA 2009). $x^2$ and Students’ t-test were used to compare qualitative and quantitative variables respectively. Statistical significance was considered at $P$ value <0.05.

**Determination of sample size**

The sample size was calculated using the formula:

$$n = \frac{2 \times (Z_\alpha + Z_\beta)^2 \times (P_1 q_1 + P_2 q_2)}{(P_1 - P_2)^2}$$

Where $n = \text{minimum sample size}$


\[ Z_\alpha = Z \text{ score at 95\% confidence interval} = 1.96 \]

\[ Z_{\beta} = Z \text{ score at 90\% statistical power} = 1.645 \]

\[ P_1 = \text{The proportion of women with PPROM with bacterial cervical microorganisms expressed as a fraction of 100\%. The organism with the highest prevalence in the Ile-Ife study was Klebsiella with a value of 32.1\%,}^{[1]} \text{In this case, 32.1\% =0.321}. \]

\[ q_1 = \text{Complementary proportion} = (1 - p_1) = 1 - 0.321 = 0.679. \]

\[ P_2 = \text{The proportion of women without PPROM with bacterial cervical microorganism (Klebsiella specie). In this case, 0\% = 0}.^{[1]} \]

\[ q_2 = \text{Complementary proportion} = (1 - p_2) = 0 = 1 \]

\[ n = \frac{2 \times (1.96 + 1.645)^2 \times [0.321 \times 0.679] + (0 \times 1]}{(0.321 - 0)^2} \]

\[ n = \frac{2 \times (3.605)^2 \times (0.218)}{0.103041} = \frac{2 \times (12.996 \times 0.218)}{0.102041} \]

\[ n = 2 \times 27.5 = 55 \]

Taking a nonresponse (attrition) rate of 10\%, \( f = \% \) of nonresponse

\[ N = n/1 - f = 55/(1 - 0.1) = 55/0.9 = 60 \]

Therefore, the minimum sample size for this study was 60 each for cases and controls in a ratio of 1:1.

Therefore, 120 patients were recruited for the study, 60 each in each arm.

**Results**

The study was commenced from 1\textsuperscript{st} February 2017 to 31\textsuperscript{st} January 2018. A total of 120 pregnant women consisting of 60 patients with PPROM and 60 matched pregnant women without PPROM (controls) were enrolled. The participants were all married.

Table 1 shows the sociodemographic characteristics of participants. The mean ages (±SD) for women with PPROM and non-PPROM groups were 27.23 ± 5.49 and 26.87 ± 5.36 years respectively, which did not show any statistically significant difference between the two groups (\( t = 0.370, P = 0.712 \)). The modal frequency of age in the PPROM group (41.7\%) and the non-PPROM group (33.3\%) was found among the 21–25 year age group, whereas the least frequency was among the 15–20 year age group in the PPROM group, and 36–40 year age group among the non-PPROM group.

The mean parity for cases and control was 2.25 ± 1.50 and 2.37 ± 1.29, respectively, which did not show any statistically significant difference between the two groups (\( t = 0.459, P = 0.647 \)). The modal frequency in the PPROM group (36.7\%) and non-PPROM group (28.3\%) was among those with parity of 2, whereas the least frequency was found among para 0 in the two groups.

There was no statistically significant association in the educational levels between the two groups (\( x^2 = 3.911, P = 0.271 \)). However, there was statistically significant association in the socioeconomic status of the two groups (\( x^2 = 11.659, P = 0.003 \)). The frequency of occurrence of PPROM showed an inverse relation with socioeconomic status in the PPROM group, with the modal frequency of 55.0\% among the low socioeconomic class, and the least frequency of 11.7\% among the high socioeconomic class. In non-PPROM group, the modal frequency of 50.0\% was among the middle socioeconomic class, whereas the high and low socioeconomic class had a frequency of 25.0\% each.

Religion did not show statistically significant association (\( x^2 = 1.443, P = 0.230 \)). The modal frequency in both group occurred among women of Islamic faith (86.7\% in the PPROM group and 78.3\% in the non-PPROM group) Table 1.

Booking status showed statistically significant association (\( x^2 = 53.494, P < 0.001 \)), with the modal frequency (61.7\%) occurring among unbooked patients in the PPROM group, whereas all the patients in the non-PPROM group were booked [Table 1].

The mean estimated gestational age at recruitment in both groups (PPROM = 31.22 ± 1.71 and non-PPROM = 31.47 ± 1.46 weeks) did not show any statistically significant difference between the two groups (\( t = 0.863, P = 0.390 \)). The modal frequency was found in both groups among the 31–33 weeks of gestation group (61.7\% among PPROM and 73.3\% among non-PPROM).

Table 2 shows the frequency of various microorganisms that were isolated from the endocervical specimen of the participating women. A total of 51 (85.0\%) and 9 (15.0\%) microorganisms including Candida albicans were isolated from both PPROM and non-PPROM groups respectively, which showed statistically significant association. (\( x^2 = 58.800, P < 0.001 \)). *E. coli* 18 (30.0\%) was the most frequently isolated organism in the PPROM group, whereas...
among the non-PPROM was Candida albicans 6 (10.0%). This was followed in order of frequency by Staphylococcus aureus 15 (25.0%), Klebsiella spp. 10 (16.7%), Streptococcus pyogenes 3 (5.0%), Candida albicans 3 (5.0%) and α-hemolytic streptococcus 2 (3.3%) in the PPROM group, and the non-PPROM group S. aureus 2 (3.3%) and E. coli 1 (1.7%). The occurrence of E. coli, S. aureus, and Klebsiella spp. were statistically significant among the PPROM group.

Table 3 shows the frequency of C. trachomatis antigen detection from the endocervical specimen of the participating women. C. trachomatis antigen was detected in 6 (10.0%) among the PPROM group and none in the non-PPROM group, which showed statistically significant association between the two groups (p= (Fisher’s)=0.027).

Table 4 shows antibiotic sensitivity pattern of the microorganisms isolated from the PPROM group. Among the microorganisms that were isolated, there were three cases of Candida albicans and 48 cases of bacteria. The antibiotic that showed the highest sensitivity to the common bacterial organisms isolated was meropenem (93.8%). It was active against 45 out of 48 bacterial pathogens isolated. Other drugs that showed excellent effectiveness of 91.7% were piperacillin and ceftazidime. Ceftriaxone (89.6%), cefixime (87.5%), ciprofloxacin (83.3%), cefoxitin (83.3%), and gentamicin (79.2%) showed very good effectiveness to the isolated organisms, whereas erythromycin (52.1%) showed good effectiveness.

Antibiotics that showed poor effectiveness (sensitivity less than 50.0%) were cefotaxime (47.9%), cefuroxime (33.3%), chloramphenicol (37.5%), and amoxiclav (27.1%). Other antibiotics that showed poor effectiveness were penicillin...
Table 4: Antibiotic sensitivity pattern of microbial isolates from the PPROM group

| Antibiotic | E. coli n=18 (%) | S. aureus n=15 (%) | Klebsiella spp n=10 (%) | S. pyogenes n=3 (%) | α-Hemo strept n=2 (%) | Total n=48 (%) | Sensitivity |
|------------|----------------|-------------------|-------------------------|--------------------|---------------------|---------------|------------|
| Cloxacillin| 1 (5.6)        | 11 (73.3)         | 0 (0.0)                 | 2 (66.7)           | 2 (100.0)          | 16 (33.3)    | Poor       |
| Penicillin | 2 (11.1)       | 12 (80.0)         | 0 (0.0)                 | 2 (66.7)           | 2 (100.0)          | 18 (37.5)    | Poor       |
| Ampicillin | 3 (16.7)       | 2 (13.3)          | 0 (0.0)                 | 1 (33.3)           | 2 (100.0)          | 8 (16.7)     | Poor       |
| Amoxicillin| 6 (33.3)       | 4 (26.7)          | 0 (0.0)                 | 2 (66.7)           | 2 (100.0)          | 14 (29.2)    | Poor       |
| Erythromycin| 7 (38.9)     | 12 (80.0)         | 2 (20.0)                | 2 (66.7)           | 2 (100.0)          | 25 (52.1)    | Good       |
| Amoxiclav  | 5 (27.8)       | 4 (26.7)          | 1 (10.0)                | 2 (66.7)           | 1 (50.0)           | 13 (27.1)    | Poor       |
| Co-trimoxazole| 1 (5.6)      | 1 (6.7)           | 0 (0.0)                 | 0 (0.0)            | 1 (50.0)           | 3 (6.3)      | Poor       |
| Gentamicin | 13 (72.2)      | 13 (86.7)         | 7 (70.0)                | 3 (100.0)          | 2 (100.0)          | 38 (79.2)    | Very good  |
| Ceftriaxone| 17 (94.4)      | 12 (80.0)         | 9 (90.0)                | 3 (100.0)          | 2 (100.0)          | 43 (86.9)    | Very good  |
| Chloramphenicol| 11 (61.1)    | 1 (6.7)           | 3 (30.0)                | 2 (66.7)           | 1 (50.0)           | 18 (37.5)    | Poor       |
| Cefuroxime | 5 (27.8)       | 6 (40.0)          | 2 (20.0)                | 1 (33.3)           | 2 (100.0)          | 16 (33.3)    | Poor       |
| Ceftazidime| 16 (88.9)      | 15 (100)          | 8 (80.0)                | 3 (100.0)          | 2 (100.0)          | 44 (91.7)    | Excellent  |
| Ciprofloxacin| 13 (72.2)     | 13 (86.7)         | 9 (90.0)                | 3 (100.0)          | 2 (100.0)          | 40 (83.3)    | Very good  |
| Meropenem  | 17 (94.4)      | 15 (100.0)        | 9 (90.0)                | 3 (100.0)          | 2 (100.0)          | 45 (93.8)    | Excellent  |
| Cefotaxime | 15 (83.3)      | 12 (80.0)         | 9 (90.0)                | 2 (66.7)           | 2 (100.0)          | 40 (83.3)    | Very good  |
| Piperacillin| 16 (88.9)      | 15 (100.0)        | 8 (80.0)                | 3 (100.0)          | 2 (100.0)          | 44 (91.7)    | Excellent  |

Table 5: Antibiotic sensitivity pattern of microbial isolates from non-PPROM group

| Antibiotic | E. coli n=1 (%) | S. aureus n=2 (%) | Total n=3 (%) | Sensitivity |
|------------|----------------|------------------|---------------|------------|
| Cloxacillin| 0 (0.0)        | 2 (100.0)        | 2 (66.7)      | Good       |
| Penicillin | 0 (0.0)        | 2 (100.0)        | 2 (66.7)      | Good       |
| Ampicillin | 0 (0.0)        | 0 (0.0)          | 0 (0.0)       | Poor       |
| Amoxicillin| 0 (0.0)        | 0 (0.0)          | 0 (0.0)       | Poor       |
| Erythromycin| 0 (0.0)      | 1 (50.0)         | 1 (33.3)      | Poor       |
| Amoxiclav  | 1 (100.0)      | 1 (50.0)         | 2 (66.7)      | Good       |
| Co-trimoxazole| 0 (0.0)      | 0 (0.0)          | 0 (0.0)       | Poor       |
| Gentamicin | 1 (100.0)      | 1 (50.0)         | 2 (66.7)      | Poor       |
| Ceftriaxone| 1 (100.0)      | 2 (100.0)        | 3 (100.0)     | Excellent  |
| Chloramphenicol| 1 (100.0) | 0 (0.0)          | 1 (33.3)      | Poor       |
| Cefuroxime | 0 (0.0)        | 2 (100.0)        | 2 (66.7)      | Good       |
| Ceftazidime| 1 (100.0)      | 2 (100.0)        | 3 (100.0)     | Excellent  |
| Ciprofloxacin| 1 (100.0)     | 2 (100.0)        | 3 (100.0)     | Excellent  |
| Meropenem  | 1 (100.0)      | 2 (100.0)        | 3 (100.0)     | Excellent  |
| Cefoxitin  | 1 (100.0)      | 2 (100.0)        | 3 (100.0)     | Excellent  |
| Cefotaxime | 1 (100.0)      | 2 (100.0)        | 3 (100.0)     | Excellent  |
| Piperacillin| 1 (100.0)      | 2 (100.0)        | 3 (100.0)     | Excellent  |

(37.5%), cloxacillin (33.3%), amoxicillin (29.2%), and ampicillin (16.7%). It was found that most of the antibiotics had excellent effectiveness against α-hemolytic streptococcus. The common pathogens isolated in this study; E. coli, S. aureus, and Klebsiella species showed very good sensitivity to meropenem, piperacillin, ciprofloxacin, cefoxitin, ceftazidime, ceftriaxone, and gentamicin. S. aureus also showed good sensitivity to erythromycin, penicillin, and cloxacillin. Table 5 shows antibiotic sensitivity pattern of the microorganisms isolated from the non-PPROM group. The only two bacterial microorganisms; E. coli and S. aureus that were isolated from the control group showed similar sensitivity pattern as the PPROM group.

Discussion

This study of sixty 60 cases of PPROM matched with 60 controls without PPROM revealed a positive culture rate of 85.0% in the PPROM group. This was a statistically significant finding between the PPROM and non-PPROM group, suggesting that there is a strong link between genital tract infections and occurrence of PPROM. This finding is similar to that of Adewumi et al. [11] and Eleje et al. [16] but much higher than 48.3% that was reported by Salou et al. [21] The study of the women did not show statistically significant difference in terms of sociodemographic characteristics between those in the PPROM group and those in the non-PPROM group, except for their socioeconomic and booking status. This may be because the husband’s occupation, which was used together with their educational status to derive their social class, was not matched. The high frequency of unbooked cases and low socioeconomic class among the women in the PPROM group compared to...
non-PPROM group in this study was also the findings by Adewumi et al.,[1] and Noor et al.[22] This may be attributed to the direct relationship between low socioeconomic class and unbooked status, which are obstetric risk factors that are responsible for the high maternal mortality and morbidity in developing countries.[23] Low socioeconomic status has been shown to be associated with high frequency of genital tract infections as a result of poverty, poor personal, and sexual hygiene,[24] which may explain the higher frequency of genital infection among the PPROM group, compared with the non-PPROM group.

Gestational age at which PPROM occurred in this study was highest in women who were between 31 and 33 weeks (61.7%). This was slightly higher than 51.8% documented by Adewumi et al.[1] but much higher than 17.1% reported by Eleje et al.[16] This may be because the circumferential dilatation of the lower uterine segment is maximal at this gestational age, which may allow ascending infection through the endocervix to the lower uterine segment, and trigger events that can cause PPROM.[25]

In this study, the prevalent microbial isolates were E. coli (30.0%), S. aureus (25.0%), and Klebsiella spp. (16.7%) in PPROM group and were statistically significantly higher in frequency than in the non-PPROM group, which is similar to the findings of Salou et al.[21] and Zeng et al.[26] from China but is at variance with the findings of other studies from Ilorin[15] and Nnewi,[16] where the most prevalent organisms were Gardnerella vaginalis and Streptococcus spp. Zeng et al.[26] in a systematic review from China found that organisms implicated in PPROM differs in each geographical location.

The high frequency of E. coli, S. aureus, and Klebsiella spp. may be a reflection of poverty and poor personal hygiene among the women in the case group, because E. coli and Klebsiella spp. are enterobactariaceae, could have access to the genital tract from the anus, which is close by, if the woman has poor anal hygiene. S. aureus on the contrary, is found on the skin, may predominate and spread to the genital tract, if the women have poor personal hygiene. This calls for strong emphasis on personal hygiene, with emphasis on anal hygiene, especially the act of swabbing from front to back only following defecation or whenever the perianal area is being cleaned.

The low frequency of Streptococcus pyogenes (5.0%), α-hemolytic streptococcus (3.3%), and Candida albicans (5.0%) among the isolates, which did not show statistically significant difference between the two groups, agrees with the findings of other studies.[1,15] Aboyeji et al.[15] found Streptococcus pyogenes to be part of wide variety of microorganism associated with PPROM.

Candida albicans was isolated in 5.0% and 10.0% among the cases and controls, respectively. Although there was no statistically significant difference in frequency of isolation of Candida albicans in the two groups, the higher frequency of isolation among the control group, may be a reflection of the strong chemical barrier protection in the vagina against microbial invasion, which may explain the lower frequency of genital infection among the control group, because Candida albicans which is a commensal in the vagina can survive in acidic environment but bacteria cannot.[27,28]

C. trachomatis antigen was detected in 6 (10.0%) of women in the case group and none in the control group, this agrees with the findings of other studies which implicated C. trachomatis as a causative agent of PPROM.[2,19] This finding may be because majority of the women in the case group were from the low socioeconomic class, which is associated with poor sexual hygiene.

The antibiotic sensitivity pattern in this study revealed that meropenem (93.8%), ceftazidime (91.7%), and piperacillin (91.7%) showed excellent sensitivity to isolated microorganisms.

Meropenem has bactericidal activity which results from inhibition of cell wall synthesis, by penetrating the cell wall of most gram-positive and gram-negative bacteria to bind penicillin-binding-protein target and has been shown to act synergistically with aminoglycosides. Meropenem, although has excellent sensitivity, its use will be limited in prophylactic treatment of PPROM because it has only intravenous preparation and may cause seizures and other central nervous system disorders,[28] which have been reported with its use. In addition, the drug is not cost-effective, all these may make it not to be recommended in pregnant women.

The criteria for selection of antibiotic agent for use as prophylactic agent in this study did not recommend antibiotic with good or poor sensitivity to the isolated organisms; hence, they were not considered during selection. Some of the antibiotics included erythromycin (52.1%), cefuroxime (33.3%), amoxiclav (27.1%), amoxicillin (29.2%), penicillin (37.5%), cloxacillin (33.3%), and ampicillin (16.7%). The reason for their poor sensitivity is probably because these drugs are readily purchased over the counter in the study area and are mostly the drug of use in the general practice. However, erythromycin, amoxiclav, and cefuroxime were shown to have very good sensitivity in a study conducted by Adewumi et
Erythromycin showed good sensitivity to isolated microorganisms. Although, it did not meet the criteria for selection of antibiotic agent for use as prophylactic in this study, erythromycin was selected based on NICHD-MFMU[26] that it is effective against *C. trachomatis*, which the antigen was detected among the cases in this study. Intravenous erythromycin was used in NICHD-MFMU study for 48 h, followed by the oral preparation to complete 7-day treatment. However, intravenous erythromycin is not available in our unit. Some studies have recommended that oral preparation of erythromycin may be used for 7 days.[11]

**Conclusion**

In this study, genital tract infection was found to be significantly related to the occurrence of PPROM, and *E. coli* was the commonest microbial organism isolated, which calls for health campaign on personal and environmental hygiene in the community through mass media, during community social events and antenatal health talk. Low socioeconomic and unbooked status were significantly associated with PPROM, which calls for improvement in the social status of the women, in order to reduce the incidence of PPROM and its sequelae in the community. Meropenem, ceftazidime, and piperacillin were antibiotics that showed excellent sensitivity to isolated microorganisms, whereas ceftriaxone, cefixime, ciprofloxacin, cefoxitin, and gentamicin showed very good sensitivity. Among these antibiotic agents that showed excellent and very good sensitivity to isolated microorganisms, intravenous ceftriaxone followed by oral cefixime met the NICHD-MFMU criteria for selection as prophylactic antibiotic in PPROM.

**Recommendation**

Based on the findings in this study, the recommended regimen that is suggested is intravenous ceftriaxone 1 g daily for 48 h, then oral cefixime 400 mg daily to complete 7-day course, and oral erythromycin 500 mg 8 hourly for 7 days for Chlamydia.

**Strength of the study**

1. This study was to determine whether microbial organisms are present in the endocervical canal in patients with early PPROM particularly the detection of Chlamydia
2. The microorganisms present in the endocervical samples were identified and antibiotic sensitivity pattern was also determined. This had helped to determine the choice of empirical antibiotics for treatment of early PPROM

3. The sample was representative of study population, relatively easy to analyze, consistent, precise, and reliable.

**Limitations of the study**

1. Amnisure ruptured fetal membranes (ROM) test which has a sensitivity of 99% and specificity of 100% and not affected by blood, semen, and cervical mucus was not used for this study because of nonavailability; however, clinical assessment was used in making diagnosis of PPROM
2. There were some antibiotics sensitivity discs that were not available and might affect the result of the antibiotic sensitivity pattern; however, the common antibiotic discs were used.

**Future direction**

1. Periodic review of this study will be necessary to ascertain antibiotic resistance to organisms implicated in PPROM in this center
2. Community-based multicenter study will be needed to confirm the findings of this hospital-based study.

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**Conflicts of interest**

There are no conflicts of interest.

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