

# Premature Rupture of the Membranes at the Sylvanus Olympio University Hospital of Lomé, Togo: Microbiological Findings and Outcomes

Mounerou Salou<sup>1,\*</sup>, Fiali Lack<sup>1</sup>, Amah Biova Adama-Hondegla<sup>2</sup>, Sika Dossim<sup>3</sup>, Novissi Tsogbalé<sup>1</sup>, Adama Gbadoé<sup>4</sup>, koffi Akpadza<sup>2</sup>, Mireille Prince-David<sup>1</sup>

<sup>1</sup>Service de Microbiologie, CHU Sylvanus Olympio, Lomé-Togo

<sup>2</sup>Servie de gynécologie obstétrique CHU Sylvanus Olympio, Lomé-Togo

<sup>3</sup>Laboratoire de Bactériologie, CHU Campus, Lomé -Togo

<sup>4</sup>Service de Pédiatrie, CHU Sylvanus Olympio, Lomé-Togo

\*Corresponding author: mounerous@gmail.com

**Abstract Introduction:** To prevent the risk of infections in cases of premature rupture of the membranes (PROM), a pregnancy complication, gynecologists of the Sylvanus Olympio University Teaching Hospital used clavulanic acid and amoxicillin as empiric antibiotic therapy intravenously. This study aims to identify and assess the susceptibility to antibiotics of bacteria involved in PROM. **Methods:** A cross-sectional study was conducted from February 25 to June 06, 2014 on 60 pregnant women presenting a PROM and their 65 newborns, recruited in the Gynecology and Obstetrics Service of the Sylvanus Olympio University Teaching Hospital of Lomé, Togo. In mothers, cytological and bacteriological examinations of vaginal and endocervix swabs were carried out and among newborns, cytological and bacteriological examinations were performed on gastric fluid and ear swabs at the Microbiology Service of the university hospital. **Results:** The frequency of PROM was 6.8% of deliveries during the study period. Pathogens were isolated among 48.3% of mothers and 26.2% of newborns. Vaginal and endocervix swabs allowed isolation of pathogens in 45% and 28.3% of cases, respectively. The most isolated pathogens were *Candida albicans* (28.6%)(14/53) and enterobacteria (41.5%)(22/53), mainly represented by *Escherichia coli* (59.1%)(13/22). We also isolated Group B Streptococci (GBS) strains (7.5%)(4/53). Pathogen isolation rate among newborns was 26.2%(17/65). Of these pathogens, *Escherichia coli* represented 60%(15/25). Pathogens found in 10.7% of newborns were phenotypically identical to those isolated from their mothers. Among newborns, *E. coli* was the most isolated strain in gastric fluid (66.7%)(4/6) as well as from ear swabs (57.9%)(11/19). **Conclusion:** Half of PROM cases in this study were associated with presence of pathogen amongst pregnant women; *E. coli* and Group B Streptococcus known to cause neonatal meningitis were found. Unfortunately, a few isolated strains of *E. coli* were resistant to clavulanic acid-amoxicillin, a combination used as empiric antibiotic therapy by healthcare practitioners in our settings.

**Keywords:** premature rupture of the membranes, pregnancy, labor, bacteriological examination, bacteria and antibiotic susceptibility testing

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## 1. Introduction

Premature rupture of the membranes (PROM) is a spontaneous rupture of the amniochorionic membrane prior to the onset of labor [1,2]. PROM affects approximately 1 to 18% or even 31% of pregnancies [3]. Etiologies of PROM are diverse and are only known in about 40% of cases [4].

The major physiopathological mechanisms mentioned involve a weakening of the membranes but causes are still poorly documented. The main assumptions are mechanical causes, deficiencies and infectious causes [1,5]. Urinary

tract and amniotic infections represent major risk factors in the occurrence of PROM [5,6]. Regardless of its etiology, the major consequence of PROM is the infectious risk for both the mother and the newborn.

In Africa, several studies have been conducted on PROM with regard to its frequency, risk and prognosis factors [1,6,7]. In Togo, few studies have focused on PROM or on the evaluation of the infectious risk for the mother and the fetus in case of its occurrence. In addition, there is no study that tracks the transfer of vaginal flora pathogens to the amniotic fluid and then to the fetus. In our settings, to prevent infectious risk for the mother-child pair, healthcare practitioners refer to an empiric antibiotic

therapy protocol based on the combination of clavulanic acid and amoxicillin intravenously.

This study aims to identify the main bacteria involved in PROM and to evaluate their susceptibility to antibiotics in order to determine if the empiric antibiotic therapy established by gynecologists at the Sylvanus Olympio University Hospital of Lomé, Togo is in line with the sensitivity profile of the bacteria isolates.

## 2. Patients and Methods

This was a cross-sectional study carried out in the Gynecology and Obstetrics Service and in the Microbiology Laboratory of the Sylvanus Olympio University Hospital (CHU-SO) of Lomé from February 25 to June 06, 2014,

### 2.1. Definition of Cases

PROM diagnosis was based on a thorough clinical examination. Women with a history suggestive of spontaneous rupture of membranes (sudden gush of fluid with continued leakage) and who had a sterile speculum examination that demonstrated pooling of fluid in the posterior vaginal fornix and Tarnier's sign were considered PROM cases.

### 2.2. Enrollment of Pregnant Women and Inclusion of Newborns

Pregnant women admitted in the Gynecology and Obstetrics Service for PROM at a gestational age greater or equal to 32 weeks of amenorrhea from February 25 to June 6, 2014 were recruited. Women who gave informed consent and who did not received antibiotic therapy for less than 24 hours before admission to the hospital were included (n=60). All women already at the active phase of cervical dilatation at the time of enrollment and women who did not gave a live birth were excluded. All live births born to pregnant women included in the sample were themselves included (n=65).

### 2.3. Samples

In mothers, after laying the speculum, separate swabs were used to sample the endocervix and the vagina. One swab was used for each site and care was taken to not cross-contaminate the samples. Among infants, the gastric aspirate fluid was collected using a stomach tube and the auditory canal was swabbed. The samples were labeled and brought immediately to the Microbiology Laboratory for cytological and bacteriological examinations.

After sampling, all included women received an empiric antibiotic therapy consisting of clavulanic acid-amoxicillin. Physicians started treatment first by parenteral route after a more than 12 hours latency phase during 24 hours and then by enteral route until delivery.

### 2.4. Samples Processing

Swabs and gastric fluid were cultured on Eosine Methylene Blue agar plates for *Escherichia coli* or others enterobacteria, on blood agar plates stored at +4°C for *Listeria monocytogenes*, on CHAPMAN agar for *Staphylococcus aureus* and on blood agar plate for *Streptococcus agalactiae* or Group B Streptococci (GBS).

Antibiotic susceptibility testing was carried out based on the disk diffusion method according to the French antibiogram committee (Comité antibiogramme de la Société Française de Microbiologie (CA-SFM) [8].

## 3. Results

### 3.1. Characteristics of Pregnant Women

During the study period, 1,388 delivery cases were admitted to the Gynecology and Obstetrics Service. Among these pregnant women, 94(6.8%) were referred for PROM. We included 60(63.8%) cases of PROM with a mean age of 27 years (range: 14-40 years). The average gestity was 2 (range: 1-4). The average parity was 1 (range: 0-4). Of the women included, six (10%) had a history of cesarean section and one (1.7%) had a history of laparotomy for ruptured ectopic pregnancy. None of them had presented a PROM before. Severe preeclampsia was the most represented gestational pathology (6.7%). The average gestational age was 38 weeks of amenorrhea (range: 32-42 weeks). However, eight (13.3%) pregnancies were early term (i.e. gestational age between 32 and 36 weeks). Most of the pregnancies (55/60) (91.7%) were single and only five (8.3%) were twins. Of the pregnancies, 33(55%) were vaginal deliveries and 27(45%) were cesarean section deliveries.

### 3.2. Microbial Examinations

Of PROM cases, bacteriological examinations of endocervix and vaginal swab samples yielded pathogens from 29(48.3%) women. Gram-negative bacilli isolated were only enterobacteria and represented 56.4% (22/39) of isolates against 43.6% (17/39) Gram-positive cocci, of which a high proportion were streptococci (82.4%)(14/17), with 28.6% (4/14) being Group B Streptococcus strains (Table 1). *Candida albicans* represented 26.4%(14/53) of the isolates (Table 1).

**Table 1. Distribution of strains depending on the origin of sample among mothers**

	Endocervix n	Vagina n	Total N (%)
<i>Escherichia coli</i>	05	08	13 (24.5)
<i>Klebsiella pneumoniae</i>	02	06	08 (15.1)
<i>Streptococcus D</i>	03	04	07 (13.2)
<i>Streptococcus B</i>	01	03	04 (7.5)
<i>Streptococcus F</i>	01	02	03 (5.7)
<i>Staphylococcus aureus</i>	02	01	03 (5.7)
<i>K. oxytoca</i>	00	01	01 (1.9)
<i>Candida albicans</i>	04	10	14 (26.4)
<b>Total</b>	<b>18</b>	<b>35</b>	<b>53 (100)</b>

Seventeen (17) cervicitis and 27 vaginitis cases were recorded. Almost all (88.2%)(15/17) cervicitis cases were associated with vaginitis. Excepted one cervicitis cases associated with a vaginitis, the pathogen isolated at the endocervix level was identical to the one isolated at the vagina level.

Bacteriological examinations from ear swabs and gastric fluid yielded isolation of microbes from 17(26.2%) newborns. Gram-positive cocci accounted for 16% (4/25) of pathogens isolated compared to 80% (20/25) for Gram-negative bacilli, of which 95% (19/20) were enterobacteria.

Only 4% (1/25) of the isolates were *Candida albicans* among newborns (Table 2).

**Table 2. Distribution of strains depending on the origin of sample among newborns**

	Ears N (%)	Gastric fluid N (%)	Total N (%)
<i>E. coli</i>	11	04	15 (60)
<i>Klebsiella pneumoniae</i>	02	01	03 (12)
<i>Streptococcus D</i>	02	00	02 (08)
<i>S. aureus</i>	01	01	02 (08)
<i>Alkalescens dispar</i>	01	00	01 (04)
<i>P. aeruginosa</i>	01	00	01 (04)
<i>Candida albicans</i>	01	00	01 (04)
<b>Total</b>	19 (76)	06 (24)	25 (100)

Among newborns where pathogens were isolated, 58.8% (10/17) were born to a mother bearing pathogens; seven of these ten newborns carried pathogens that were identical to those isolated from their mothers.

Overall, in mothers (i.e. endocervix and/or vagina) and newborns (i.e. ears and/or gastric fluid) bacterial and fungal strains accounted for 80.7% (63/78) and 19.3% (15/78) of isolated pathogens, respectively (Table 1 and Table 2). Fungi consisted of *Candida albicans* strains exclusively, of which 93.3%(14/15) were isolated from the mothers.

### 3.3. Antibiotics Susceptibility Testing

Twenty-eight (28) strains of *Escherichia coli* and 11 strains of *Klebsiella Pneumoniae* were isolated. Three (3) *Escherichia coli* strains, 4 *Klebsiella Pneumoniae* strains and one *Alkalescens dispar* strain were extended-spectrum beta-lactamase (ESBL) producing strains. None of the enterobacteria strains isolated were sensitive to ampicillin. One-third of isolated strains remain resistant to the amoxicillin-clavulanic acid combination. All strains isolated were sensitive to common antibiotics such as netilmicin and ciprofloxacin. The four Group B Streptococci strains isolated were all sensitive to penicillin, amoxicillin-clavulanic acid combination and 2<sup>nd</sup> and 3<sup>rd</sup> generation cephalosporin. Five strains of *Staphylococcus aureus* were isolated and they were all resistant to penicillin G, ampicillin and oxacillin, but 80% sensitive to gentamicin and ofloxacin.

The suites layers were simple in all women and we did not found any cases of chorioamnionitis. Overall, 20 newborns (30.8%) had an infection or were carried a germ. Some of the newborns (12.3%)(8/65) developed neonatal infections but we did not record any case of death

## 4. Discussion

The frequency of PROM found in this study is similar to those reported by Bisembo Wa Bisembo MC. et al. in Democratic Republic of Congo [9] and Adisso S. et al. in Benin [6] respectively, 2% and 4.2%. In our study, pathogens were isolated in one out of two women (48.3%) suffering for PROM. In 45% of the cases, pathogens were isolated from vaginal swabs. Findings also showed that one out of two women who had a PROM developed bacterial or mycological vaginitis. These proportions are close to those reported in 2005 by Aboyeji A et al. who isolated pathogens in 44% of PROM cases at a Nigerian

teaching hospital [10]. Our findings are similar to those reported in studies from Chinese population. These Chinese's studies review showed that pathogens derived from women with PROM were predominantly *Staphylococcus* and *Escherichia coli* and the causes of sepsis in their infants were primarily *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Escherichia coli* [11]. This bacterial pattern differs from the pattern in western countries where GBS constitutes most of the isolates from women with PROM and their babies [11,12,13]. Thus, geographical regions can influence the organisms cultured from women with PROM and their infants. The Group B Streptococcus rate found in our study (7.5%) is somewhat higher than what we reported in a previous study (2.5%) using healthy women [14,15] but the sample sizes are too low for comparison. Furthermore the lack of large scale antenatal GBS screening in Togo may also contribute to the low prevalence of GBS in healthy pregnant women. Moreover, the method of specimen collection, transportation, and storage can also change the rate of positive cultures [16,17]. These factors may also contribute to the variance in colonized bacteria in different areas. In Uganda, a case control study conducted in Mulago hospital showed also no association between Group B Streptococcus infection and risk of PROM [18]. The 28.6% *Candida albicans* rate is in agreement with the vaginal carriage rate of *Candida albicans* among pregnant women ranging between 33.3% and 38% as reported by Cocho in 2012 in France [19]. Our result is also similar to 23% reported by Aboyeji et al. in 2005 in Nigeria with a study population of 108 women [10]. Herbretau C et al. in 2010 isolated *Candida albicans* in 4% of PROM cases in France [20]. This lower rate as compared to our finding could be explained by an increased frequency of vaginal candidiasis in tropical countries. However, the case control study from Uganda showed that candidiasis was found to be protective for PROM; patients with PROM were 73 % less likely to have candidiasis compared with those without PROM [18]. Thus, The association between candidiasis and rupture of membranes is still unclear. There is evidence of release of inflammatory cytokines during candida infestation [21] and these cytokines would cause membrane rupture [18]. Some studies conducted in resources limited settings have shown a positive association between having an abnormal vaginal during pregnancy and PROM [22,23]. The association between PROM and abnormal discharge, a common symptom of genital infections is most likely via inflammatory mediators [24].

Pathogens were isolated from cytological and bacteriological examinations of endocervix swabs among one-third (28.3%) of the women. This rate is comparable to that reported by Herbretau et al. who found 23.2% of positive endocervix samples [20]. The comparison of pathogens found at the endocervix and the vagina demonstrated that 88,2% of isolates found at the endocervix was identical to those isolated at the vagina. We assume that these pathogens are of the same type but this assumption cannot be confirmed, as we did not include serotyping or biotyping of the isolated pathogens. Our study has some limitations, as the sampling technique at the endocervix could be a limiting factor. In fact, we could not prove cases of contamination by one who realizes the collection. To avoid this risk of contamination, the solutions may be for example the dosage of interleukin

6, with or without other protein biomarkers as a reasonable screening test for the presence or absence of microbial invasion of the amniotic cavity by analysis of cervicovaginal proteins in women with preterm [25,26,27].

Pathogens isolated from newborns on the basis of basic laboratory diagnostic methodology, were phenotypically identical to those isolated from their mothers in 41.2% (7/17) of cases. Pathogen isolation rate was 9.2% from gastric fluid and 24.6% from ear swabs. It has been reported that Group B Streptococci and *Escherichia coli* represent about 45% of pathogens isolated from fetal samples in case of infection of the amniotic cavity [28].

The important *Escherichia coli* isolation rate could be explained by the fact that it was also the most isolated pathogen among mothers. This observation may be explained by ascending maternal-fetal contamination or a contamination during the passage of the newborn through the vaginal canal. It would be interesting to perform serogrouping of the *Escherichia coli* strains to determine K1 serotype which is more pathogenic and known as the second cause of maternal-fetal infection [28].

No complications found during the puerperium in this study. Our result is comparable to report from Morocco [1]. These positive outcomes could be explained by the systematic antibiotic therapy established after a period of 6 to 12 hours after PROM occurrence to manage cases [29]. No maternal death was recorded, which is consistent with studies of some other authors [1,7]. Of newborns even among those who were suffering for neonatal infection, we did not isolate GBS, which is been described since the 1960's as a significant causative organism for life threatening infections in infants less than 3 months of age [30].

Concerning enterobacteria, the antibiotic susceptibility testing showed some limitations of the current empiric antibiotic therapy. About 20% of the enterobacteria strains isolated, produced ESBL. This rate of ESBL is similar to the 17.6% found in the same hospital in 2011 [31]. However, the empirical antibiotic therapy is appropriate for the Group B Streptococci strains isolated.

All *Staphylococcus aureus* strains were methicillin-resistant and this resistance rate is substantially higher than 24% reported by a previous study [31] conducted in the same hospital but our sample size is too small to build a comparison.

## 5. Conclusion

Although etiologies are diverse as reported in the literature, the first objective in the case of PROM is to prevent infectious complications in the mother and the fetus. This study showed the presence of pathogens from the endocervix and vagina in almost half of women presenting with PROM. The most isolated pathogens were *E. coli* followed by *Candida albicans*. This finding demonstrates that the infectious risk remains important in PROM cases in our settings, for the couple Mother-child, especially for the newborn. Most of isolated strains were sensitive to antibiotics. However, the empiric antibiotic therapy based on amoxicillin-clavulanic acid used by gynecologists in the Sylvanus Olympio teaching hospital has some limitations due to antimicrobial resistance. As we found pathogens known to be responsible for perinatal infections,

it is important to undertake bacterial examinations at least in vaginal swabs in women experiencing PROM for better pregnancy outcomes. In a future study, it would be interesting to study factors that influence the carriage or the transmission of pathogens in case of PROM.

## Conflict of Interest

All authors declare that none of them have any conflict of interest.

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