

## Outcomes of Pre-Term Premature Rupture of Fetal Membranes at Komfo Anokye Teaching Hospital, Kumasi, Ghana

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### Abstract

Context: Pre-term premature rupture of fetal membranes (pPROM) contributes to maternal and fetal morbidity and mortality. These include chorioamnionitis, prematurity and still-births. Various microbial organisms have been implicated. Few studies have been done on pPROM in this environment.

Objectives: To determine pregnancy outcomes and microbial organisms in cultures from the endocervix, high vagina and urine of patients with pPROM.

Design: Cross-sectional descriptive survey.

Setting: Komfo Anokye Teaching Hospital (KATH), Ghana.

Subjects: Patients admitted to KATH with fluid loss per vaginam during 1<sup>st</sup> April, 2005 to 30<sup>th</sup> September, 2005.

Methods: Structured pre-tested questionnaires were administered to patients who presented with fluid loss per vaginam followed by physical examination. Microbiology cultures were obtained from patients with proven pPROM between gestational ages 28 to 37 completed weeks. The data was analysed using Epi Info software.

Main Outcome Measures: Maternal morbidity and mortality; delivery outcomes; microbial organisms from cultures and drug sensitivities.

Results: Total antenatal admission was 1459 and eighty-five patients (5.8%) satisfied the study criteria. There was no maternal mortality but four patients (4.7%) developed chorioamnionitis. There were sixty-four (75%) live births, nineteen (22%) stillbirths and liquor loss stopped in two (3%) resulting in normal term deliveries. The commonest organisms from the cultures were high vagina, *Candida spp.* (29%); endocervix, *Candida spp.* (23%); and urine, *E. coli* (19%). All bacterial isolates were sensitive to norfloxacin

Conclusions: Pregnancy outcomes in pPROM at KATH are unsatisfactory. Further controlled studies on pPROM are advocated and use of norfloxacin in pregnancy needs reconsideration.

Keywords: Fetal membranes, microbial organisms.

### Introduction

Preterm premature rupture of the membranes (pPROM) is the spontaneous rupture of the fetal membranes before 37 completed weeks of pregnancy and before the onset of labour<sup>1, 2</sup>. There is considerable morbidity and mortality to the neonate<sup>3, 4</sup>. The mother is also at risk of chorioamnionitis. Among the primary aetiological mechanisms for pPROM is infection/inflammation<sup>5</sup>. Organisms which have been implicated include *Chlamydia trachomatis*, *Neisseria gonorrhoea*, group B streptococcus (GBS), causative agents of bacterial vaginosis<sup>6</sup>, *Mycoplasma hominis* and *Ureaplasma urealyticum*<sup>7</sup>, bacteroides species, *Haemophilus* species<sup>8</sup> and *T. vaginalis*<sup>9</sup>.

Maternal risk factors associated with pPROM include previous pPROM, previous preterm delivery, early pregnancy bleeding and cigarette smoking<sup>10</sup>. Premature rupture of membranes (PROM) is commonly diagnosed by patient history, visualization of pooling of amniotic fluid in the vagina, identification of vaginal fluid microscopic ferning and finding of an alkaline pH using nitrazine paper<sup>11</sup>. Mothers with PROM should receive repeated and focused evaluation

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**Table 1**

Maternal characteristics (n =85)		
	n	%
<b>Parity</b>		
0	35	41.2
1 to 5	49	57.6
>5	1	1.2
<b>Marital status</b>		
Single	21	24.7
Married	57	67.1
Cohabiting	7	8.2
<b>Occupation</b>		
Skilled	22	25.9
Semi-skilled	47	55.3
Unskilled	16	18.8
<b>Education</b>		
No formal education	21	24.7
Primary	53	62.3
Secondary	10	11.7
Tertiary	1	1.3
<b>Previous pPROM</b>		
Nil	78	92.9
1	3	3.5
2	2	2.3
>2	2	1.3

for signs and symptoms of maternal and fetal infection and inflammation<sup>12</sup>. In the mother, the search for infection should focus on the upper and lower reproductive and urinary tracts. Organisms grown from culture material obtained from the vaginal fluid may not correspond to the microorganisms present in intrauterine fluid or tissues. Given the 5% to 25% rate of positive cultures from amniotic fluid in research studies<sup>13</sup>, many experienced clinicians attempt to obtain amniotic fluid in all patients.

There is sufficient evidence of better maternal and fetal outcomes to justify the routine administration of antibiotics after pPROM<sup>14</sup>. When PROM complicates cervical cerclage, the ligature should be promptly removed to avoid a twofold risk of infectious morbidity<sup>15</sup> and even mortality.

From 1<sup>st</sup> January 2004 to 31<sup>st</sup> December 2004 pPROM for gestational ages 28 to 37 weeks accounted for 6.1% of all admissions to the antenatal wards at KATH. This study was therefore undertaken to determine the pregnancy outcomes of patients admitted with pPROM over the six month period 1<sup>st</sup> April to 30<sup>th</sup> September 2005. It was also to find out microorganisms from cultures obtained from the endocervix, high vagina and urine and their drug sensitivities. The Kwame Nkrumah University of Science and Technology/School of Medical Sciences Committee of Human Research Publications and Ethics (KNUST/SMS CHRPE) approved the study.

### Patients and Methods

All patients who were admitted to the antenatal ward during the study period complaining of loss of fluid per vaginam were interviewed and examined after the study had been explained to

**Table 2**  
Current pregnancy outcomes.

	n	%
<b>Duration of pPROM before admission (days) (n = 85)</b>		
<1 day	29	34.1
2-7 days	55	64.7
8-14 days	1	1.2
<b>pPROM to delivery interval (latency) (weeks) (n = 85)</b>		
<1 week	68	80.0
1-2 weeks	14	16.4
2-3 weeks	0	0.0
3-4 weeks	1	1.2
>4 weeks	2	2.4
<b>Loss of liquor stopped (n = 2)</b>		
<b>Live births (n = 66)</b>		
Spontaneous vaginal delivery (SVD)	50	75.8
Vacuum extraction	2	3.0
<b>Caesarean section (C/S) (n = 14)</b>		
Fetal distress*	9	13.7
2 previous C/S	1	1.5
pPROM/unfavourable cervix	2	3.0
Breech presentation	1	1.5
Twins-1 <sup>st</sup> + 2 <sup>nd</sup> breech	1	1.5
<b>Still births (n = 19)</b>		
Fresh **	15	78.9
Macerated ***	4	21.1

\* 1 case of chorioamnionitis  
 \*\* 1 case of chorioamnionitis  
 \*\*\* 2 cases of chorioamnionitis

them and verbal consent had been obtained. The doctor admitting the patient administered a standardized questionnaire and relevant information and clinical findings were noted. The questionnaire had been pre-tested on 20 patients and modifications were made following

a departmental meeting.

The inclusion criteria were- gestational ages between 28 to 37 completed weeks, fetal heart tones present at the time of admission and confirmed loss of liquor. Exclusion criteria were

established labour and use of antibiotics within the previous two weeks prior to admission. The following items were recorded for each patient - age, occupation, marital status, parity, and duration of pPROM. The gestational age was determined from the known last menstrual period, ultrasound measurements of biparietal diameter, femur length, and abdominal circumference. The symphysio-fundal height is not reliable in pPROM. A physical examination of the patient was done and the pulse rate and temperature were recorded.

A sterile speculum examination was done to confirm loss of liquor (liquor seen coming from the cervical os or pool in the posterior vaginal fornix). Where no liquor loss was seen, the patient was made to rest in bed for one hour and the examination repeated. Specimens were thus obtained only when there was unequivocal loss of liquor. Sterile swabs were used to obtain specimens from the endocervix and the posterior vaginal fornix and placed in separate Amies (DIFCO) transport media. A mid-stream urine specimen (MSSU) was then collected into a sterile universal container and all specimens immediately sent to the microbiology laboratory. The endo-cervical swab (ECS) and high vaginal swab (HVS) were cultured on chocolate agar and Thayer-Martin plates whilst the MSSU was cultured on a well-dried cystine-lysine-electrolyte-deficient (CLED) (OXOID) plate for 48 hours. Sensitivity tests were done using antibiotic impregnated multi-disks (BRITANNIA). Mueller-Hinton agar (OXOID) was the base medium for sensitivity testing for *N. gonorrhoea*. Bacterial vaginosis was diagnosed using Amsel's criteria<sup>16</sup>.

The clinical course of each patient up to delivery or other outcome was carefully documented. At the time of this study, the departmental policy on pPROM included prophylactic antibiotic combination of amoxicillin, metronidazole and gentamycin for seven days. Each patient was observed for any evidence of infection such as rising pulse rate, rising temperature, tender uterus/abdomen and foul smelling liquor. The researcher checked each questionnaire for omissions and errors prior to the patient's discharge from hospital. The data were analysed

using Epi Info 6.

#### Results

Eighty-five patients satisfied the criteria for this study out of a total antenatal admission of 1459 (5.8%)

**Maternal Characteristics.** The maternal characteristics are shown in Table 1. The ages ranged from 16 years to 42 years with a mean of 28.1 ± 5.8 years, and a mode of 32 years. Most of the patients (78 out of 85 or 92.9%) had not had previous pPROM.

**Current Pregnancy Outcomes.** The outcomes for the current pregnancies are shown in Table 2. There were 66 live births and 19 stillbirths. Almost all the patients (84 out of 85 or 99.8%) reported to hospital within one week of noticing loss of liquor. The pregnancies of 68 out of 85 patients (80%) ended within one week of admission whilst in 2(2.4%) the pregnancies continued for more than four weeks. Seventy-five percent of the live births occurred by spontaneous vaginal delivery (SVD). The average Apgar scores of the SVD babies were 5 and 8 at 1 and 5 minutes respectively. One baby delivered by vacuum extraction and four babies delivered by caesarean section were admitted to the neonatal intensive care unit for an average of 4 days because of breathing difficulties.

Febrile morbidity (defined here as an oral temperature = 38°C on any occasion during admission without other signs and symptoms of chorioamnionitis) occurred in 4 out of 85 or 4.7% of patients. The temperatures settled when antimalarials were added to their antibiotics. Four (4.7%) of the 85 patients developed chorioamnionitis (raised temperature, tender abdomen/uterus, offensive lochia). An emergency caesarean section for fetal distress was done for one at 36 weeks resulting in a live birth. For the remaining three, there was one fresh still-birth and two macerated still-births.

Three (3.5%) of patients had cervical cerclage inserted in the current pregnancy. One of these presented at 32 weeks with pPROM of 2 days duration. The suture was removed and she went into labour four days later resulting in a live birth.

*Staph. aureus* were isolated from both the ECS and HVS and *E. coli* from the MSSU. The antibiotic regime of amoxycillin, gentamycin and metronidazole was changed to cefuroxime when the sensitivity results were available. In the remaining two, one had a pre-term delivery and the other a full term live birth.

The loss of liquor stopped in 2 (2.3%) of the patients. They were discharged after no further loss of liquor could be seen on speculum examination and maternal and fetal well being judged to be satisfactory. They were followed up at the antenatal clinic and delivered normal live babies at term.

#### Microbiology:

**MSSU:** Urine cultures were positive in 36 out of the 85 patients who had no signs or symptoms of urinary tract infection giving an asymptomatic bacteriuria rate of 42.3%.

*Escherichia coli* was the commonest organism and was isolated from 16 out of 36 (44.4%) of the positive MSSU. Other organisms were *Providencia sp.*, *Klebsiella sp.*, *Proteus sp.* and *Coliforms*. All the organisms were sensitive to norfloxacin and nitrofurantoin and uniformly resistant to ampicillin. There was varying susceptibility to other antibiotics. The urine samples were sterile in 49 (57.6%) of patients.

**HVS:** Bacterial vaginosis (BV) was found in 12 out of 85 (14.1%) of the patients. *Candida sp.* was isolated from 24 (28.2%) of the patients. *T. vaginalis* was isolated from 3 (3.5%) of patients. *Staph. aureus* was also isolated from 3 (3.5%) of patients and all were sensitive to norfloxacin. One patient had both BV and Candidiasis.

**ENDOCERVIX:** *Neisseria gonorrhoeae* and *Staph. aureus* were isolated from the endocervix of 3 (3.5%) and 2 (2.3%) of patients respectively as was *Candida sp.* from 19 (22.3%) of patients. Pus cells of at least 3+ (suggestive of infection)<sup>18</sup> but with no bacterial growth were reported in 34 (40%) of patients. Isolates of *N. gonorrhoeae* and *Staph. aureus* were sensitive to norfloxacin.

#### Discussion

In this study, the diagnosis of ruptured

membranes was based on direct visualisation of amniotic fluid. Other methods such as use of nitrazine paper to determine pH and ferning on microscopic examination were not available at the time. In general, patients reported to the hospital early which could be an indication that advice given to attendants at antenatal clinics was effective. The overall still-births comprising 22% of the study population is disappointing considering that antibiotic cover was given on admission. Although the sample size is small, this finding gives cause for concern. It would have been useful to follow up the surviving babies for one year or more to find out about possible late developmental sequelae. Surveillance of this nature is very difficult to conduct with resources currently available.

The diagnosis of chorioamnionitis was clinical based on findings such as fever, rising pulse rate, abdominal/uterine tenderness and foul smelling lochia. The incidence of chorioamnionitis in this study was 4.7%. This contrasts markedly with the study of Morales<sup>17</sup>, who reported that in a study of nearly 700 women between 26 and 34 weeks with preterm ruptured membranes, 13% developed chorioamnionitis diagnosed by oral temperatures of 38°C and no other cause for fever. It is noted that Morales' study included more patients and was based on oral temperatures. Febrile morbidity occurred in 4.7% of patients. Malaria is endemic in this region and should also be excluded as was done in these cases.

The organisms isolated from this study (not proven to be causative) included *Neisseria gonorrhoeae* and *Staph aureus* from the endocervix, *Candida sp.*, *T. vaginalis*, *Staph aureus* and BV related organisms from HVS and *E. coli*, *Klebsiella sp.*, *Providencia sp.*, *Coliforms* and *Proteus sp.* from urine. Cultures and assays for Chlamydiae were not done because the necessary facilities were not available. However the findings of moderate to high numbers of pus cells with no bacterial growth on the endocervix of patients could suggest the involvement of Chlamydiae<sup>18</sup>. At the time of the study patients admitted to the antenatal ward in KATH with pPROM were given prophylactic antibiotics comprising a combination of amoxycillin,

metronidazole and gentamycin. This combination covered all the bacterial isolates from this study.

This study suggests that norfloxacin (a quinolone) would cover the potential associated pathogens. Although there is no evidence from animal studies that norfloxacin has teratogenic or mutagenic effects, it has been shown to cause arthropathy in immature animals and therefore its use during pregnancy is not recommended<sup>19</sup>. Quinolones may also interfere with absorption of iron and multivitamins, which are commonly used in pregnancy. Perhaps norfloxacin could be used in the latter parts of pregnancy. This will

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