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Premature Rupture of Membranes after Twenty-Eight Complete Weeks of Gestation and Pregnancy Outcome

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Abstract

Purpose : To study the outcomes of pregnancies complicated with premature rupture of membranes (PROM).

Materials and Methods : This comparative prospective cohort study was carried out between 1st February and 31st July 2023. Women whose pregnancies were complicated with PROM from the 28th week of gestation or not were recruited and followed up from admission, then delivery till their discharge from the hospital and their newborn as well. The main variables recorded included maternal age and parity, medical and obstetrical past-histories, gestational age at delivery, birth weight, sex of newborn, Apgar score, maternal and perinatal outcomes. Fisher exact test and t-test were used for comparison. P<0.05 was considered statistically significant.

Results : Our frequency of PROM was 6.2% (96/1540 births). PROM occurred mostly at term (77.6%). Significant maternal adverse outcomes associated with PROM were increased risk of cesarean section (RR 2.52, 95%CI 1.63-3.88) and puerperal or surgical site infection (RR 3.00, 95%CI 1.10-8.15), while adverse perinatal outcomes were cord prolapse (RR 8.00, 95%CI 0.91-70.48), premature delivery (RR 2.24, 95%CI 1.23-4.07), neonatal asphyxia (RR 3.71, 95%CI 1.54-8.97), neonatal infection (RR 19.00, 95%CI 7.01-51.48), admission in the neonatal intensive care unit (RR 4.35, 95%CI 2.61-7.26) and perinatal death (RR 3.50, 95%CI 1.53-8.02).

Conclusion : PROM is associated with adverse maternal and perinatal outcomes. Therefore, pregnancies complicated with PROM should be managed in settings where cesarean sections and neonatal intensive care are available.

Keywords: Cesarean section; Neonatal asphyxia; Néonatal infection; Périnatal death; Prémature rupture of membranes

Abbreviations: CI: Confidence interval; COVID-19: Coronavirus disease-2019; CS: Cesarean section; NICU: Neonatal intensive care unit; NNA: Neonatal asphyxia; NNI: Neonatal infection; PAMG-1: Placental α-microglobulin-1; PROM: Premature rupture of membranes; SPSS: Statistical package for social sciences; RR: Relative risk.

Introduction

Premature rupture of membranes (PROM) is defined as the spontaneous tear of both the amnion and chorion before the beginning of uterine contractions [1]. PROM usually affects about 5% to 10% of all births [2]. A PROM rate as high as 13.7% has been noticed in singleton deliveries in Ethiopia [3]. PROM can occur at term or not. When it occurs preterm it is thon called preterm PROM. The latter represents about 40% of cases of PROM. The risk factors for PROM are not all known. Known risk factors are cervical incompetency, history of PROM, smoking, polyhydramnios, fetal mal presentation, cervical infections, urinary tract infections and multiple pregnancies [4, 5]. PROM is usually diagnosed under vaginal speculum examination in a woman not in labor. Direct observation of the cervix can reveal flow of amniotic fluid from the endocervical canal. In certain cases, the liquid flow is so little that some tests such as the placental α-microglobulin-1 (PAMG-1) assay or the Nitrazine test should be done to confirm the diagnosis [6, 7].

It is a major concern in Obstetrics, given that it is associated with high risk of premature deliveries when it occurs before term [8]. Other complications include cord prolapse, cesarean section risk, endometritis, neonatal infections and perinatal death [9, 10]. Neonatal infection risks increase when the time interval between PROM and delivery increases [11], and when the gestational age is low. Hence, prompt delivery should be carried out when the fetal lungs are mature. Neonatal infection is also favored by concomitant cervical or vaginal infection. Because of these adverse maternal and perinatal outcomes, PROM should be prevented. If not, its management should be adequately done. The magnitude of these adverse outcomes in our environment is not well known. To the best of our knowledge, no recent study has evaluated the outcome of pregnancies complicated with PROM in our country, hence this study which aimed at evaluating these outcomes.

Methods

This comparative prospective cohort study was carried out between 1st February and 31st July 2023 in two University Teaching Hospitals. From the 28th week of gestation, women whose pregnancies were complicated with PROM (group A) or not (group B) were recruited and followed up from admission, then delivery till their discharge from the hospital and their newborn as well. Women of group B had intact fetal membranes at four cm cervical dilatation. The two eligible women without PROM who delivered immediately after the delivery of each woman with PROM were taken in the comparative group. Women who refused to participate to this survey and those lost at follow-up were excluded. A written informed consent was obtained from each woman or from their relatives. This study was approved by the two institutional ethics committees. The variables recorded in both groups on a pre-established questionnaire included maternal age and parity, marital status, gestational age at PROM (confirmed by an ultrasound scan performed before 20 weeks' gestation), fetal presentation, whether there was PROM or not, medications received after PROM, time interval between PROM and delivery, gestational age at delivery, mode of delivery, birth weight, sex of newborn, Apgar scores, maternal and neonatal outcomes. Severe pre-eclampsia was defined as blood pressure ≥160/110 mm Hg, with or without headache, visual disturbances, epigastric pain or oliguria.

The minimum sample size was calculated as needing at least 42 cases of PROM, using the following formula [12]: N= 2 (1/1-f)((p)(1-p) ($Z\alpha+Z_{\beta}$)^2)/(P0-P1)^2 , where f is the percentage of women lost at follow-up (10%), Zα =1.96 corresponds to a type I error of 2.5%, Zβ =1.96 corresponds to a power of 97.5%, P0 the percentage of babies transferred to the NICU amongst women with PROM (41.7%) [13], P1 the percentage of babies transferred to the NICU amongst women without PROM (3.7%) and P is (P0+P1)/2. To increase the power of our study, we decided to recruit two women without PROM for each woman with PROM. Data were analyzed using SPSS 26.0. Data of women of group A were compared to those of group B. Fisher's exact test was used to compare categorical variables and t-test to compare continuous variables. We used relative risks (RRs) with their 95% confidence intervals (CIs) to present the comparison between the two groups. Logistic regression was used to control for potential confounders. P<0.05 was considered statistically significant.

Results

During the study period, we had a total of 96 PROMs out of 1540 deliveries performed, giving a PROM rate of 6.2%. A total of 11 (11.4%) women were excluded, eight (8.3%) for refusal to participate and three (3.1%) lost at follow-up. The 85 remaining women with PROM and 170 women without PROM took part to this survey. Some sociodemographic and obstetrical variables are given in (Table 1). PROM occurred between 28 and 44 weeks gestation (mean 38.4 ± 2.3 weeks), with five cases (5.9%) occurring before 32 weeks, four (4.7%) between 32 and <34 weeks, 10 (11.8%) between 34 and < 37 weeks, 61 (71.8%) at term (37 to 42 weeks inclusive) and 5 (5.9%) post-term (>42 weeks gestation). GA <32 weeks at delivery were found more in group A (6 or 7.1% vs. 2 or 1.2%, RR 6, 95%CI 1.24-29.10, P=0.018). A total of 61 (71.8%) women with PROM received antibiotics until delivery. Amongst women with gestational age at admission <34 weeks' gestation, betamethasone for lungs maturation was given to all the nine women (10.6%) with PROM and to six women (3.5%) without PROM. Short term tocolytics (24-48 hours duration) were administered to 12 (14.1%) and four (2.4%) women respectively. The PROM-delivery interval varied between five and 48 hours in 71 cases (83.5%), between three and seven days in nine cases (10.6%) and between eight and 14 days in five cases (5.9%).

Table 1: Some sociodemographic characteristics of the population under study RR: Relative risk, CI: Confidence interval, NICU: neonatal intensive care unit.

Variables	Group A women (n=85) N (%)	Group B women (n=170) N (%)	RR	95% CI	P-value
Mother's age (y)	28.8 ± 6.1 (17-42)	29.4 ± 6.2 (16-44)	-	-	0.465
Parity	2.5 ± 1.9 (0-9)	2.6 ± 1.5 (0-7)	-	-	0.647
Single women	57 (67.1)	101 (59.4)	1.13	0.93-1.37	0.147
Non-cephalic presentation	6 (7.0)	8 (4.7)	1.54	0.51-4.58	0.306
Labor induction	13 (15.3)	14 (8.2)	1.86	0.91-3.77	0.068

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Cord prolapse	4 (4.7)	1 (0.6)	8	0.91-70.48	0.044
Cesarean delivery	34 (40)	27 (15.9)	2.52	1.63-3.88	<0.001
Premature delivery (<37w)	19 (22.4)	17 (10)	2.24	1.23-4.07 1.24-29.10	0.008
· <32 w	6 (7.1)	2 (1.2)	6	0.34-6.55	0.018
· 32-<34 w	3 (3.5)	4 (2.4)	1.5	0.80-4.11	0.429
· 34-<37 w	10 (11.8)	11 (6.5)	1.82		0.115
Still births	3 (3.5)	4 (2.4)	1.5	0.34-6.55	0.429
Male sex	35 (41.2)	88 (51.8)	0.79	0.59-1.07	0.072
Mean birth weight (g)	3028.5 ± 754.0 (550-4790)	3242.9 ± 618.4 (1100-5500)	-	-	0.016
Neonatal asphyxia	13 (15.3)	7 (4.1)	3.71	1.54-8.97	0.003
Early neonatal death	11(12.9)	4 (2.4)	5.5	1.8-16.76	0.001
Neonatal infection	38 (44.7)	4 (2.4)	19	7.01-51.48	<0.001
Transfer to NICU	37 (43.9)	17 (10)	4.35	2.61-7.26	<0.001

Amongst women with PROM, 69 (81.2%) delivered more than 6 hours and 49 (57.6%) more than 24 hours after PROM. With regards to mode of delivery, cesarean sections (CSs) were carried out more amongst women with PROM, the main indications been acute fetal distress and scarred uterus (Table 2). We noticed more puerperal infection (defined as a fever of 38°C or more from the second day after delivery on two separate occasions associated with hypogastric tenderness with/without offensive vaginal discharge) (seven or 8.2% vs. five or 2.9%) and surgical site infection (two or 2.4% vs. One or 0.6%) amongst women with PROM. Globally, maternal infectious complications were found more amongst women with PROM (9 or 10.6% vs. 6 or 3.5%, RR 3, 95%CI 1.10-8.15, P=0.027). Low birth weight (<2500g) were significantly more observed amongst women with PROM (Table 3). Neonatal infection (diagnosed with a C-reactive protein >6mg/l on the first day of life, a leucocytosis >25x103 white blood cells/ml or a positive urine or blood culture) and neonatal asphyxia (defined as a 5th minute Apgar score <7) were more found in group A. Perinatal death was also noticed more amongst babies of women with PROM (14 or 16.5% vs. 8 or 4.7%, RR 3.5, 95%CI 1.53-8.02, P=0.002), even after adjustment for very preterm births (28-<32 weeks) (aRR 3.03, 95%CI 1.19-7.67, P=0.017) (Table 4) summarizes significant adverse outcomes associated with PROM.

Table 2: Indications for cesarean sections amongst the study population RR: Relative risk, CI: Confidence interval, CPD: Cephalo-pelvic disproportion.

Variables	Group A women (n=85) N (%)	Group A women (n=170) N (%)	RR	95% CI	P-value
Acute fetal distress	17 (20)	5 (2.9)	6.8	18.81-20.91	<0.001
Scarred uterus	6 (7.1)	3 (1.8)	4	1.03-17.34	0.04
CPD	5 (5.9)	9 (5.3)	1.11	0.38-3.21	0.526
Mal presentation	4 (4.7)	4 (2.4)	2	0.51-7.80	0.256
Placenta praevia	1 (1.2)	2 (1.2)	1	0.09-10.87	0.741
Severe pre-eclampsia	1 (1.2)	4 (2.4)	0.5	0.06-4.40	0.46
Total	34 (40.0)	27 (15.9)	2.51	1.63-3.88	<0.001

Table 3: Distribution of birth weights amongst the study population RR: Relative risk, CI: Confidence interval.

Variables	Group A women (n=85) N (%)	Group A women (n=170) N (%)	RR	95% CI	P-value
<2500	15 (17.6)	14 (8.2)	2.14	1.09-4.23	0.027
2500 - 2999	22 (25.9)	22 (12.9)	2	1.17-3.40	0.009
3000 - 3499	28 (32.9)	70 (41.2)	0.8	0.56-1.14	0.127
3500 - 3999	12 (14.1)	50 (29.4)	0.48	0.27-0.85	0.005

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4000 - 4499	6 (7.1)	10 (5.9)	1.2	0.45-3.19	0.453
≥4500g	2 (2.4)	4 (2.4)	1	0.19-5.35	0.682

Table 4: Summary of adverse maternal and perinatal outcomes associated with PROM, RR: Relative risk, CI: Confidence interval, PROM: premature rupture of membranes, NICU: Neonatal intensive care unit.

Adverse outcome	RR	95%CI	P-value
A) Maternal			
Cesarean section	2.52	1.63-3.88	<0.001
Puerperal or wound infections	3	1.10-8.15	0.027
B) Perinatal			
Cord prolapse	8	0.91-70.48	0.044
Premature delivery	2.24	1.23-4.07	0.008
Neonatal asphyxia	3.71	1.54-8.97	0.003
Neonatal infection	19	7.01-51.48	<0.001
Transfer to NICU	4.35	2.61-7.26	<0.001
Perinatal death	3.5	1.53-8.02	0.002

Discussion

Our rate of PROM was 6.2%. The two groups were similar as concerns maternal age, parity, marital status, fetal presentation and fetal sex. Adverse maternal outcomes associated with PROM were increased risks of CS and puerperal or surgical site infections, while adverse perinatal outcomes were high risks of cord prolapse, preterm delivery, neonatal asphyxia, neonatal infection, transfer of the newborn to the neonatal intensive care unit (NICU) and perinatal death. Our PROM rate is within the 5-10% rate found in the literature. Our rate of CS amongst women with PROM (40%) is similar to the 42.3% rate reported in China. It was mainly attributed to acute fetal distress and scarred uterus. In the UK scarred uterus is a main indication for CS amongst women with PROM [14]. CS is preferred to labor induction in women with scarred uterus since labor induction is not universally admitted amongst women with scarred uterus.

Surgical site infection rate in our survey was 2.4% amongst women with PROM. A rate of surgical site infection of 9.7% in women with PROM has been reported in Ethiopia [15]. In our study, antibiotics were not given to all women with PROM, though they were prescribed to all of them. Only 71.8% of women received antibiotics. The remaining 28.2% of women could not afford it. Our 8.2% rate of puerperal infection might have been lower if all women with PROM had received antibiotics, given that antibiotics reduce the risk of endometritis [16]. With regards to perinatal complications, preterm deliveries were more observed in the group with PROM. With rupture of membranes, there is release of membranous prostaglandins, hence, spontaneous labor is frequent within the first 24 hours [17]. Cord prolapse occurred in 4.7% of cases of PROM in our study. PROM is a risk factor for cord prolapse, as observed in Japan [18]. The increased rate of cord prolapse could be attributed to the rapid flow of amniotic fluid especially when the woman was going to the hospital in a sitting position, as lying down position reduces the risk of cord prolapse after PROM [19]. Our neonatal asphyxia rate amongst women with PROM in our series (15.3%) was higher than that of 8% observed in India and was due to cord prolapse, acute fetal distress and prematurity, though in our series women with PROM and gestational age <34 weeks received corticosteroids. Treatment with antenatal corticosteroids reduces the risk of respiratory distress syndrome in early and even late preterm infants [20,21]. Our 44.7% rate of neonatal infection is higher than that of 4% reported in India. This huge difference can be attributed to the fact that the study carried out in India did not include babies born before 34 weeks gestation. Moreover, our high rate can be explained also by the fact that some women did not received antibiotics. Broad spectrum antibiotics reduce the risk of NNI [22]. Lastly, so many babies (57.6%) were born more than 24 hours after rupture of membranes. This was due to the fact that in certain cases spontaneous labor was being awaited. Induction of labor should be carried out latest six hours after PROM if there is no spontaneous labor [23], especially if the gestational age is above 34 or 35 weeks [24]. Delivery within a short time after PROM is associated with reduced rate of neonatal sepsis.

Our transfer rate of the newborn to the NICU (43.3%) was higher than the 26% noticed in India. This high rate is due to our high rates of NNA and NNI. Finally, our perinatal death rate of 16.5% amongst babies with PROM was higher than the 6.5% observed in USA [25] and was attributed in our series to preterm deliveries especially before 32 weeks gestation, NNA and NNI. Our limitations are firstly our small sample size attributed to the COVID-19 pandemic. Indeed, due to fear of being contaminated, some women refuse to attend at our hospitals Secondly, our rate of PROM might be higher than what we reported since we recruited only cases with obvious endocervical flow of amniotic fluid. Therefore, similar studies with large sample sizes should be carried out to verify these findings.

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Conclusion

PROM was associated with adverse maternal and perinatal outcomes. Therefore, efforts should be made to prevent it. Moreover, women with PROM should be managed in well-equipped centers where CS and intensive neonatal care are available.

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