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Research Article

Risk Factors for Premature Rupture of Membranes After Twenty-Eight Complete Weeks of Gestation

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ABSTRACT

Purpose: To identify the risk factors for premature rupture of membranes (PROM).

Materiel and Methods: This case-control study was carried out between 1st February and 31st July 2021. Files of women who delivered after having PROM or not were examined. The main variables recorded included maternal age and parity, familial, medical and obstetrical histories, the presence or not of nuchal cord at delivery, gestational age at delivery, birth weight and sex of newborn. Fisher exact test, t-test and logistic regression were used for comparison. P<0.05 was considered statistically significant.

Results: Our frequency of PROM was 6.2% (94/1524 births). PROM occurred mostly at or after 37 weeks gestation (77.6%). Significant risk factors for PROM were 1st degree family history of PROM (aOR 31.36, 95%CI 2.57-382.11), fetal weight ≥4000g (aOR 14.78, 95%CI 2.72-80.20), cord round neck (aOR 6.36, 95%CI 1.17-34.66), past history of preterm delivery (aOR 3.42, 95%CI 1.02-11.52) and parity 4 or 5 (aOR 3.27, 95%CI 1.25-8.56).

Conclusion: Women with these risk factors should be well followed up during pregnancy, especially during the third trimester, to allow prevention, if not, early diagnosis of PROM.

KEYWORDS

Premature rupture of membranes, Risk factors, Fetal macrosomia, Nuchal cord entanglement, Multiparity.

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List of Abbreviations

aOR: adjusted odds ratio, CI: Confidence interval, COVID-19: Coronavirus disease-2019, PAMG-1: Placental α-microglobulin-1, PROM: Premature rupture of membranes, SPSS: Statistical package for social sciences, OR: Odds ratio.

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 affects about 5% to 10% of all births [2]. It affects up to 13.7% of singleton deliveries in Ethiopia [3]. PROM occurs mostly at term. When it occurs preterm as it is the case in about 30-40% of cases it is then called preterm PROM [2,4].

It is a major concern in Obstetrics, given that it is associated with high risk of preterm deliveries when it occurs before term [5,6]. Other complications of PROM include cord prolapse, cesarean section risk, neonatal infections and perinatal death [7,8].

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 small that some tests such as the placental α-microglobulin-1 (PAMG-1) assay or the Nitrazine test should be done to confirm the diagnosis [9,10].

With regards to pathogenesis, there are four mechanisms that explain the occurrence of PROM. The first is an increased intra-amniotic pressure as seen in polyhydramnios, the second is congenital or acquired defects in the fetal membranes as seen in collagen diseases or smoking. The third mechanism is the lysis of fetal membranes proteins by enzymes produced by germs and the fourth is direct trauma of the fetal membranes within the cervical canal as seen in women with incompetent cervix.

The risk factors for PROM are probably not all known, given the scarcity of publications on the topic. Known risk factors for PROM are cervical incompetency, past history of PROM, smoking, polyhydramnios, fetal mal presentation, cervical infections, and multiple pregnancies [1,11]. Smoking leads to decrease of collagen and proteins in membranes by increasing cadmium levels and decreasing the availability of Cu2+ for collagen synthesis in amnion mesenchymal cells [12].

Some other risk factors might exist in our environment, given the higher incidence in developing world. Identifying the risk factors helps in the prevention of some cases of PROM. To the best of our knowledge, no study has evaluated the risk factors for PROM in our country, hence this study which aimed at seeking for such risk factors.

Materials and Methods

This case-control study was carried out between 1st February and 31st July 2021 in two University Teaching Hospitals. Files of women who delivered at ≥28th week's gestation after having PROM were recruited as cases (group A). Those of two women who delivered immediately after each case without having PROM (intact fetal membranes noticed at four cm cervical dilatation) were recruited as controls (group B). Women who refused to participate to this study 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 on a pre-established questionnaire in both groups included maternal age and parity, familial, medical and obstetrical histories, number of gestations, number of antenatal visits, health care provider, gestational age at diagnosis of PROM (confirmed by an ultrasound scan performed before 20 weeks' gestation), pathologies that occurred during pregnancy, fetal presentation, birth weight, presence or not of nuchal cord at delivery and sex of newborn.

The necessary minimum sample size was calculated as needing at least 73 cases of PROM, using the following formula [13]: $N=2\frac{(p)(1-p)(Z\alpha+Z_{\beta})^2}{(P0-P1)^2}$,

where 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 previous PROM amongst women with PROM (33.8%) [14], P1 the percentage of previous PROM amongst women without PROM (6.2%) [14] and P is (P0+P1)/2. To increase the power of our study, we then decided to recruit two controls for each case.

Data were analyzed using SPSS 26.0. Data of cases were compared to those of controls. Fisher's exact test was used to compare categorical variables and t-test to compare continuous variables. We used odds ratios (ORs) with their 95% confidence intervals (CIs) to present the comparison between the two groups. Logistic regression was used to control for confounders. P<0.05 was considered statistically significant.

Results

During the study period, we had a total of 94 PROMs out of 1524 deliveries performed, giving a PROM rate of 6.2%. A total of nine (9.6%) women were excluded because they refused to take part to this study. The 85 remaining women and 170 controls were recruited. Some sociodemographic and obstetrical variables are given in Table 1.

PROM occurred between 28 and 44 weeks gestation with a mean of 38.4 ± 2.3 Amongst the 85 women with PROM, seven (8.2%) occurred before 32 weeks, five (5.9%) between 32 and <34 weeks, seven (8.2%) between 34 and <37 weeks gestation, 61 (71.8%) at term (37 to 42 weeks inclusive) and 5 (5.9%) post-term (>42 weeks gestation).

We found no significant differences between the two groups as concerns mean maternal ages and mean parities. We also observed

no association between PROM and history of late abortion, placenta praevia and non-cephalic fetal presentation (Table 1). Women with less than four antenatal contacts were more exposed to PROM after univariate analysis (Table 1).

As concerns fetal weights, women with fetal weight <2500 g or ≥4000 g were more exposed to PROM after univariate analysis (Table 2).

Table 3 shows significant risk factors for PROM after multivariate analysis.

Table 1: Some sociodemographic characteristics of the population under study.

Variables	Group A women (n=85) Mean ± SD (range)	Group B women (n=170) Mean ± SD (range)	OR	95% CI	P-value
Mother's age (y)	28.2 ± 6.3 (17-42)	29.2 ± 7.0 (16-53)	-	-	0.268
Parity	2.4 ± 1.6 (0-7)	2.5 ± 1.8 (0-9)	-	-	0.665
1st degree family PROM	7 (8.2)	1 (0.6)	15.17	1.83-125.40	0.002
Past history of PROM	10 (11.8)	6 (3.5)	3.64	1.28-10.40	0.013
Past history of Preterm delivery	19 (22.4)	15 (8.8)	2.97	1.42-6.20	0.003
Past history of late abortion	11 (12.9)	17 (0.1)	1.34	0.60-3.00	0.305
Smoking (passive)	2 (2.4)	3 (1.8)	1.33	0.23-7.83	0.540
Pregnancies followed up by nurses	19 (22.4)	14 (8.2)	3.20	1.52-6.78	0.002
Multiple pregnancies	4 (4.7)	2 (1.2)	4.15	0.74-23.12	0.097
<4 antenatal visits	19 (22.4)	10 (5.9)	4.60	2.03-10.43	<0.001
Cervico-vaginitis*	9 (10.6)	1 (0.6)	20.01	2.49-160.79	<0.001
Malaria in pregnancy	29 (30.1)	18 (10.6)	4.37	2.25-8.49	<0.001
Placenta praevia	5 (5.9)	3 (1.8)	3.48	0.81-14.92	0.084
non-cephalic presentation	6 (7.0)	8 (4.7)	1.54	0.51-4.58	0.306
Male sex	35 (41.2)	88 (51.8)	0.79	0.59-1.07	0.072
Nuchal cord at delivery	13 (15.3)	3 (1.8)	10.05	2.78-36.35	<0.001

* Trichomonas vaginalis.
OR: Odds ratio, CI: Confidence interval, PROM: premature rupture of membranes.

Table 2: Birth weights distribution in the population under study.

Birth weight (g)	Group A women (n=85) N (%)	Group B women (n=170) N (%)	OR	95%CI	P-value
< 2500	11 (12.9)	8 (4.7)	3.01	1.16-7.79	0.020
2500- <3000	22 (25.9)	32 (18.8)	1.51	0.81-2.80	0.128
3000- <3500	33 (38.8)	92 (54.1)	0.54	0.32-0.91	0.015
3500- <4000	8 (9.4)	35 (20.6)	0.40	0.18-0.90	0.017
≥ 4000	11 (12.9)	3 (1.8)	8.27	2.24-30.53	<0.001

OR: Odds ratio, CI: Confidence interval.

Table 3: Independent risk factors for premature rupture of membranes.

Variables	OR	95%CI	P-value	aOR	95%CI	P-value
1st degree family PROM	15.17	1.83-125.40	0.002	31.36	2.57-382.11	0.007
Fetal weight ≥4000g	8.27	2.24-30.53	<0.001	14.78	2.72-80.20	0.002
Cord round neck	10.05	2.78-36.35	<0.001	6.36	1.17-34.66	0.032
Past history of preterm delivery	2.97	1.42-6.20	0.003	3.42	1.02-11.52	0.047
Parity 4 or 5	1.88	1.01-3.52	0.035	3.27	1.25-8.56	0.016
Cervico-vaginitis	20.01	2.49-160.79	<0.001	8.01	0.60-106.73	0.115
<4 antenatal visits	4.60	2.03-10.43	<0.001	3.22	0.93-11.20	0.065
Malaria in pregnancy	4.37	2.25-8.49	<0.001	2.30	0.84-6.37	0.107
Birth weight <2500 g	3.01	1.16-7.79	0.020	2.09	0.52-8.49	0.301
Past history of PROM	3.64	1.28-10.40	0.013	1.12	0.23-5.55	0.887
Pregnancy followed up by nurses	3.20	1.52-6.78	0.002	1.10	0.30-4.08	0.882

OR: Odds ratio, CI: Confidence interval, aOR: adjusted odds ratio, PROM: premature rupture of membranes.

Discussion

Our rate of PROM was 6.2%. Risk factors for PROM were 1st degree family history of PROM, fetal weight ≥4000g, cord round neck, past history of preterm delivery and parity 4 or 5. We found no association between PROM and maternal age, parity, history of late abortion, number of antenatal visits, non-cephalic presentation, placenta praevia or birth weight <2500 g.

Our PROM rate is within the 5-10% rate found in the literature [2]. PROM occurred mostly at term or post-term in our series (77.6%). This is explained by the fact that fetal membranes resistance decreases with increasing gestational age. First degree family history of PROM was a risk factor for PROM in our study. Fetal membranes resistance is reduced in some families, due to some hereditary connective tissue disorders, as observed in the USA where many inherited gene mutations have been identified [15]. These hereditary disorders also include Marfan and Erler Danlos syndromes [15]. Investigations should be carried out in such families to determine the type of hereditary disorders. Moreover, women from such families should be closely followed up during the third trimester.

Fetal macrosomia was another risk factor. This might be due to uterus overdistension with resultant increased intra-amniotic pressure, leading to PROM. Another explanation is the fact that fetal macrosomia is usually associated with advanced gestational age [16], and therefore with decreased fetal membranes resistance. The combination of these two mechanisms in fetal macrosomia can lead to PROM. Other studies are needed to confirm these findings.

Nuchal cord was another risk factor for PROM in our survey. Nuchal cord can be associated in certain cases with post-term, hence with diminished membranes resistance, given that post-term is a known risk factor for nuchal cord at delivery [17]. More studies are needed to confirm and explain these findings. The adverse perinatal outcome observed with nuchal cord may be favored by PROM.

History of preterm birth was also a risk factor for PROM in our study. Preterm PROM can induce preterm birth as a result of the release of membranous prostaglandins. Some cases of preterm birth are related to incompetent cervix [5]. Indeed, rapidly dilating cervical internal os might lead to protrusion of fetal membranes into the cervical canal, and might favor PROM, as observed in Thailand [2]. This phenomenon might also explain why women of parity 4 and 5 were at risk of PROM in our survey. Indeed, we have observed in our daily practice some multiparous women with the cervix dilated up to 4 cm, without them being in labor.

We also found increased risk of PROM in multiple pregnancies (OR 4.15), even though it was statistically insignificant (P=0.097), attributable to uterus over-distension with increased intra-amniotic pressure. The lack of significance as concerns multiple pregnancies in our study is probably due to our small sample size since we had only six women with multiple gestations.

Cervico-vaginitis is a known risk factor for PROM [18,19]. The enzymes produced by the germs or by monocytes/macrophages of the decidua (leucocyte elastase, matrix metalloproteinases) can lyse the fetal membranes proteins [20], which then rupture without the intra-amniotic pressure being increased. The lack of significance of cervico-vaginitis as a risk factor for PROM in our study (P=0.115) might be due to the fact that the infection was rapidly treated or might be due to our small sample size since we had only 10 women with documented cervical infections.

Our limitations are firstly our small sample size attributed to the Covid-19 pandemic. Indeed, because of fear of being contaminated, only few women attended our hospitals Furthermore, our rate of PROM might be higher than what mentioned given that 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.

Conclusion

PROM was more observed amongst women with 1st degree family history of PROM, fetal weight ≥4000g, cord round neck, history of preterm delivery and parity 4 or 5. Such women should be well followed up during pregnancy, especially during the third trimester, to allow prevention, if not, early diagnosis of PROM

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