



Research Article

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# Outcome of Neonates Born to Mothers with Prolonged Premature Rupture of Membranes Admitted to Neonatal Intensive Care Unit at Omdurman Maternity Hospital



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## Abstract

**Objectives:** This study aims to identify the most common neonatal complications following prolonged premature rupture of membranes (PROM) and the risk factors contributing to them. **Methods:** This cross-sectional study was conducted in the neonatal intensive care unit (NICU) at Omdurman maternity hospital in Sudan between February to August 2017. The population included live born neonates delivered following prolonged PROM after exclusion of other pregnancy related complications and chronic maternal illnesses. The effect of this on the neonates was studied. Also, we studied the association between this effect and many variables in relation to PROM.

**Results:** A total of 216 neonates met the case definition, almost a third of them developed neonatal sepsis and prematurity. There was a significant statistical association between the onset and duration of prolonged PROM with these complications ( $P=0.000$ ). Among the maternal evidence of infection, raised C reactive protein (CRP) and oligohydramnios showed significant statistical association with adverse neonatal outcome. This was not seen with the mode of delivery. Use of antibiotics in the mothers didn't affect the development of neonatal sepsis ( $P=0.289$ ) while use of steroids had significant statistical association with neonatal sepsis ( $P=0.008$ ), prematurity and RDS ( $P=0.000$ ). Death was seen in 7.9% of the cases. Most of them (82.3%) were associated with duration of PROM more than 72 hours.

**Conclusion:** Neonatal sepsis and prematurity were the most common adverse neonatal outcome following prolonged PROM. Different risk factors were identified including timing and duration of PROM, maternal raised CRP and leukocytosis and oligohydramnios. Neonatal mortality was seen more with duration of PROM more than 72 hours. Use of antibiotics in the mothers didn't affect the risk of neonatal sepsis in this study. To find an explanation for that, we recommend further studies to be done including the duration of the use of antibiotics and any delay in administration.

**Keywords:** Neonatal Sepsis, Oligohydramnios, Prematurity, Prolonged Premature Rupture of Membranes, Respiratory Distress Syndrome

**Abbreviations:** PROM: Premature Rupture of Membranes; NICU: Neonatal Intensive Care Unit; CRP: C Reactive Protein; CBC: Complete Blood Count; SPSS: Statistical Package for Social Sciences; WHO: World Health Organization

## Introduction

Normally fetal membranes rupture at the time of delivery, when this happens more than one hour before the delivery, it is called premature rupture of membranes (PROM). [1] This is found in almost 5-10% of pregnancies. [2,3] It is defined as prolonged PROM when it lasts for more than 18-24 hours. [4] According to the timing at onset, it is considered as preterm

PROM when it happens prior to 37 weeks gestation, and this is seen in 3% of pregnancies. [5] Open membranes provide an entry route for bacteria and place the fetus and mother at risk for life-threatening complications. One of these complications is decreasing the amount of fluid surrounding the fetus which affects the development of the fetal lungs early in pregnancy. Also, it can

lead to umbilical cord compression later in pregnancy. [6] While prenatal care has been improved, sever complications among mothers and neonates related to PROM are still seen. [7] About 19/1,000 live births is the neonatal mortality rate as reported by World Health Organization (WHO). [8] Almost 26% of them are due to neonatal sepsis. In developed countries, 1-10/1,000 live births represent the incidence of neonatal sepsis. While in developing countries it has been reported as triple this. [2] One of the significant risk factors for prematurity and sepsis in the neonates is prolonged PROM. Several studies have described both complications as serious and potential complications following prolonged PROM especially if the two happen together. [7] In addition to neonatal morbidity and mortality, PROM is important in the long-term complications in the living neonates. [9] Despite much research, most aspects of prolonged PROM and its effect on the born neonates remain unclear and represent an interesting and clinically relevant subject. To the best of our knowledge there is no study done before in Sudan to assess the outcome of neonates born to mothers following prolonged PROM. This study aims to identify the most associated neonatal complications following prolonged PROM and the risk factors contributing to them.

**Methods**

This study was done in the period of February 2017 to August 2017 in the NICU at Omdurman Maternity Hospital which is the first and largest maternity hospital in Sudan and the first specialized maternity hospital in Africa. Data were collected prospectively from all neonates delivered after a singleton pregnancy complicated by prolonged PROM for more than 24 hours and after exclusion of other pregnancy related complications and chronic maternal illnesses. These data included neonatal characteristics such as gender, gestational age at birth and birth weight. Many adverse neonatal outcomes were studied such as neonatal sepsis, prematurity and respiratory distress syndrome. Neonatal sepsis was identified based on the presence of signs and symptoms consistent with sepsis, positive complete blood count (CBC) and C reactive protein (CRP). Also, we collected data on pregnancy

characteristics (timing and duration of PROM, maternal fever, leukocytosis more than 12,450 x 10<sup>9</sup> /L and raises CRP more than 4,9 mg/dl [10], oligohydramnios and mode of delivery) to find association between these and the adverse neonatal outcome. In addition, we studied the relation between the use of antibiotics and steroids in the mothers after the onset of PROM and the neonatal outcomes. Mothers who presented to the hospital early before delivery received them, while those who presented late did not. All of these data were collected, organized and coded then analyzed using version 20.0 of the Statistical Package for Social sciences (SPSS). For various variables a descriptive analysis was performed. P value is considered significant when it is less than 0.05.

**Results**

During the study period almost 1972 neonates were admitted to the NICU. Of them, 216 (11%) were included in the study as they met the case definition. Table 1 summarizes the characteristics of the included mothers. Almost two thirds of the cases had PROM at 37 weeks gestational age or beyond that, while in 22% the onset was at less than 34 weeks. It lasted for more than 72 hours in 39% of the cases and less than that in 61%. In most of the included neonates (64.8%), PROM did not cause any signs or symptoms of infection in the mothers. Among those who had raised CRP was the commonest (19.4%), followed by leukocytosis (10.6%) and oligohydramnios (8.8%). Antibiotics and steroids were given to the mothers after PROM in 48% and 39% respectively. The characteristics of the born neonates are shown in Table 2. Most of the included neonates were delivered by vaginal delivery (65.3%) and 31% by emergency cesarean section (C/S). Male gender was seen in 54.6%. Birth weight was 2,500 grams or more in 52.8% and only 0.9% had birth weight less than 1,000 grams. Most of the neonates (59.3%) had gestational age of 38 weeks or more at time of delivery and only 4.2% were less than 30 weeks. Regarding the outcome among the born neonates, two thirds had neonatal complications. These associated complications included prematurity (33.7%), neonatal sepsis (33.3%) and RDS (25.5%).

**Table 1:** Characteristics of pregnant mothers.

		Frequency	Percent (%)
Onset of PROM	37 wks. or more	130	60.2
	34 wks. to 36 wks+6 days	38	17.6
	Less than 34 weeks	48	22.2
Duration of PROM	24-48 hrs.	78	36.1
	49-72 hrs.	54	25
	More than 72 hrs.	84	38.9
Evidence of maternal infection	Not present	140	64.8
	Fever	5	2.3
	Abdominal tenderness	1	0.5
	Foul smelling liquor	13	6
	Oligohydramnios	19	8.8
	Raised CRP	42	19.4
	Leukocytosis	23	10.6

Use of antibiotics	Yes	104	48.1
	No	112	51.9
Use of steroids	Yes	84	38.9
	No	132	61.1
Mode of delivery	Elective C/S	7	3.2
	Emergency C/S	67	31
	Vaginal delivery	141	65.3
	Instrumental	1	0.5

**Table 2:** Characteristics of the born neonates and their complications.

		Frequency	Percent (%)
Gender	Male	118	54.6
	Female	97	44.9
	Unidentified gender (ambiguous genitalia)	1	0.5
Gestational age at birth	38 weeks or more	128	59.3
	34-37 weeks	41	19
	30-33 weeks	38	17.6
	< 30 weeks	9	4.2
Birth weight	2,500 g or more	114	52.8
	2,499 – 1,500 g	76	35.2
	1,499 -1,000 g	24	11.1
	< 1,000 g	2	0.9
Associated neonatal Complications	None	85	39.4
	Prematurity	73	33.7
	Neonatal sepsis	72	33.3
	Respiratory distress	55	25.5
	Birth asphyxia	10	4.6

Different risk factors were identified for these associated neonatal complications as shown in Table 3. Of all the neonates with sepsis (72 cases), in 31 cases PROM occurred at 37 weeks gestational age or beyond and in 23 cases at less than 34 weeks. Respiratory distress increased from 11 cases in term PROM to 12 and 32 cases when PROM occurred at 34-36 weeks + 6 days and less than that respectively. Frequency of absence of complications decreased with earlier PROM. Of all neonates without complications (85 cases), in 78 of them PROM occurred at term. All neonates with PROM less than 34 weeks developed complications. The frequency of neonatal sepsis increased from 11 cases when PROM lasted 24-48 hours to 12 cases in 49-72 hours and 49 cases in more than 72 hours. The reverse was seen in the absence of complications, where 47 cases of the neonates did not develop complications when PROM lasted 24-48 hours compared to 11 cases when it lasted more than 72 hours (P=0.000). There was no significant

statistical association between mode of delivery with presence or absence of neonatal complications (P=0.644). Some of the maternal evidence of infection following PROM had significant statistical association with some of the associated neonatal complications. Raised maternal CRP with neonatal sepsis (P=0.029), respiratory distress (P=0.013) and prematurity (P=0.001). Also, maternal leukocytosis had significant statistical association with neonatal respiratory distress (P=0.009) and prematurity (P=0.027) but not with neonatal sepsis (P=0.755). Significant statistical association was seen also between maternal oligohydramnios with neonatal sepsis (P=0.000), prematurity (P=0.002) and respiratory distress (P=0.004). Maternal fever had no significant statistical association with any of the adverse neonatal outcomes. Antenatal antibiotics had significant statistical association with neonatal sepsis (P=0.289) or with lack of complications in the neonates (P=0.123). On the other hand, antenatal steroid administration

had significant statistical association with respiratory distress (P=0.000), prematurity (P=0.000). About 90% of the cases were discharged from the NICU. Death was reported in 7.9%. Most of the deaths (82.3%) were associated with PROM lasting more than 72 hours (P=0.010, Table 4).

**Table 3:** Relation between neonatal complications and pregnancy characteristics.

Risk factor		Neonatal complications			
		Non	sepsis	Prematurity	RDS
Onset of PROM	37 wks. or more	78	31	0	11
	34 wks. to 36 wks+6 days	7	18	25	12
	Less than 34 wks.	0	23	48	32
	Total	85	72	73	55
	P value	0	0.001	0	0
Duration of PROM	24-48 hrs.	47	11	9	10
	49-72 hrs.	27	12	15	8
	More than 72 hrs.	11	49	49	37
	Total	85	72	73	55
	P value	0	0	0	0
Mode of delivery	Elective C/S	4	2	0	0
	Emergency C/S	27	25	18	18
	Vaginal delivery	54	44	56	37
	Instrumental	0	1	0	0
	Total	85	72	73	55
	P value	0.644	0.418	0.05	0.42
Asymptomatic mothers	No symptoms or signs	61	42	36	27
	Presence of symptoms or sign	24	30	37	28
	Total	85	72	73	55
	P value	0.085	0.158	0	0.01
Maternal fever	Present	2	1	0	1
	Not present	83	71	73	54
	Total	85	72	73	55
	P value	0.976	0.522	0.46	0.19
Maternal leukocytosis	Present	8	7	11	11
	Not present	77	65	62	44
	Total	85	72	73	55
	P value	0.635	0.755	0.027	0.01
Maternal raised CRP	Present	12	20	22	17
	Not present	73	52	51	38
	Total	85	72	73	55
	P value	0.111	0.029	0.001	0.01
Oligohydramnios	Present	1	14	11	10
	Not present	84	58	62	45
	Total	85	72	73	55
	P value	0.001	0	0.002	0

Antibiotics after PROM	Used	35	38	49	33
	Not used	50	34	24	22
	Total	85	72	73	55
	P value	0.123	0.289	0	0.03
Steroids after PROM	Used	20	37	52	37
	Not used	65	35	21	18
	Total	85	72	73	55
	P value	0	0.008	0	0

**Table 4:** Outcome of neonates and its relationship with duration of PROM.

P-value = 0.010*			Duration of PROM in hours			Total
			24-48	49-72	72	
Outcome of neonate	Discharged	Count	75	53	68	196
		% of Total	34.70%	24.50%	31.50%	90.70%
	Referred to other hospital	Count	1	0	2	3
		% of Total	0.50%	0.00%	0.90%	1.40%
	Death	Count	2	1	14	17
		% of Total	0.90%	0.50%	6.50%	7.90%
Total		Count	78	54	84	216
		% of Total	36.10%	25.00%	38.90%	100.00%

## Discussion

In this study we found that two thirds of the born neonates following prolonged PROM had neonatal morbidities, while 39.4% did not develop any complications. The commonly observed associated complications were prematurity (33.7%), neonatal sepsis (33.3%), and respiratory distress syndrome (25.5%). This was similar to the finding reported by Adetunju O and Oluseyi O in a study done in Nigeria where they found prematurity in 30% and neonatal sepsis in 42.7%. [11] In India a similar study was done by Manjul Vijay, Tejaswi Nandan and Binay Ranjan and found that 48% of the neonates had complications. The most common of them were respiratory distress syndrome (36%) and septicemia (8%). [12] This difference could be explained by the small sample size (50 neonates) in their study and inclusion of cases with shorter duration of PROM (18-24 hours). In Iran higher frequencies of complications were reported in a study done by Boskabadi H, Zakeri Hamidi and others. The commonest was prematurity (73%), followed by neonatal infection (52%), respiratory distress (30.4%) and asphyxia (17%). [13] These higher reported frequencies of neonatal complications in Iran may be due to the higher cases of maternal complications and the high frequency of neonates delivered at 32-37 weeks (54.2%); in our study most of the neonates (52.8%) when delivered had gestational age of 38 weeks or more.

A significant statistical association was found between timing of PROM with neonatal prematurity (P=0.000), respiratory distress (P=0.000), neonatal sepsis (P=0.001) and with absence of neonatal complications (P=0.000). The same was reported in the study published in American Journal of Obstetrics and Gynecology. In it higher rates of neonatal sepsis (15% vs. 6.1%, P <0.001) and respiratory distress (0.6 vs. 0.002, P=0.001) were reported in neonates with late PPRM compared to term PROM group. [14] Also, Priscilla Frenette and Linda Dodds reported higher rates of neonatal infection in the group of early PPRM (11.1%) compared to late PPRM (1.9%). [15] All these studies support the fact from literature review that the earlier the onset of PROM the higher the risk for neonatal morbidity. [5] Also, duration of PROM showed significant statistical association with neonatal sepsis, respiratory distress, prematurity and with absence of complications in the neonates (P=0.000 in all). Muhammad Matloob, Ali Faisal saleem and others in Pakistan reported an association between neonatal sepsis and duration of PROM (P = <0.001). [2] However, they did not study the change in the frequencies of RDS and prematurity with different durations of PROM. Unlike our study, Manjul Vijay found significant statistical association between duration of PROM with neonatal sepsis only (P <0.001) but not with RDS. [12] This difference may be due to the differences in the reported frequencies of these complications between the



two studies. On the other hand, there was no observed increase in the odds of neonatal infection following any of the duration of PROM at or more than 24 hours compared to less than 24 hours in the Canadian study. [15] This could be explained by the small percentage of reported neonatal infection in the Canadian study that may fail to demonstrate a difference.

We identified a significant statistical association between some of the maternal evidence of infection and neonatal complications. Maternal raised CRP and oligohydramnios had significant statistical association with neonatal sepsis, respiratory distress and prematurity. Also, a significant statistical association was seen between maternal leukocytosis with respiratory distress ( $P=0.009$ ) and prematurity ( $P=0.027$ ), but not with neonatal sepsis ( $P=0.755$ ). On the other hand, maternal fever did not have significant statistical association with any neonatal complications. However, in Pakistan they reported a significant statistical association of neonatal sepsis with maternal fever and chorioamnionitis ( $P < 0.001$ ). [2] This may be due to the high incidence of maternal fever (17%) in their study compared to only 2.3% in our study. They did not report any other maternal evidence of infection. In our study, of all neonates with sepsis (72 cases), about 20 cases (27.7%) were born to mothers with raised CRP, 14 cases (19.4%) had oligohydramnios and seven cases (9.7%) with leukocytosis. In Nigeria, 80% of neonates with infection were born to mothers with chorioamnionitis. 11 No significant statistical association was found between mode of delivery with presence or absence of neonatal complications. The same also was reported in Iran. [13] Regarding the outcome of neonates, death was seen in 7.9% of our cases. Most of these deaths (82.3%) were associated with duration of PROM more than 72 hours compared to 24-48 hours (11.4%,  $P=0.010$ ). A study done at Guru Gobind Singh Hospital in India, reported a lower incidence of death (2.9%) among neonates born after prolonged PROM. [16] This could be explained by the lower incidence of reported neonatal complications. In Pakistan, it was reported that, almost all neonates who died following PROM were premature with duration of PROM more than 48 hours. [2]

## Conclusion

Prolonged PROM is a common problem among pregnant women and a big challenge for neonatologist. It can cause different neonatal morbidities and mortality. This study found that neonatal prematurity and sepsis were the most associated neonatal complications following prolonged PROM. Different risk factors for these complications were identified including onset of PROM and its duration, maternal raised CRP and leukocytosis and oligohydramnios. We found that antenatal antibiotics use did not show significant statistical association with neonatal sepsis. Most of the neonates who died had duration of PROM more than 72 hours. We recommend early identification, monitoring and management of pregnant mothers with prolonged PROM to

improve the outcome of the born neonates. Further studies are recommended to study the long-term effect of prolonged PROM on the surviving neonates.

## Ethical approval

The research was accepted and approved by the Sudan Medical Specialization Board's ethics committee.

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