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ORIGINAL ARTICLE

MATERNAL AND PERINATAL OUTCOME OF PREGNANCIES WITH PRETERM PREMATURE RUPTURE OF MEMBRANES (PPROM) AT TIKUR ANBESSA SPECIALIZED TEACHING HOSPITAL, ADDIS ABABA, ETHIOPIA

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ABSTRACT

Introduction*: Preterm premature rupture of membranes is a common complication of pregnancy associated with significant maternal, fetal and neonatal risks. An understanding of its magnitude and consequences is critical in providing appropriate intervention to prevent poor pregnancy outcomes.*

Objective: *To describe maternal and perinatal outcomes of preterm premature rupture of membranes at Tikur Anbessa Hospital, Addis Ababa, Ethiopia.*

Methodology*: A Retrospective cross-sectional descriptive study done at Tikur Anbessa Hospital from June, 2010 G.C. to June, 2013 G.C.*

Results: *The prevalence of preterm premature rupture of membranes in this study was 1.4%. Intra-amniotic infection, seen in 31.5% (35/111), was the commonest maternal complication. The mean latency period from rupture of membranes to delivery was 6.6 days. Twenty-six (23.2%) neonates were delivered by cesarean section. There were a total of 12 perinatal deaths, 4 (3.6%) stillbirths (2 antepartum and 2 itrapartum) and 8 (7.1%) early neonatal deaths, making the gross perinatal mortality rate to be 107 per 1000 live births. Prematurity was the commonest cause of neonatal death.*

Conclusion and recommendations*: Although the prevalence of preterm premature rupture of membranes in this study appears lower than many prior reports, the level of maternal and perinatal morbidity is high compared to many prior reports from similar setups. Especially the proportion of mothers presenting with established chorioamnionitis is high. Therefore, it is important that women be well informed regarding maternal, fetal and neonatal complications of premature rupture of membranes so that proper and timely management is provided.*

Key words: *PROM, Pre-term PROM, PPROM, Chorioamnionitis*

INTRODUCTION

Premature rupture of membranes (PROM) is defined as spontaneous rupture of membrane before onset of labor. Membrane rupture that occurs between the gestational ages (GA) of 28 and 37 completed weeks is referred to as preterm PROM (PPROM). PPROM occurs in 1%–3% of all pregnancies and is responsible for approximately one third of all preterm births (1-3). Latency period, the time from membrane rupture until delivery, is inversely correlated with the gestational age at membrane rupture. Regardless of management or clinical presentation, birth within 1 week is the most likely outcome of any patient with PPROM. A review of 13 randomized trials reported that approximately 75% of patients with preterm PROM who were managed expectantly delivered within 1 week (4).

PPROM is associated with significantly increased risk of maternal, fetal and neonatal morbidity and mortality resulting from associated complications. Among women with preterm PROM, clinically evident intraamniotic infection occurs in approximately 15–25% (5). Abruptio placentae can cause PROM or occur subsequent to membrane rupture and affects 4% to 12% of these pregnancies (6). The frequency and severity of neonatal complications after PROM vary inversely with gestational age at membrane rupture and at delivery. The rates of these complications are higher in the setting of chorioamnionitis (7).

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Management of PROM is primarily dependent on gestational age and the presence of complicating factors. It requires evaluation of the risks and benefits of expectant management or expeditious delivery. In expectant management of PPROM adjuvant antibiotic and corticosteroid therapy are widely shown to reduce GA–dependent and infectious complications significantly improving perinatal outcome. A Cochrane review of 22 placebo-controlled randomized trials involving 6800 women showed the benefits of using antibiotics following PPROM (5). According to the review; the use of antibiotics was associated with a statistically significant reduction in chorioamnionitis (RR 0.57, 95%; CI 0.37 to 0.86) and neonatal infections (RR 0.68, 95% CI 0.53 to 0.87). There was a reduction in the numbers of babies born within 48 hours (RR 0.71, 95% CI 0.58 to 0.87) and seven days of rupture of membrane (RR 0.80, 95% CI 0.71 to 0.90). In addition, a meta-analysis regarding antenatal corticosteroid administration after PPROM has confirmed steroid therapy to significantly reduce the risks for Respiratory Distress Syndrome (RDS) (20% versus 35.4%), Intra Ventricular Hemorrhage (IVH) (7.5% versus 15.9%), and necrotizing enterocolitis (0.8% versus 4.6%) (8).

Understanding the magnitude and consequences of Preterm PROM is vital in providing appropriate intervention to prevent poor pregnancy outcomes. Information regarding PPROM in Ethiopian setup, however, is very limited. The 2011 Ethiopia Demographic and Health Survey (EDHS) revealed complications of preterm birth, intrapartum related events, and sepsis and meningitis to be the leading causes of neonatal deaths in the country. The survey also showed that only about one-fifth (22 percent) of pregnant women were informed of vaginal gush or fluid as signs of pregnancy complications during their ante natal care (ANC) follow up (9).

This study was conducted at Tikur Anbessa Specialized Teaching Hospital where PPROM is managed following a management protocol prepared based on the current global recommendations and practice. According to the management protocol, all pregnant women with PPROM are admitted either for expectant management or immediate delivery. The study is designed primarily to give a baseline description of perinatal and maternal outcomes of PPROM cases.

SUBJECTS AND METHODS

This is a hospital based retrospective cross sectional descriptive study done from June, 2010 G.C. to June, 2013 G.C. at Tikur Anbessa Hospital (TAH), a specialized central referral Hospital, Addis Ababa, Ethiopia. All mothers admitted to the Hospital with a diagnosis of PPROM during the study period were included. Their medical record numbers (MRN) identified from admission log books in the maternity ward and neonatal intensive care unit (ICU) were used to retrieve medical records/charts. Data was collected by the investigator using a pre-tested questionnaire from medical records of the study participants. Data was cleared prior to entry and data analysis was made using SPSS version 20.0 soft ware. Summary tables and charts were used for describing data.

Ethical clearance was obtained from the research and publication committee of the department of Obstetrics & Gynecology and IRB of Addis Ababa University. Permission was also obtained from the Hospital to access the medical records of mothers included in the study.

RESULT

During the three years study period, a total of 8,283 mothers delivered in the study hospital. A total of 111 mothers (1 twin) had pregnancies complicated with Preterm PROM and gave birth to 112 neonates. The overall prevalence of Preterm PROM was 1.4% (111 / 8,283). The age of the study subjects ranged from 15-to-39 years while the mean age was 26.31 years. Majority were married, housewives, and from outside of Addis Ababa with proportions of 96.4% (107/111), 67% (75/111) and 82% (91/111) respectively. (Table-1)

Table 1: Socio demographic characteristics of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 G.C. (n=111)

Characteristics		Frequency	Percentage (n=111)
Age	15-19	4	3.6%
	20-24	36	32.4%
	25-29	37	33.3%
	30-34	24	21.6%
	35-39	10	9%
	≥ 40	0	-
Address	Addis Ababa	91	82%
	Out of Addis Ababa	20	18%
Marital Status	Married	107	96.4%
	Single	4	3.6%
Occupation	House Wife	75	67.6%
	Governmental Employee	17	15.3%
	Private Employee	7	6.3%
	Student	6	5.4%
	Daily Laborer	4	3.6%
	Others	2	1.8%

Fifty three percent (59/111) were nulliparous. All except one (110/111) had ANC follow up. Health centers and Tikur Anbessa Hospital were the sites of ANC follow up for 54.5% (60/111) and 24.5% (27/111) of the mothers respectively. Information on danger signs of pregnancy was given to 81.8% (90/111) of the mothers during their ANC follow up. The mean gestational age at ROM was 33.83 weeks (SD of 2.4).

The ROM occurred at less than 34 weeks in 41.4% (46/111), and between 34 and 37 weeks in 58.6% (65/111) of the mothers. Fetal presentation at the time of admission was cephalic, breech and shoulder in 80.4% (90/112), 14.3% (16/112) and 5.4% (6/112) of the fetuses respectively. (See Table-2 below)

Prophylactic antibiotics were administered to 84 % (93/111) of the mothers. In addition, dexamethasone was administered in 87 % (40/46) of the mothers with ROM at less than 34 weeks. There was no documented use of tocolysis in the study group.

Time of Delivery: The mean gestational age at delivery was 34.57 weeks (SD of 2.2). Majority, 61.3% (68/111), gave birth at gestational age of ≥34 weeks but <37 weeks. The mean latency period from PROM to onset of labor was 6.6 days with a median of 3.0 and range of 1-65 days. Twenty four percent (27/112) of the neonates were born within the first day while 46.4% (52/112) were born with in the first week of rupture of membrane. One case of PPROM was admitted at GA of 29 weeks with GA at ROM of 27 weeks. She ultimately delivered at 37 weeks, after a latency period of 65 days, by Cesarean Section (C/S) for failed induction with an outcome of a female neonate weighing 2,880 grams and APGAR score of 8 and 9 in the first and fifth minutes. Excluding this outlier case; the mean, median and range of the latency period becomes 6.08, 3 (SD of 8.01 days) and 1-47 days respectively.

Mode of Delivery: Labor started spontaneously in 58.5% (65/111) of the mothers. Pregnancy was terminated by induction in 30.6% (34/111) and cesarean section before onset of labor in 10.8% (12/111). Indications for termination of pregnancy were chorioamnionitis, anticipated fetal lung maturity because of GA considered to be near term, confirmed lung maturity by amniocentesis and NRBPP in 54.3% (25/46), 21.7% (10/46), 17.4% (8/46) and 6.5% (3/46) respectively. The cesarean section delivery rate in the study group was 23.2% (26/112). Failed induction, chorioamnionitis with breech presentation and chorioamnionitis with previous caesarian scar were the main indications for C/S each accounting for 19.2% (5/26), 19.2% (5/26) and 15.3% (4/26) of cesarean deliveries respectively. The other indications include; shoulder presentation, footling breech, non reassuring biophysical profile (NRBPP), non reassuring fetal heart rate pattern (NRFHRP) and prolonged latent stage of labor with breech presentation in 11.5% (3/26), 11.5% (3/26), 11.5% (3/26), 7.7% (2/26) and 3.8% (1/26) of the cesarean deliveries respectively. (Table -3)

Table 2: Obstetric characteristics of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 G.C. (n=111)

Characteristics	Frequency	Percentage, %
Parity (n=111)		
Nuliparous	59	53.2
Multiparous	52	46.8
GA at rupture of membrane (n=111)		
< 34weeks	46	41.4
≥ 34weeks	65	58.6
ANC follow up (n=111)		
Yes		
At health centre	60	54.1
At Tikur Anbessa Hospital	27	24.3
At private facility	15	13.5
Other governmental hospital	8	7.2
Sub total	110	99.1
No	1	0.9
Type of pregnancy (n=111)		
Singleton	110	99.1
Twin	1	0.9
Fetal presentation (n=112)		
Cephalic	90	80.4
Breech	16	14.3
Shoulder	6	5.4

Maternal Morbidity: Clinical chorioamnionitis, seen in 31.5% (35/111) of the mothers, was the commonest maternal complication. Twenty five (22.5%) mothers presented with clinical chorioamnionitis, while additional 10 (9%) developed chorioamnionitis after admission. Puerperal endomyometritis, superficial abdominal wound infection and sepsis occurred in 13.5% (15/111), 4.5% (5/111) and 2.7% (3/111) of cases. There were no reported cases of maternal mortality or long term morbidity.

A multivariate binary logistic regression analysis showed statistical significant association between prophylactic antibiotic administration and Chorioamnionitis. Those who were not given prophylactic antibiotic had 339 times increased risk of developing chorioamnionitis (AOR 339.73 (95% CI: 31.09-3712.46). (Tables 3and 4)

Table 3: Maternal outcome of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 G.C.

Characteristics	Frequency	Percentage (%)
Gestational age at delivery (n=111)		
≥ 28 weeks and < 34 weeks	37	33.3
≥ 34 weeks and < 37 weeks	68	61.3
≥ 37 weeks	6	5.4
Mode of delivery (n=112)		
Vaginal	86	76.8
Cesarean section	26	23.2
Indication for cesarean section (n=26)		
Failed induction	5	19.2
Chorioamnionitis with breech presentation	5	19.2
Chorioamnionitis with previous C/S	4	15.3
Shoulder presentation in labor	3	11.5
Footling breech	3	11.5
Non reassuring biophysical profile (NRBPP)	3	11.5
Non reassuring fetal heart rate pattern (NRFHRP)	2	7.7
Prolonged latent stage of labor with breech presentation	1	3.8
Maternal morbidity (n=111)		
Clinical chorioamnionitis	35	31.5
Puerperal endomyometritis	5	4.5
Sepsis	3	2.7

Perinatal Outcome: A total of 112 neonates, 57 (50.9%) males and 55 (49.1%) females, were born. The mean birth weight of the neonates was 2,315 grams (SD of 558.5). Fifty percent (56/112) weighed 1500 - 2500 grams while 39.3% (44/112), 8% (9/112) and 2.7% (3/112) weighed >2500 grams, 1000 - 1499 grams and < 1000 grams respectively. The APGAR score at the first and fifth minutes was less than seven in 23.2% (26/112) and 5.4% (6/112) of the neonates respectively. The rate of admission to neonatal ICU was 48.2% (54/112). There were a total of 12 perinatal deaths out of the 112 births; 4 being stillbirths (2 antepartum and 2 intrapartum) and 8 early neonatal deaths. The gross perinatal mortality rate, hence, was 107 per 1000 live births. Most of the perinatal deaths had birth weight of <2500grams and GA at ROM of <34 weeks with proportions of 92% (11/12) and 75% (9/12) respectively. (Table -5).

Prematurity was the commonest stated reason for the perinatal mortality accounting for 66.7% (8/12) of perinatal deaths. Other stated causes include congenital anomaly, birth asphyxia and intra uterine growth restriction (IUGR) accounting for 16.7% (2/12), 8.3% (1/12) and 8.3% (1/12) respectively. A multivariate binary logistic regression analysis showed statistical significant association between GA at rupture of membrane and APGAR score at five minutes, and perinatal outcome. Rupture of membrane at <34 weeks of gestation had five times higher risk of being dead on discharge from the hospital AOR 5.03 (95% CI: 1.28-19.76). APGAR score of <7 was also seen to have seventy times higher risk of being dead on discharge from the hospital AOR 70.00 (95% CI: 7.16- 684.24).

Table 4: Multivariate binary logistic regression analysis of Selected Variables with Chorioamnionitis of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 G.C.

Selected Variables		Chorioamnionitis no	yes	AOR	95% CI
GA <34 and GA >=34	<34 weeks	27	20	2.99	.72-18.43
	>= 34 weeks	50	15		
Administration of Prophylactic Antibiotics to the	yes	74	19	339.73	**31.09-3712.46****
	no	2	16		
Corticosteroid administration to the Mother	yes	24	16	8.55	**1.42-51.45****
	no	52	19		
Onset of Labor	Spontaneous	54	13		
	Induced	18	15	7.98	**1.73-36.82****

AOR= Adjusted Odds Ratio, CI= Confidence Interval, **Statistically Significant Adjusted for Gestational Age, Informed about danger sign, Marital Status, and Address of the Mother

Table 5: Perinatal outcome of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 G.C. (n=112)

Characteristics	Frequency	Percentage (%) n=112
Sex		
Male	37	33.3
Female	6	5.4
Birth weight in grams		
<1,000	3	2.7
1,000 – 1,499	9	8.0
1,500 – 2,499	56	50
³ 2,500	44	39.3
APGAR score		
First minute		
< 7	26	23.2
³ 7	86	76.8
Fifth minute		
< 7	6	5.4
³ 7	106	94.6
NICU admission		
Yes	54	48.2
No	58	51.8
Perinatal outcome		
Still born	4	3.6
Early neonatal death	8	7.1
Alive on discharge	100	89.3

DISCUSSION

Preterm PROM, occurring globally in 1%–3% of all pregnancies, is associated with significant maternal, fetal and neonatal risks. The 1.4% prevalence of PPROM in this study is generally with in the global range. However, it is significantly lower than reported prevalences from similar developing countries including that of Nigeria and Pakistan with reported prevalences of 3.3% and 16% respectively (10, 11). Compared to prior local reports, it is higher than the prevalence of 0.9% in the study done at three teaching hospitals TAH, St Paul's Hospital (SPH) and Gandhi Memorial Hospital (GMH) in the year 2007 (12). It, however, is lower than the reported prevalence in the study at SPH and TAH which are 7.5% of women age <35yrs and 12.6% of women age>/=35yrs in a period of 21 months (13). The local reported prevalence of PPROM appears widely variable despite similar study methodology and setup.

There is currently no effective way of preventing most preterm PROMs as it is mostly unpredictable. However, its early and accurate diagnosis would allow for gestational age–specific obstetric interventions designed to optimize maternal and perinatal outcome, and minimize serious complications (3). It is therefore important that all pregnant women be well informed regarding maternal, fetal and neonatal complications, and the need to immediately seek medical care when it occurs. In our study; although nearly all the study mothers had ANC follow-up, only 81.8% (90/111) were told about danger signs of pregnancy during their follow up. This finding still is much higher than the national reported figure of only 22 percent (2011 EDHS) (7). This could be due to the fact that this study was done at a tertiary university hospital where most of the clients are from Addis Ababa with better access to ANC and information.

The management of pregnancies complicated with preterm PROM, is individualized, highly controversial and challenging. Administration of adjunctive prophylactic antibiotics is one of the interventions known to improve obstetric outcome. The goal of antibiotic therapy is to reduce the frequency of maternal and fetal infection and delay the onset of preterm labor (ie, prolong latency period). The mean latency period from PPROM to delivery in our study was 6.6 days, and 46.8% of the neonates were born within the first week of rupture of membrane. This latency period in this study is better than a previously reported latency period in a review of 13 randomized trials involving PPROM cases managed expectantly where 75% of patients delivered within 1 week (14).

The risk of clinically evident infection is significant following PPROM. Intraamniotic infection was the commonest maternal complication of PPROM in this study. The infection rate of 31.5% (35/111) was comparable to the reported prevalence of 32.7% in the study done in the same set up in 2007 but much higher than the infection rate of 13.9 percent reported in the Nigerian study (10, 12). This high level of maternal morbidity could be due to significant number of mothers in this study who came to the study hospitals with already established chorioamnionitis 22.5% (25/111). Many of these cases could have been prevented had they come to the facility earlier as soon as ROM occurs.

Caesarean section rate was 23.2 % for this study. This is comparable to a rate of 23.1% reported in the study done in the three teaching hospitals TAH, SPH and GMH but higher than the 14% rate reported in Ayub medical college, Abbottabad, Pakistan (11).

The most significant risks to the fetus after preterm PROM are complications of prematurity. Similarly, the most common complication of PROM related to perinatal outcome in this study was prematurity and its side effect. The perinatal mortality rate of 98.2 per 1000 births in this study, as a result, is more than twice higher than the national overall perinatal mortality rate of 46 per 1,000 pregnancies reported in DHS-2011 (7). The finding, however, is comparable to reported perinatal mortality rate of 89/1000 in the Nigerian study and reported rate of 105/1000 in other prior studies (10, 15).

The major limitation of this study was the restriction of the study population to a central referral hospital with a selected group of women. In addition, it is a small scale retrospective study and it was not possible to assess risk factors associated with PPROM because of incomplete information in the medical records. Hence the findings of this study may not reflect the true situation in the general population and should be interpreted with caution. Despite the limitations, this study has provided baseline information on PPROM in our setup and is a stepping stone towards further research on PPROM among Ethiopian women.

Conclusion and Recommendation: Although the prevalence of PPROM in this study appears lower than many prior reports, the level of maternal and

perinatal morbidity is high compared to reports from similar setups. Intraamniotic infection and prematurity with its side effects were the commonest maternal and perinatal complications of PPROM respectively in this study. The proportion of mothers presenting with established chorioamnionitis was high contributing to the high intraamniotic infection rate. It is, therefore, important that all pregnant women be well informed regarding potential complications of PPROM during their ANC follow to avoid delay in presentation. The practice of antibiotic administration during management of Preterm PROM should be encouraged as significant reduction in chorioamnionitis was seen in agreement with most other prior studies.

To obtain more representative information on PPROM among Ethiopian women and come up with more reliable recommendations further large scale prospective research is recommended.

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