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PREVALENCE OF PRETERM PREMATURE RUPTURE OF MEMBRANE AND ASSOCIATED FACTORS AMONG PREGNANT WOMEN ADMITTED IN HIWOT FANA COMPREHENSIVE SPECIALIZED UNIVERSITY HOSPITAL, EASTERN ETHIOPIA

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ABSTRACT

BACKGROUND: Preterm premature rupture of membrane (PPROM) affects approximately 3% of all pregnancies and is responsible for one-third of all preterm births. Despite its contribution to maternal and neonatal mortality and morbidity, evidence on the burden of PPRM and its associated factors in the study area is scarce. Therefore, this study was aimed to assess the prevalence and associated factors of PPRM among preterm pregnancies managed from May 2019 to September 2020 at Hiwot Fana Comprehensive Specialized University Hospital University Hospital, Eastern Ethiopia.

METHODS: A hospital-based retrospective cross-sectional study was conducted among 449 preterm pregnancies selected by systematic random sampling technique. Data related to socio-demographic variables, obstetric and reproductive health conditions, and labor and related pregnancy outcomes were extracted from their medical records using a structured checklist. Factors associated with PPRM were identified using bivariable and multivariable logistic regression. Association was presented using an adjusted odds ratio (AOR) along with 95% confidence interval (CI). P-value <0.05 in the final model was considered as statistically significant.

RESULTS: Of 449 preterm pregnant women included in the study, 64 (14.3%; 95% CI:11.1% -17.5%) had PPRM. Preterm PROM was significantly associated with urinary tract infections (AOR=6.33; 95% CI:3.26-12.29), vaginal bleeding (AOR=2.62; 95% CI:1.23-5.57), history of abortion (AOR= 3.07; 95% CI:1.33-7.06) and mid upper arm circumference <23 (AOR=7.06; 95% CI: 4.02-12.43). A total of 3 (4.3%) stillbirth and 16 (22.9%) early neonatal deaths occurred corresponding with a gross perinatal mortality rate of 271 per 1000 births.

CONCLUSION: This study showed that one in seven preterm pregnancies in eastern Ethiopia had PPRM. Urinary tract infection, vaginal bleeding, previous history of abortion, and undernutrition were associated with PPRM. Early screening and treatment of urinary tract infections and nutritional assessments are essential to reduce the risk of PPRM.

KEYWORDS: Associated factors, Eastern Ethiopia, Preterm, Premature Rupture of Membrane

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INTRODUCTION

Premature rupture of the membrane (PROM) is the rupture of fetal membranes before the onset of labor and it can occur as preterm PROM or term PROM¹. Preterm premature rupture of membrane (PPROM) is the spontaneous rupture of the amniotic membrane with a release of amniotic fluid before the onset of labor before 37 weeks of gestation². The incidence of PROM ranges from 5% to 10% of all pregnancies worldwide². The prevalence of PROM varies widely in different countries and it ranges from 6.3% to 13.8% in African populations³⁻⁶. Preterm PROM affects approximately 3% of all pregnancies and is responsible for one-third of all preterm births^{2,7,8}. Although PPRM occurs both in developed and developing countries, its prevalence is high in African and Asian countries. The prevalence of PPRM accounts for 3.1% in Brazil⁹, 2.2% in India¹⁰, 3.3% in Nigeria¹¹, and it ranges from 6.6% to 13.7% in Ethiopia^{12,13}.

Although the causes of PPRM are complex and multifactorial¹⁴⁻¹⁶, intrauterine infection has been implicated as a major etiological factor in the pathogenesis and subsequent complications¹⁷. Moreover, PPRM will end up in preterm birth, becoming one of the leading causes of perinatal morbidity and mortality with severe subsequent problems^{7,18}. Studies showed that history of PPRM increased the risk of recurrent PPRM and preterm delivery by 20 and four-folds, respectively¹⁹. In addition, preterm infants may be vulnerable to a variety of problems including respiratory distress syndrome, hyaline membrane disease, intraventricular hemorrhage, periventricular leukomalacia, neurologic impairment, bacterial infection, and necrotizing enterocolitis²⁰. Given the fact that preterm babies have higher risk of death from prematurity or bacterial infection as a result of the ruptured membrane, and there is increased maternal risks and infections, assessing burden of PPRM and identifying associated factors is essential for designing appropriate interventions^{2,21}.

Burden of PPRM ranges from maternal and neonatal mortality and morbidity to national economic loss due to drug expense, hospitalization, absence from the workplace, and expense to the health professionals²¹. Despite its contribution to maternal and neonatal mortality and morbidity, very few studies have addressed PPRM and its associated management and related pregnancy outcomes in Ethiopia. Therefore, this study was conducted to assess the prevalence and associated factors of PPRM among all preterm pregnancies managed in Hiwot Fana Comprehensive Specialized University Hospital, Eastern Ethiopia.

MATERIAL AND METHODS

Study design, and area

A hospital based retrospective cross-sectional study was conducted at the department of obstetrics of Hiwot Fana Comprehensive Specialized University Hospital (HFCSUH). Hiwot Fana Comprehensive Specialized University Hospital is a tertiary academic center of Haramaya University found in Harar town serving as a comprehensive referral center for more than 5.8 million population in eastern Ethiopia. As a comprehensive hospital, it plays a major role in providing teaching, research, and community service, including a well-established neonatal intensive care unit. During the study period, the department was run by 14 consultants, 28 residents, and 33 midwives.

Study participants

In this retrospective study, all preterm pregnant women who were admitted from May 2019 to September 2020 were included. On the other hand, all preterm pregnancies with incomplete data, and unknown weeks of gestation were excluded from the study.

Sample size determination and sampling technique

Double population proportion formula was used and sample size was determined using Epi Info version 7 stat Cal by considering the proportion of women with a history of urinary tract infection (UTI) in pregnancy than those who did not have UTI (AOR = 2.62, 95% CI = 1.32-5.19), in a previous

study done in Debre Tabor General Hospital¹³ and the following assumptions was considered: 95% confidence level, 80% power, 1:1 ratio and 15% non-response rate. The final minimum required sample size was determined to be 449. A total of 1346 preterm deliveries were identified during the admission period (from May 2019 to September 2020) and 449 participants were selected using systematic random sampling technique. When the total population for the admission period (1346) was divided by the sample size (449), the sample interval (K) was found 3. The first study participant was selected randomly between one and K using the lottery method, and the next subject was selected in accordance with K value until the sample size was reached.

Data collection methods

Data was collected using pretested structured data extraction checklist by trained senior midwives and two resident doctors under the supervision of a senior resident. The data extraction checklist was developed after reviewing relevant literature and contextualized to fit the research objective. The checklist was designed to obtain data related to socio-demographic variables (maternal age, marital status, residence, occupation, and educational status), obstetric variables (prenatal care, vaginal bleeding, gravidity, parity, gestational age, history of abortion and PPRM), maternal medical, fetal, and health-related factors (urinary tract infections, mid-upper arm circumference, (pre)eclampsia, diabetes mellitus, malpresentation, intrauterine growth restriction, ancephaly, number of fetus, and anemia).

Quality assurance and management

A one-day training was given to the data collectors before the actual data collection. In addition, the data abstraction checklist was pre-tested on 5% of the sample size in Jugal Hospital. Completeness of information and clarity of the collected data were checked on a daily basis. Data was double entered independently by two individuals.

Data processing and analysis

Data were coded, cleaned, and entered in Epi-Data 3.1 (Epi data Association, Odense Denmark) and exported to SPSS 25 (IBM Corporation, USA) for analysis. The results were reported as frequency and percentages for categorical variables and using mean (\pm SD) for normally distributed continuous variables. Bivariable and multivariable logistic regression was fitted to identify factors associated with PPRM. Association was described using an adjusted odds ratio (AOR) along with their corresponding 95% confidence interval (CI). Associations with a p -value <0.05 in the multivariable regression were considered statistically significant.

Ethical considerations

Ethical clearance was obtained from the Institutional Health Research Ethics Review Committee of Haramaya University College of Health and Medical Sciences (Ref No: IHRERC/146/2021). The purpose and objective of the study were explained to the hospital administrative body and written informed consent was obtained from the chief clinical director of the hospital and head of the labor ward before the data collection. Confidentiality of information was kept throughout the study through the use of anonymous identifiers. The study was carried out according to the Declaration of Helsinki.

RESULTS

Socio-demographic characteristics

A total of 449 preterm pregnant women were enrolled in the study. The mean age of participants was 28.9 ± 1.12 , ranging from 16 to 40 years. The majority of the study participants were married (97.3%), housewives 374 (83.3%), and Oromo 365 (81.3%). Half of them were urban residents 228 (50.8%) (Table 1).

Table 1: Sociodemographic characteristic of preterm pregnant women admitted in Hiwot Fana Comprehensive Specialized University Hospital, Eastern Ethiopia, (n=449).

Variable	Categories	Frequency (n)	Percentage (%)
Age in years	<18	24	5.3
	18-35	410	91.7
	>35	15	3.3
Residence	Urban	228	50.8
	Rural	221	49.2
Ethnicity	Oromo	365	81.3
	Harari	73	16.3
	Amhara	8	1.8
	Somali	3	0.7
Occupation	House wife	374	83.3
	Marchant	45	10.0
	Government employee	15	3.3
	Civil servant	3	0.7
	Others	12+3	2.7+0.7
Marital status	Single	9	2.0
	Married	437	97.3
	others	3+9	0.7+2
Women's educational Status	No formal education	220	49.0
	Primary school	154	34.3
	Secondary school	45	10.0
	Higher education	30	6.7

Reasons for Admission

Nearly one-fifth (22%) of the women were admitted for the indications of preterm labor followed by preeclampsia 74 (16.5%), PPRM 64 (14.3%), and APH 63 (14%) (Table 2).

Table 2: Reasons for admission of preterm pregnant women in Hiwot Fana Comprehensive Specialized University Hospital, Eastern Ethiopia, (n = 449).

Indication for admission	Frequency (n)	Percent (%)
Preeclampsia/eclampsia	74	16.5
APH	63	14
Oligohydramnios	14	3.1
PPROM	64	14.3
Preterm labor	99	22
Diabetes mellitus	4	0.9
Malpresentation	20	4.5
IUGR	5	1.1
Anencephaly /hydrocephalus	21	4.7
Non-reassuring biophysical profile	8	1.8
Twin pregnancy	31	6.9
Severe anemia	10	2.2
Intrauterine fetal death	19	4.2
Others	17	3.8
Total	449	100

About 155 (35.0%) were nulliparous and two third of them 300 (66.8%) had ANC follow up.

The majority of the pregnancies were singleton 405 (90.2%) (Table 3).

Table 3: Obstetric profile of women admitted with preterm pregnancy in Hiwot Fana Comprehensive Specialized University Hospital, Eastern Ethiopia, (n=449).

Variable	Categories	Frequency (n)	Percentage (%)
Gravidity	I	144	32.1
	II-IV	205	45.7
	>IV	100	22.3
Parity	Nullipara	155	34.5
	Primipara	86	19.2
	II-IV	125	27.8
	>IV	83	18.5
History of abortion	Yes	53	11.8
	No	396	88.2
ANC	Yes	300	66.8
	No	149	33.2
Number of ANC visit	No visit	149	33.2
	One	29	9.7
	Two	131	43.7
	> two	140	46.7
Number of fetus	Singleton	405	90.2
	Multiple	44	9.8

The burden of PPRM and associated factors

A total of 64 (14.3%; 95% CI 11.1-17.5) of the women had PPRM, all of whom were managed expectantly. Bivariable and multivariable logistic regressions were done to assess the factors associated with PPRM. In bivariable analysis, gravidity, residence, history of PROM, history of abortion, vaginal bleeding, maternal nutritional status, and urinary tract infections (UTI) were identified as potential candidate variables to be considered in the multivariable analysis by setting a p-value <0.25. In the final multivariable logistic regression model, PPRM was found to be associated with history of abortion, vaginal bleeding, maternal nutritional status, and UTI. The odds of having PPRM were 6 times higher (AOR=6.33; 95% CI:3.26-12.29, P=0.001) among women with UTI as compared

to women without UTI. Similarly, the odds of PPRM among women with vaginal bleeding were almost 3 times higher (AOR=2.62;95% CI:1.23-5.57, P=0.012) compared with their counterparts. The odds of having PPRM was 3 times higher (AOR= 3.07,95% CI:1.33-7.06, P=0.008) among women with a history of abortion. The odds of developing PPRM were 7 times higher (AOR=7.06; 95% CI:4.02-12.43, P=0.001) among women with undernutrition (MUAC <23) compared with their counterparts (Table 4).

Table 4: Factors associated with PPRM among women admitted with preterm pregnancy in Hiwot Fana Comprehensive Specialized University Hospital, Eastern Ethiopia, (n=449).

Variable	Categories	PPROM		COR (95% CI)	P-value	AOR (95% CI)	P-value
		Yes	No				
Gravidity	1	16(11.1%)	128(88.9%)	1		1	
	2-4	31(15.1%)	174(84.9%)	1.43 (0.75-2.72)	0.389	1.37 (0.72-2.62)	0.122
	>4	17(17.0%)	83(83.0%)	1.64 (0.78-3.42)	0.282	1.82 (0.86-3.86)	
Residence	Urban	38(16.7%)	190(83.3%)	1		1	
	Rural	26(11.8%)	195(88.2%)	0.67 (0.39-1.14)	0.139	0.63 (0.34-1.09)	0.139
History of abortion	No	48(12.1%)	348(87.9%)	1		1	
	Yes	16(30.2%)	37(69.8%)	3.14 (1.62-6.06)	0.001	3.07 (1.33-7.06)	0.008*
Previous PROM	No	53(12.6%)	368(87.4%)	1		1	
	Yes	11(39.3%)	17(60.7%)	4.49 (1.99-10.2)	0.001	2.76 (0.98-7.72)	0.053
Vaginal bleeding	No	47(12.2%)	337(87.8%)	1		1	
	Yes	17(26.2%)	48(73.8%)	2.54 (1.35-4.78)	0.004	2.62 (1.23-5.57)	0.012*
UTI	No	31(8.2%)	345(91.8%)	1		1	
	Yes	33(45.2%)	40(54.8%)	9.18(5.09-16.55)	0.001	6.33(3.26-12.29)	0.001*
MUAC	<23cm	38(36.5%)	66(63.5%)	7.06(4.02-12.43)	0.001	7.18(3.71-13.91)	0.001*
	≥23 cm	26(7.5%)	319(92.5%)	1		1	

Note: *p<0.05 considered as statistically significant, COR, crude odds ratio; AOR, adjusted odds ratio; CI, Confidence interval

DISCUSSION

In this study, we assessed the burden of PPRM and its associated factors among pre-term pregnant women admitted to a university hospital in eastern Ethiopia. In our sample, we found that one in seven preterm women had PPRM. Preterm PROM was more likely among women with urinary tract infection, history of abortion, vaginal bleeding, and undernutrition. Our finding is comparable with the finding from Debre Tabor General Hospital, North West Ethiopia (13.67%)¹³. In our study, the prevalence of PPRM was higher than the global prevalence of (1% - 3%)²² and other studies in Rio Grande Brazil (3.1%)⁹, in India (2.01% - 2.2%)^{10,23}, in Nigeria (3.3%)¹¹, in Uganda (7.5%)⁶ and southern Ethiopia (6.6%)¹². This might be due to the differences in the study population; in this study, data was collected from a selected high-risk population which may increase the magnitude of PPRM. On the other hand, this finding is

lower than the study findings in Jiangsu Province Hospital in China (19.2%)²⁴. The difference could be attributed to the time gap between the studies and the absence of behavioral risk factors for PPRM such as smoking, cocaine use, and alcohol consumption in the present study.

We found that PPRM was associated with UTI, which is consistent with previous reports from Debre Tabor, Ethiopia (13), and northeastern India,²³. This might be linked with elevations in the inflammatory mediators such as prostaglandins, cytokines, and proteinases in the local tissue which plays a causative role in the disruption of fetal membrane integrity triggering uterine contractility as part of the physiologic defense mechanism²⁵. We also found that undernutrition (MUAC <23 cm) was significantly associated with PPRM, a finding consistent with studies from Debre Tabor, northern Ethiopia¹³. Nutritional deficiency particularly micronutrients deficiencies such as vitamin C or

ascorbic acid affects collagen formation which protects the body against degenerative processes resulting from oxidative stress leading to collagen weakness and capillary hemorrhage. Similarly, women with vaginal bleeding were more likely to develop PPRM compared to their counterparts. This finding was consistent with the study conducted at Debre Tabor General Hospital¹³. This might be related to thrombin release from the decidual cells as a result of decidual hemorrhage which might result in tissue necrosis and degradation of the extracellular matrix²⁶.

We also found that history of abortion was found to be significantly associated with PPRM. The likelihood of having PPRM among mothers who have a history of abortion was three times higher than compared with those who did not have a history of abortion. Our study was supported by previous reports from China²⁷, rural Uganda⁶, Tigray, northern Ethiopia¹⁶, and southern Ethiopia¹². This might be related to the weakening of the membranes secondary to the trauma that lies on the uterine wall. In addition, it might be related to the tendency for increased systemic inflammation and stimulation of the infection pathway or vascular complications which raised secondary to the abortion²⁰.

The current study has to be interpreted with some limitations. First, the study is institution-based and focused on the high-risk population who might affect the actual prevalence of PPRM in the study area as well as in the country. Second, we did not collect data on some variables such as interpregnancy interval, BMI and income which may be associated with PPRM because of incomplete information in the medical records.

CONCLUSIONS

Overall, one in seven preterm women included in our study had PPRM. Preterm PROM was found to be significantly associated with urinary tract infections, vaginal bleeding, maternal nutrition, and history of abortion. Hence, improving the nutritional statuses of pregnant women including

pre-conception nutrition and early screening and treatments of UTIs is recommended to reduce the risk of PPRM. Further study on the appropriateness of management of women with PPRM and related pregnancy outcomes is essential for designing tailored recommendations.

DECLARATIONS

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Availability of Data and Materials

All relevant data are included in this manuscript. However, the datasets used or analyzed during the current study available from the corresponding author on reasonable request.

Conflict of interests

The authors declare no conflict of interest.

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The funder (Haramaya University) has no role in the design of the study, collection, analysis, and interpretation of data, and in writing the manuscript.

Contribution of authors

ST conceived the study, supervised the data collection, run the statistical analysis and interpretation, and drafted the manuscript. TG and AKT supervised the overall research process. TG, AKT, AA, and MA participated in the design of the study, data analysis, interpretation, and drafting of the manuscript. All authors have approved the final manuscript for submission and agreed to be accountable for the entire work of this research.

Abbreviations

ACOG: Americans College of Obstetricians and Gynecologist,

AOR: Adjusted odds ratio, APH: Antepartum

Hemorrhage,

COR: Crude odds ratio,

HFCSUH: Hiwot Fana Comprehensive Specialized
University Hospital,

IUGR: Intrauterine Growth Restriction,

PPROM: Preterm Premature Rupture of the
Membrane,

PROM: Premature Rupture of of the Membrane,

SPSS: Statistical Package for Social Science,

MUAC: Mid Upper Arm Circumference,

UTI: Urinary Tract Infection

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