

Research

Khat chewing in pregnant women associated with prelabor rupture of membranes, evidence from eastern Ethiopia



Tesfaye Assebe Yadeta^{1,*}, Gudina Egata², Berhanu Seyoum³, Dadi Marami⁴

¹School of Nursing and Midwifery, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia, ²School of Public Health, College of Health and Medical Sciences, Addis Ababa University, Addis Ababa, Ethiopia, ³Armauer Hansen Research Institute, Addis Ababa, Ethiopia, ⁴Department of Medical Laboratory Sciences, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia

*Corresponding author: Tesfaye Assebe Yadeta, School of Nursing and Midwifery, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia

Key words: PROM, Khat plant, *Catha edulis*, khat chewing, pregnancy, Harar, Ethiopia

Domain: Obstetrics and gynecology, Maternal and child health, Reproductive Health

Received: 27 Mar 2020 - Accepted: 04 Apr 2020 - Published: 01 May 2020

Abstract

Introduction: prelabor rupture of membranes (PROM) is a major factor that affects pregnancy outcome. Results from previous studies have suggested that there is an association between pregnant women, khat chewing and preterm birth, but evidence of association with PROM is sparse. This study therefore aims at identifying association between khat chewing in pregnancy and premature rupture of membranes in eastern Ethiopia.

Methods: A health facility-based cross-sectional study was conducted among 1688 pregnant women who came for delivery service in Harar town, Eastern Ethiopia between June to October in 2016. Data were collected using a pre-tested structured questionnaire and checklist to extract data from the medical record. The association between khat and PROM was examined using logistic regression analysis. A statistical significance was declared at p-value < 0.05.

Results: Of the 1688 pregnant women who participated in the study, 397 had prelabor rupture of the membranes, representing a proportion of 23.5% [(95% CI: (21.5, 25.6%)]. Of these 397 prelabor rupture of the membranes 198 (31.53%) were from Khat chewing mothers and, 199(18.77%) were from non-khat chewing mothers. After controlling for potential confounders, the multivariable logistic regression analysis revealed the odds of PROM was 1.51 times higher among khat chewed pregnant women [AOR = 1.51; 95% CI; (1.11, 2.07)] were had no khat chewing. **Conclusion:** this study found a significant association between khat chewing in pregnancy and PROM. Efforts to reduce PROM need to consider prevention of khat chewing in pregnancy. A specific strategy need to protect pregnant women from khat chewing.

Research | Volume 36, Article 1, 01 May 2020 | 10.11604/pamj.2020.36.1.22528

This article is available online at: <http://www.panafrican-med-journal.com/content/article/36/1/full/>

© Tesfaye Assebe Yadeta et al. Pan African Medical Journal (ISSN: 1937-8688). This is an Open Access article distributed under the terms of the Creative Commons Attribution International 4.0 License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Prelabor rupture of membranes (PROM) is rupture of membranes that occurs before the onset of labor. Membranes rupture before labor and before 37 weeks of gestation is referred to as preterm PROM. Term Prelabor Rupture of Membranes (term PROM) is defined as rupture of the membranes prior to the onset of labor at or beyond 37 weeks gestation [1]. Prelabor rupture of membranes complicates approximately 8% of pregnancies. Prelabor rupture of membranes has been shown to increase the risk of cord prolapse, cord compression and placental abruption, maternal chorioamnionitis, infectious endometritis, neonatal sepsis, and perinatal death. Preterm PROM is responsible for 1 of every 3 preterm births and is associated with significant morbidity for both women and neonate [2-7]. Widespread khat chewing in pregnancy, in east African countries, including Ethiopia is recognized as an important public health concern [8,9]. Khat is chewed for its central nervous system stimulant properties. The major pharmacologically active constituent of the fresh khat leaf is cathinone which is extracted by mastication [10]. Khat chewing in pregnancy women were at risk for preterm labor, labor induction and fetal distress, intra uterine fetal death (IUFD), lower mean hemoglobin concentration at delivery, low birth weight, higher perinatal mortality and congenital malformations [11]. During khat chewing, the leaves are simply kept in the side of the cheek to masticate over time. Prolonged mastication of khat affects oral hygiene status of chewers. The incidence of gingival bleeding, inflammation, ulcers on the oral mucosa, and gingival recession was significantly higher in khat-chewers [12]. Khat use increase the risk of esophageal cancer [13]. Periodontal disease is associated with PROM [14,15]. Exposure to contaminated sources during khat chewing was reported to cause bacteremia and meningitis [16]. Khat chewing grown with chemical pesticides may cause considerable adverse health effects in khat users [17]. Khat may be a contributing factor in the pathological diseases found among khat users like liver disease, coronary problems, cancers of the digestive tract and incidents of domestic violence [18,19]. Despite impact of khat on adverse pregnancy outcome, pregnant women in the study area were khat chewing. This may be due to lack of information on the health impact of khat during pregnancy. The aim of this study was to perform an investigation on the association of khat chewing in pregnancy and PROM among pregnant women.

Methods

Study setting: this study was performed in three health facilities (Hiwot Fana Specialized University Hospital, Jugal Hospital and Arategna Health Center) found in Harar town, Eastern Ethiopia. Harar is located 510 km east of the capital city of Ethiopia, Addis Ababa. Ethiopia is among widely distributed khat chewing country of east Africa [8,20].

Study design and sampling: a cross-sectional study was done between June and October 2016. The study participants were 1688 singleton pregnant women who came for delivery services at labour and delivery rooms of the selected health facilities. Study participants were taken proportional to the client load of the selected health facilities.

Data collection: data were collected using a pretested and structured questionnaire. In addition, a checklist was used to extract data from the medical record. The data collection tools were developed by reviewing various previous related data collection instruments and articles [1,21-23]. The questionnaire included socio-demographic characteristics of the participant like (age of mothers, residence of mothers, educational status, and khat chewing in pregnancy), obstetric and gynecologic history (history of abortion, history of preterm, history of PROM,), current pregnancy obstetric and gynecologic situation (ANC, parity and anemia). The original questionnaire was prepared in English language and later translated into the local languages (Amharic and Afan Oromo) for data collection. Forward and backward translations were performed by language experts. A six-day training was given to attending midwives and the supervisors who worked as data collectors. The training for data collectors and supervisors addressed issues related to data collection procedures and tools, interviewing techniques, medical record review procedures. A research manual was prepared to guide training, data collection and management.

Measurement: prelabor rupture of membranes (PROM) is rupture of membranes that occurs before the onset of labor. Membranes rupture before labor and before 37 weeks of gestation is referred to as preterm PROM. Term Prelabour Rupture of Membranes (term PROM) is defined as rupture of the membranes prior to the onset of labour at or beyond 37 weeks gestation [1]. Premature rupture of membranes was the dependent variable in this study and this information was obtained from medical records. It was labelled as "yes" and "no" with

a code of 1 and 0, respectively. Khat chewing in pregnancy, age of mothers, residence of mothers, educational status, history of abortion, history of preterm, history of PROM, ANC, parity and anemia were independent variables. Khat chewing in pregnancy was collected based on maternal reply for the question "have you chewed khat during current pregnancy?", and labeled as "yes" and "no" and coded with 1 and 0, respectively. Age of the mother was documented based on maternal reply and later grouped as 15-19 and 20+ with code 1 and 2, respectively for analysis. Maternal education was grouped as "literate" for those who could read and write and all others as "illiterate" and was coded 0 and 1, respectively. Antenatal care visit was obtained from maternal reply and labeled as "yes" and "no" and coded with 1 and 0, respectively. Number of births (parity) were grouped as one primiparity (one delivery), multiparous (2-4 delivery) and grand multiparous (= 5 deliveries) and code with 1, 2 and 3, respectively [20]. History of abortion, history of preterm, and history of PROM was documented based on maternal reply and labeled as "yes" and "no" and coded with 1 and 0, respectively.

Statistical analysis: data were double entered and cleaned using Epi-Data version 3.1 and analyzed using STATA version 14. Summary and proportions of the variables were computed against PROM. The logistic regression model was used to assess the association between independent and the outcome variable (PROM). Multicollinearity was tested using the Variance Inflation Factor (VIF) and the tolerance test. Correlation matrix and covariate matrix were tested for the final model. The Hosmer-Lemeshow goodness-of-fit tests were used to test for model fitness [24]. Bivariate analysis was first made and the variables with a p-value less than 0.25 were considered for multivariable analysis, along with maternal age, important predictors of PROM, regardless of the cut-off point for p value. The association between khat chewing in pregnancy and the outcome variable (PROM) was analyzed by controlling for other potential confounding variables, a p value of less than 0.25 in bivariate analysis and maternal age. Adjusted Odds Ratio (AOR) along with 95% confidence interval was estimated to assess the strength of the association. Statistical significance was declared at a p-value < 0.05.

Ethical approval and consent to participate: the study material was reviewed and approved by the Institutional Health Research Ethics Review Committee of the College of Health and Medical Sciences at Haramaya University. Permission was obtained from each of the health facilities involved in the study. Written consent was obtained from each woman before commencement of data collection.

Women experienced PROM was treated. Neonates with health problems were treated and immediate referral was also facilitated.

Results

Of the 1688 pregnant women who participated in the study, 397 had prelabor rupture of the membranes, representing a proportion of 23.5% [95% CI:(21.57, 25.6%)]. Of these 397 prelabor rupture of the membranes 198(31.53%) were from mother had khat chewing and, 199(18.77%) were from non-khat chewing (Table 1). Bivariable analysis revealed, khat, educational status, history of abortion, history of preterm, history of PROM, ANC, parity, and anemia were found to have a significant association with PROM (Table 1).

Multicollinearity test: multicollinearity was tested using the Variance Inflation Factor (VIF) and tolerance test. VIF for all variables was less than 10, and tolerance test was greater than 0.2. This indicate there was no multicollinearity problem [25] (Table 2).

The multivariable logistic regression analysis: the multivariable logistic regression analysis revealed the odds of PROM was 1.51 times higher among khat chewed pregnant women [AOR = 1.51; 95% CI; (1.11,2.07)] who had no khat chewing. In addition, the odds for pregnant women who had history of PROM [AOR = 4.77; 95% CI; (3.35,6.79)], and mother experience anemia [AOR = 3.18; 95% CI; (2.09,4.85)] had increased odds of experiencing PROM. Age twenty and above year 51% [AOR =0.49; 95% CI; (0.27, 0.87)], rural resident 44% [AOR =0.56; 95% CI; (0.39, 0.80)], and attended ANC follow-up 37% [AOR =0.63; 95% CI; (0.44,0.89)] had lower odds of experiencing PROM (Table 3).

Discussion

This study showed an association between PROM and khat chewing in pregnancy, after controlling for other potential confounders. Similar findings were reported from Yemen [11]. Khat is consumed by plucking off the leaves of the tree and rolling them into little balls that are pushed into the side of the cheek, where they form a large bolus (soft mass of leaves). The practice is usually referred to as khat chewing, but in fact the leaves are simply kept in the side of the cheek to masticate over time. Prolonged mastication of khat affects oral hygiene status of chewers. The incidence of ulcers on the oral mucosa,

gingival bleeding, gingival recession is high [12]. Khat use increase the risk of esophageal cancer [13]. Periodontal disease is associated with PROM [14,15]. The link between periodontal disease and preterm delivery is a possible translocation of periopathogenic bacteria to the placenta and amniotic fluid as well as a systemic response to this chronic inflammatory disease [25,26]. Other studies have reported, khat chewing pregnant women were at risk for infection, due to exposure to contaminated sources during chewing [16]. Infection in the female reproductive tract can cause prelabor rupture of the membranes and induce premature labor [5]. Prolonged PROM significantly increases the risk of placental infection [6]. Histological chorioamnionitis (HCA) and funisitis increase the risk of adverse perinatal outcome in PPROM pregnancies [7]. Preterm prelabor rupture of membranes is associated with Intra-amniotic infection and perinatal deaths [2]. The implication of khat chewing grown with chemical pesticides may cause considerable adverse health effects in khat users need further investigation [17]. At term, programmed cell death and activation of catabolic enzymes, such as collagenase and mechanical forces, result in ruptured membranes [8]. The aetiology of PROM has been shown to be multifactorial, and increasing evidence has regarded exposure to environmental pollutants as risk factors for PROM like lead exposure [9,27].

Experiencing anemia was one of the predictors' of PROM. Similar findings were reported [11,28]. Khat chewing results in lowering mean hemoglobin concentration at delivery [11]. Maternal anemia results in hypoxic conditions of the fetoplacental unit and thus is a suitable model to study the effects of hypoxia on villous proliferation in human placenta [29]. Additionally, in this study pregnant woman who had history of PROM was an increase the risk of PROM. Similar findings were reported in other studies conducted in different part of the world [30-32]. The cause of PROM is obscure, however the reason may be due to maternal genital bacterial colonization, maternal medical and obstetric complications that are predictors for PROM, there may be recurrence, in the study area where there is no screening [33]. Women presenting with premature rupture of the membranes, intrauterine infection, and oligohydramnios are at risk of placental abruption [34]. Aspirin and progesterone may be used in preventing and delaying preterm birth recurrence [35,36]. In this study, antenatal care follow up was one of the predictors. Similar findings were reported in Pakistan [37]. The reason may be treatment was given when the pregnant women come to health center with problems. Despite this, ANC follow up was a protective for PROM. Only 32% of pregnant women had four recommended ANC visits in Ethiopia [15]. To achieve the sustainable development goal to end all

preventable maternal and perinatal mortality and morbidity in relation with PROM, health promotion programs must better target those communities where maternal health care utilization is low. Effective interventions are therefore needed to improve the ANC coverage as part of a PROM reduction strategy. Age twenty and above and being a rural resident were reduced PROM recurrence. This needs further investigation. There are a number of initiatives that are currently being worked on improving maternal and newborn health care delivery in Ethiopia. The Health Extension Program, launched by the Federal Ministry of Health of Ethiopia in 2003, involves the placement of Health Extension Workers (HEW) in rural villages to deliver mostly disease prevention and health promotion activities. There is an increase in the reporting of sick children, access to ANC and post-natal care [38]. Despite these successes, khat chewing in pregnancy is spreading very fast. The community may have no understanding on its associated risk. Our study findings reveal that there is still much work to be done at the community level to protect pregnant women from the adverse effect of khat chewing.

Strengths and limitations of this study: this study was conducted with a large sample size which allowed us to adjust for other potential risk factors for prelabor rupture of membranes. Although many potential confounders were taken into account for analysis, other confounding factors may remain. Clinical assessment and periodontal status was not done.

Funding: this study was financially supported by Haramaya University. The funding body did not play any role in the design of the study, collection, analysis, interpretation of data, and in writing the manuscript.

Conclusion

This study demonstrated a significant association between khat chewing in pregnancy and PROM. Efforts to reduce PROM need to consider prevention of khat chewing in pregnancy. Policy and programmatic efforts to optimize pregnancy outcome should consider khat use as an important determinant.

What is known about this topic

- Khat chewing affects oral hygiene status of chewers;
- Periodontal disease is associated with prelabor rupture of membranes;

- Prelabor rupture of the membranes increase the risk of infection.

What this study adds

- Possible translocation of periopathogenic bacteria to the placenta and amniotic fluid as well as a systemic response to this chronic inflammatory disease;
- This study rises the discussion around the association between khat chewing in pregnancy and prelabor rupture of the membranes.

Competing interests

The authors declare no competing interests.

Authors' contributions

TA, GE, BS, and DM conceived and designed the paper, involved in data collection, performed the statistical analysis, interpreted the results, wrote and reviewed the manuscript.

Acknowledgments

The authors would like to thank Haramaya University for financial support, the study participants, data collectors, and supervisors for their kind cooperation.

Tables

Table 1: basic characteristics of study subjects by premature rupture of the membranes and unadjusted odds ratio, Harar town, Eastern Ethiopia, 2016

Table 2: multicollinearity test output among predictor variables, Harar, Eastern Ethiopia, 2016

Table 3: multivariable output of factors associated with PROM among pregnant women, Harar, Eastern Ethiopia, 2016

References

1. Kuba K, Bernstein PS. ACOG Practice Bulletin No. 188: Prelabor Rupture of Membranes. *Obstetrics & Gynecology*. 2018; 131(6):1163-1164. **PubMed**
2. Kassa EM, Sirak B. Maternal and perinatal outcome of pregnancies with preterm premature rupture of membranes (pprom) at tikur anbessa specialized teaching hospital, addis ababa, ethiopia. *Ethiopian medical journal*. 2015; 52(4). **Google Scholar**
3. Ibishi V, Isjanovska R. Prelabour Rupture of Membranes: Mode of Delivery and Outcome. *OA Maced J Med Sci*. 2015. **PubMed | Google Scholar**
4. Patkai J, Schmitz T, Anselem O, Mokbat S, Jarreau P-H, Goffinet F *et al*. Neonatal and two-year outcomes after rupture of membranes before 25 weeks of gestation. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2013; 166(2):145-150. **PubMed | Google Scholar**
5. Knox I, Hoerner J. The role of infection in premature rupture of the membranes. *American Journal of Obstetrics & Gynecology*. 1950; 59(1):190-194. **PubMed | Google Scholar**
6. Wu T, Shi J, Bao S, Qu Y, Mu D. Effect of premature rupture of membranes on maternal infections and outcome of preterm infants. *Zhongguo dang dai er ke za zhi= Chinese journal of contemporary pediatrics*. 2017; 19(8):861-865. **PubMed | Google Scholar**
7. Tsiartas P, Kacerovsky M, Musilova I, Hornychova H, Cobo T, Sävman K *et al*. The association between histological chorioamnionitis, funisitis and neonatal outcome in women with preterm prelabor rupture of membranes. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2013; 26(13):1332-1336. **PubMed | Google Scholar**

8. Lifson AR, Workneh S, Shenie T, Bezabih L, Desalegn Admassu Ayana, Behailu Dagne *et al.* Frequent Use of Khat, an Amphetamine-Like Substance, as a Risk Factor for Poor Adherence and Lost to Follow-Up Among Patients New to HIV Care in Ethiopia. *AIDS RESEARCH AND HUMAN RETROVIRUSES*. 2017; 33(10). **PubMed | Google Scholar**
9. Wallace ME, Grantz KL, Liu D, Zhu Y, Kim SS, Mendola P. Exposure to ambient air pollution and premature rupture of membranes. *American journal of epidemiology*. 2016; 183(12):1114-1121. **PubMed | Google Scholar**
10. Kuczkowski K. Herbal ecstasy: cardiovascular complications of khat chewing in pregnancy. *Acta Anaesthesiol Belg*. 2005; 56(1):19-21. **PubMed | Google Scholar**
11. Abdel-Aleem MA, Al-Aghbari A, Mustafa M, Nasr AA, Assad A. Khat chewing during pregnancy: an insight on an ancient problem impact of chewing Khat on maternal and fetal outcome among Yemeni pregnant women. *Journal of Gynecology and Neonatal Biology*. 2015; 1(2):28-31. **Google Scholar**
12. Al-Kholani AI. Influence of khat chewing on periodontal tissues and oral hygiene status among Yemenis. *Dental research journal*. 2010; 7(1):1. **PubMed | Google Scholar**
13. Leon ME, Assefa M, Kassa E, Bane A, Gemechu T, Tilahun Y, Endalafer N, Ferro G, Straif K, Ward E. Qat use and esophageal cancer in Ethiopia: A pilot case-control study. *PloS one*. 2017;12(6):e0178911. **PubMed | Google Scholar**
14. Michalowicz BS, Durand R. Maternal periodontal disease and spontaneous preterm birth. *Periodontology*. 2007; 44(1):103-112. **PubMed | Google Scholar**
15. Radochova V, Stepan M, Kacerovska Musilova I, Slezak R, Vescicik P, Menon R *et al.* Association between periodontal disease and preterm prelabour rupture of membranes. *Journal of clinical periodontology*. 2019;46(2):189-196. **PubMed | Google Scholar**
16. Martínez-Balzano C, Kohlitz PJ, Chaudhary P, Hegazy H. *Campylobacter* fetus bacteremia in a young healthy adult transmitted by khat chewing. *Journal of Infection*. 2013; 66(2):184-186. **PubMed | Google Scholar**
17. Hassan AA, Abdullah SM, Khardali IA, Oraiby ME, Shaikain GA, Fageeh M *et al.* Health Impact of Khat Chewing and Pesticides: Detection of 8 Pesticides Multi-Residues in Khat Leaves (*Catha edulis*) From Jazan Region, KSA. *Advances in Environmental Biology*. 2016; 10(8):30-36. **Google Scholar**
18. Thomas S, Williams T. Khat (*Catha edulis*): A systematic review of evidence and literature pertaining to its harms to UK users and society. *Drug Science, Policy and Law*. 2013; 1:2050324513498332. **Google Scholar**
19. Daba D, Hymete A, Bekhit AA, Mohamed AMI, Bekhit AE-DA. Multi residue analysis of pesticides in wheat and khat collected from different regions of Ethiopia. *Bulletin of environmental contamination and toxicology*. 2011; 86(3):336-341. **PubMed | Google Scholar**
20. Ayano G, Yohannis K, Abraha M. Epidemiology of khat (*Catha edulis*) consumption among university students: a meta-analysis. *BMC public health*. 2019; 19(1):150. **PubMed | Google Scholar**
21. Getachew A, Ricca J, Cantor D, Rawlins B, Rosen H, Tekleberhan A *et al.* Quality of care for prevention and management of common maternal and newborn complications: a study of Ethiopia's hospitals. *Baltimore: Jhpiego*. 2011. **Google Scholar**
22. Central Statistical Agency (CSA) [Ethiopia] and ICF. Ethiopia Demographic and Health Survey 2016. In Addis Ababa, Ethiopia, and Rockville, Maryland, USA CSA and ICF. 2016.
23. Maine D. *Monitoring emergency obstetric care: a handbook*. Geneva, Switzerland World Health Organization. 2009.
24. Midi H, Sarkar SK, Rana S. Collinearity diagnostics of binary logistic regression model. *Journal of Interdisciplinary Mathematics*. 2010; 13(3):253-267. **Google Scholar**
25. Ercan E, Eratalay K, Deren O, Gur D, Ozyuncu O, Altun B *et al.* Evaluation of periodontal pathogens in amniotic fluid and the role of periodontal disease in pre-term birth and low birth weight. *Acta Odontologica Scandinavica*. 2013; 71(3-4):553-559. **PubMed | Google Scholar**

26. Madianos PN, Bobetsis YA, Offenbacher S. Adverse pregnancy outcomes (APO s) and periodontal disease: pathogenic mechanisms. *Journal of clinical periodontology*. 2013; 40:S170-S180. **PubMed** | **Google Scholar**
27. Huang S, Xia W, Sheng X, Qiu L, Zhang B, Chen T. Maternal lead exposure and premature rupture of membranes: a birth cohort study in China. *BMJ open*. 2018; 8(7):e021565. **PubMed** | **Google Scholar**
28. Zhang Q, Ananth CV, Li Z, Smulian JC. Maternal anaemia and preterm birth: a prospective cohort study. *International journal of epidemiology*. 2009; 38(5):1380-1389. **PubMed** | **Google Scholar**
29. Kosanke G, Kadyrov M, Korrr H, Kaufmann P. Maternal anemia results in increased proliferation in human placental villi. *Placenta*. 1998; 19:339-357. **Google Scholar**
30. Lee T, Carpenter MW, Heber WW, Silver HM. Preterm premature rupture of membranes: risks of recurrent complications in the next pregnancy among a population-based sample of gravid women. *American journal of obstetrics and gynecology*. 2003; 188(1):209-213. **PubMed** | **Google Scholar**
31. Getahun D, Strickland D, Ananth CV, Fassett MJ, Sacks DA, Kirby RS *et al*. Recurrence of preterm premature rupture of membranes in relation to interval between pregnancies. *American journal of obstetrics and gynecology*. 2010; 202(6):570. e571-570. e576. **PubMed** | **Google Scholar**
32. Assefa NE, Berhe H, Girma F, Berhe K, Berhe YZ, Gebrehet G *et al*. Risk factors of premature rupture of membranes in public hospitals at Mekele city, Tigray, a case control study. *BMC pregnancy and childbirth*. 2018; 18(1):386. **PubMed** | **Google Scholar**
33. Patras KA, Rösler B, Thoman ML, Doran KS. Characterization of host immunity during persistent vaginal colonization by Group B *Streptococcus*. *Mucosal immunology*. 2015; 8(6):1339. **PubMed** | **Google Scholar**
34. Ananth CV, Oyelese Y, Srinivas N, Yeo L, Vintzileos AM. Preterm premature rupture of membranes, intrauterine infection, and oligohydramnios: risk factors for placental abruption. *Obstetrics & Gynecology*. 2004; 104(1):71-77. **PubMed** | **Google Scholar**
35. Visser L, de Boer MA, de Groot CJ, Nijman TA, Hemels MA, Bloemenkamp KW *et al*. Low dose aspirin in the prevention of recurrent spontaneous preterm labour—the APRIL study: a multicenter randomized placebo controlled trial. *BMC pregnancy and childbirth*. 2017; 17(1):223. **PubMed** | **Google Scholar**
36. Dodd JM, Jones L, Flenady V, Cincotta R, Crowther CA. Prenatal administration of progesterone for preventing preterm birth in women considered to be at risk of preterm birth. *Cochrane Database of Systematic Reviews*. 2013(7). **PubMed** | **Google Scholar**
37. Rozi S, Butt ZA, Zahid N, Wasim S, Shafique K. Association of tobacco use and other determinants with pregnancy outcomes: a multicentre hospital-based case-control study in Karachi, Pakistan. *BMJ open*. 2016; 6(9):e012045. **PubMed** | **Google Scholar**
38. Banteyerga H, Kidanu A. Rapid appraisal of health extension program: Ethiopia country report. Addis Ababa: The L10K project and MHRC. 2008.

Table 1: basic characteristics of study subjects by premature rupture of the membranes and unadjusted odds ratio, Harar town, Eastern Ethiopia, 2016

| Characteristics | Total n=1688 | Experience PROM | | Crude OR CI | | | P value |
|-----------------------------|-----------------|-----------------|---------|-------------|------|------|---------|
| | | No (%) | Yes (%) | | | | |
| Khat | | | | | | | |
| No | 1,060 | 81.23 | 18.77 | 1 | | | |
| Yes | 628 | 68.47 | 31.53 | 1.99 | 1.58 | 2.50 | 0.000 |
| Age of mothers | | | | | | | |
| ≤19 | 301 | 75.08 | 24.92 | 1 | | | |
| 20 and above | 1,387 | 76.78 | 23.22 | 0.911 | 0.68 | 1.21 | 0.528 |
| Residence of mothers | | | | | | | |
| Urban | 943 | 75.19 | 24.81 | 1 | | | |
| Rural | 745 | 78.12 | 21.88 | 0.84 | 0.67 | 1.06 | 0.158 |
| Educational status | | | | | | | |
| Literate | 894 | 78.52 | 21.48 | 1 | | | |
| Illiterate | 794 | 74.18 | 25.82 | 1.27 | 1.01 | 1.59 | 0.036 |
| History of abortion | | | | | | | |
| No | 1,388 | 78.82 | 21.18 | 1 | | | |
| Yes | 300 | 65.67 | 34.33 | 1.94 | 1.48 | 2.55 | 0.000 |
| History of preterm | | | | | | | |
| No | 1,657 | 77.07 | 22.93 | 1 | | | |
| Yes | 31 | 45.16 | 54.84 | 1.62 | 1.21 | 2.17 | 0.001 |
| History of PROM | | | | | | | |
| No | 1,456 | 81.66 | 18.34 | 1 | | | |
| yes | 232 | 43.97 | 56.03 | 3.38 | 1.64 | 6.97 | 0.001 |
| ANC | | | | | | | |
| No | 561 | 70.23 | 29.77 | 1 | | | |
| Yes | 1,127 | 79.59 | 20.41 | 0.60 | 0.47 | 0.76 | 0.000 |
| Parity | | | | | | | |
| 1 | 722 | 81.72 | 18.28 | 1 | | | |
| 2-4 | 755 | 74.30 | 25.70 | 1.54 | 1.20 | 1.98 | 0.001 |
| ≥5 | 211 | 66.35 | 33.65 | 2.26 | 1.60 | 3.19 | 0.000 |
| Anemia | | | | | | | |
| No | 1,535 | 79.54 | 20.46 | 1 | | | |
| Yes | 153 | 45.75 | 54.25 | 4.61 | 3.27 | 6.48 | 0.000 |

Table 2: multicollinearity test output among predictor variables, Harar, Eastern Ethiopia, 2016

| Variable | Variance inflation test (VIF) | Tolerance test (1/VIF) |
|-----------------------------|-------------------------------|------------------------|
| Khat chewing in pregnancy | 1.07 | 0.930794 |
| Age of mother | 1.06 | 0.944123 |
| Residence of mothers | 1.36 | 0.734311 |
| Maternal education | 1.44 | 0.695489 |
| History of abortion | 1.15 | 0.869117 |
| History of preterm delivery | 1.05 | 0.949141 |
| History of PROM | 1.18 | 0.849108 |
| Antenatal care follow up | 1.25 | 0.801577 |
| Parity | 3.40 | 0.293837 |
| | 3.64 | 0.274827 |
| Anemia in mother | 1.08 | 0.925358 |
| Mean | 1.61 | |

Table 3: multivariable output of factors associated with PROM among pregnant women, Harar, Eastern Ethiopia, 2016

| Characteristics | | AOR | 95% Conf. Interval | | P value |
|------------------------------------|--------------|------|--------------------|-------|---------|
| Khat chewing in pregnancy | No | 1 | | | |
| | Yes | 1.51 | 1.11 | 2.07* | 0.009 |
| Age of mother | ≤19 | 1 | | | |
| | 20 and above | 0.49 | 0.27 | 0.87* | 0.017 |
| Residence of mothers | Urban | 1 | | | |
| | Rural | 0.56 | 0.39 | 0.80 | 0.002 |
| Maternal education | Literate | 1 | | | |
| | Illiterate | 1.04 | 0.72 | 1.51 | 0.813 |
| History of abortion | No | 1 | | | |
| | Yes | 1.22 | 0.86 | 1.73 | 0.244 |
| History of preterm delivery | No | 1 | | | |
| | Yes | 1.83 | 0.80 | 4.15 | 0.146 |
| History of PROM | No | 1 | | | |
| | yes | 4.77 | 3.35 | 6.79* | 0.000 |
| Antenatal care follow up | No | | | | |
| | Yes | 0.63 | 0.44 | 0.89* | 0.01 |
| Parity | 1 | 1 | | | |
| | 2-4 | 1.22 | 0.64 | 2.34 | 0.531 |
| | ≥5 | 1.01 | 0.48 | 2.13 | 0.962 |
| Anemia in mother | No | 1 | | | |
| | Yes | 3.18 | 2.09 | 4.85* | 0.000 |

AOR: Adjusted Odds Ratio