

Prevalence of premature rupture of membrane and its associated factors among pregnant women in Ethiopia: A systematic review and meta-analysis

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Abstract

Background: Premature rupture of the membrane is a serious public health problem, especially in low- and middle-income countries with significant maternal and perinatal morbidity and mortality. Despite its substantial contributions to fetomaternal complications, the burden of premature rupture of the membrane was not systematically analyzed in Ethiopia. Hence, this review aimed to identify the burden of premature rupture of the membrane and associated factors among pregnant women in Ethiopia.

Methods: PubMed/Medline, Scopus, and African journal online databases and Google Scholar were searched for articles published in the English language. Independent review authors selected and screened studies. Appraisal for methodological quality of studies was conducted using the Joanna Briggs Institute assessment checklist. RevMan 5.3 software was used for meta-analysis. The I^2 statistical significance and Egger's test were used to assess heterogeneity and publication bias, respectively.

Results: The pooled prevalence of premature rupture of the membrane among pregnant women in Ethiopia was 9.2% (95% confidence interval=5.0, 16.4). Factors significantly associated with premature rupture of the membrane were no antenatal care visit (odds ratio=2.87, confidence interval=1.34, 6.14), history of premature rupture of the membrane (odds ratio=4.09, 95% confidence interval=2.82, 5.91), history of abortion (odds ratio=3.13, confidence interval=1.63, 6.01), abnormal vaginal discharge (odds ratio=6.78, confidence interval=4.11, 11.16), and urinary tract infection (odds ratio=3.04, confidence interval=1.21, 7.63).

Conclusion: Nearly one in ten pregnancies in Ethiopia encounters premature rupture of the membrane complications. The finding highlights improving antenatal care utilization, thus preventing or treating urinary and reproductive tract infections, and tailored interventions for pregnant women with a history of premature rupture of the membrane or abortion contribute to reduced premature rupture of the membrane.

Keywords

Premature rupture of membrane, meta-analysis, Ethiopia

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Introduction

Premature rupture of the membranes (PROMs) are defined as the disruption of fetal membranes before the onset of labor, which is characterized by a painless gush of watery fluid out of the vagina.¹ A PROM that occurs before 37 and after 37 weeks of gestation is referred to as preterm and term premature rupture of membranes, respectively.^{2,3} The occurrence of PROM ranges from 5% to 15% of all pregnancies worldwide.^{4,5}

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Globally, preterm birth is among the three major causes of neonatal death,⁶ and PROM contributes to more than 40% of preterm deliveries⁷ and is linked with the cause of 18%–20% and 21.4% of perinatal mortalities and morbidity, respectively.^{8,9} It is a significant cause of perinatal, neonatal, and maternal morbidity and mortality both in high- and low-income countries.¹⁰

Premature rupture membrane causes fetal distress (i.e. due to umbilical cord compression or placental abruption), sepsis, and intraventricular hemorrhage; it increases the risk of cesarean delivery due to non-reassuring fetal heart rate.^{9,11} In addition to significant mortality, PROM accounts for around 10%–40% of respiratory distress syndrome.^{12,13} It has been also related to the causes of long-term adverse neurodevelopmental outcomes such as visual or hearing difficulties, intellectual disabilities, developmental and motor delay, cerebral palsy, or death.^{12,14}

PROM contributes to maternal infections (15%–25%),¹⁰ chorioamnionitis (13%–60%), placental abruption (9%–12%), and increase risk of disseminated intravascular coagulopathy and operative deliveries.⁹ It rarely causes serious complications such as retained placenta, hemorrhage accompanied by dilation and curettage, and maternal death.^{15–17} The prevalence and impacts of PROM are disproportionately higher among adolescent women,¹⁸ where they account for more than 11% of births worldwide,¹⁹ suggesting that nutritional deficiencies may play an important role in this complication.²⁰ Furthermore, the burden of PROM is not limited only to maternal and neonatal mortality and morbidity but also causes a nationwide economic loss due to drug expense, hospitalization, and burden to the health professionals.^{7,14}

Several strategies such as preparing a training manual and guidelines on Basic Emergency Obstetric and Newborn Care to enhance the competency of health professionals in managing obstetric emergencies including PROM, capacitating health facilities, and free maternity service decree to tackle maternal and neonatal mortality were implemented in Ethiopia.^{21,22} Thus, a significant stride has been made in the past decade in the reduction of maternal and neonatal mortality from 871 per 100,000 and 49 per 1000 in 2000 to 412 and 28 in 2016, respectively.²³ However, maternal and neonatal mortality remained unacceptably high in the world; and to date, the decline for neonatal mortality remained stagnant.²⁴ Furthermore, PROM is responsible for the significant causes of adverse birth outcomes and common contributor to the three leading causes of neonatal mortality such as preterm birth (26%), intrapartum-related complications (30%), and sepsis (18%) in Ethiopia.^{25,26} Therefore, failure to improve birth outcomes by 2035 will result in an estimated 116 million deaths and 99 million survivors with disability in the globe.²⁷ Moreover, the complication of PROM such as low birth weight, birth asphyxia, neonatal infection, puerperal sepsis, and chorioamnionitis is among the serious public health problems in Ethiopia.²⁸

The primary studies in Ethiopia indicated a varying prevalence of PROM, that is, 3.8% in Oromia²⁹ and 23.5% in the

Harari Region.³⁰ Moreover, the studies found inconsistent factors associated with PROM, that is, studies stated that history of abortion,^{13,31} history of smoking,⁷ abnormal vaginal bleeding,^{13,32} and urinary tract infection (UTI)³² were associated with PROM. On the contrary, abnormal vaginal bleeding,^{7,30} history of smoking,¹³ and UTI^{13,30} were not significantly associated with PROM in Ethiopia.

Therefore, robust data on the burden of PROM and its associated factors would offer strong evidence for policy-makers and program managers to design programs and strategies to prevent neonatal and maternal complications. Hence, this systematic review and meta-analysis aimed to determine the pooled prevalence of PROM and associated factors among pregnant women in Ethiopia.

Materials and methods

The current systematic review and meta-analysis was written following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline checklist³³ (Supplemental file, Table S1).

Eligibility criteria

All peer-reviewed observational (cross-sectional, case-control, and cohort) studies conducted in Ethiopia reported prevalence and/or associated factors of PROM among pregnant women, studies that defined PROM as loss of amniotic fluid before the onset of labor but after fetal viability (>28 weeks of gestation), and English language articles regardless of publication period were eligible. However, studies that reported the outcome of interest emanated from review, commentary, fact sheet, and policy brief was not eligible.

Search and identification of studies

Articles were independently searched systematically from PubMed, Scopus, and African Journals Online (AJOL) databases and Google scholar using appropriate keywords. Database-specific subject headings and free-text terms (premature rupture of membrane OR prelabor rupture of membrane OR premature rupture of fetal membrane OR PROM) AND (risk factors OR determinants OR epidemiological factors OR precipitated factors OR protective factors OR correlates OR predictors) AND Ethiopia were used as appropriate search terms (Supplemental file, Table S2). The two review authors (G.T. and A.M.) independently searched for both published and unpublished studies available until 23 February 2021 G.C.

Study selection

The study selection process had several steps. First, the title and abstract were selected independently by two review authors (G.T. and A.M.) based on eligibility criteria. Second,

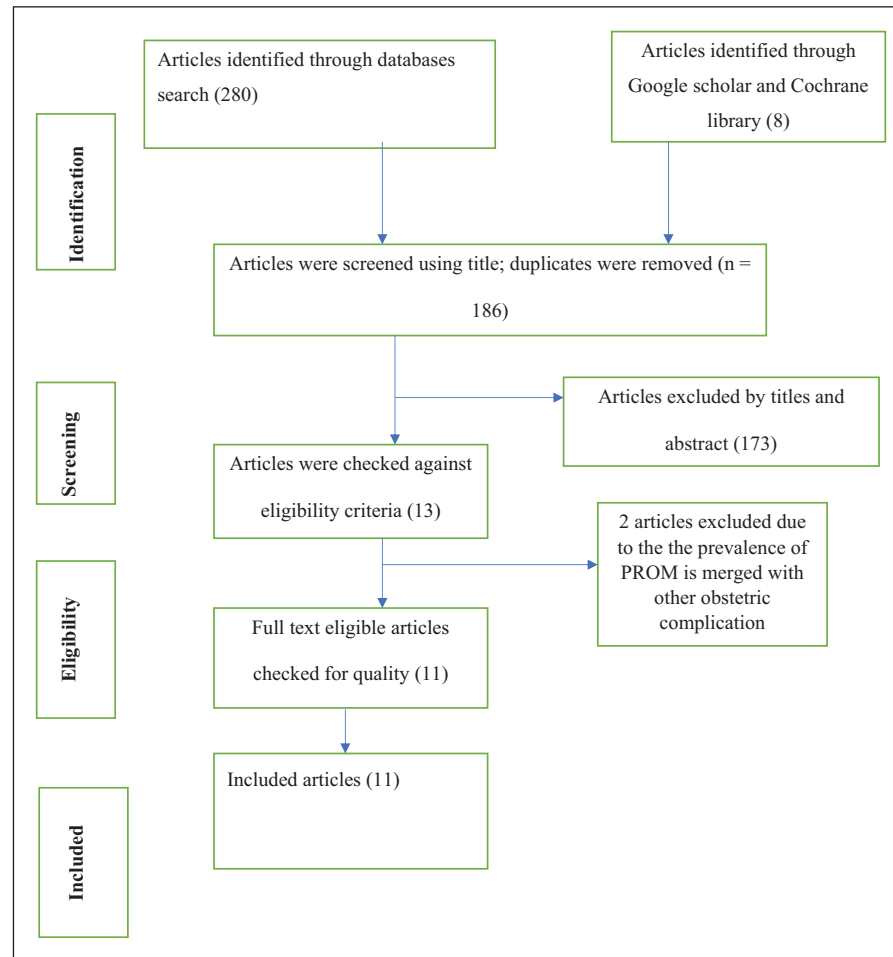


Figure 1. Flowchart showing the procedure of selecting studies for the systematic review and meta-analysis, until 23 February 2021.

removing the duplicates, the potentially relevant full-text articles based on the predetermined eligibility criteria were selected through discussion. In the case of disagreement between review authors on the status of studies, the other review authors (K.S., A.K.T., or A.D.) were consulted for the final decision. Finally, the full-text eligible articles were checked for quality. The overall selection process of the studies is available on the PRISMA flow diagram (Figure 1).

Data extraction

The data extraction template was prepared using a Microsoft Excel spreadsheet to record data. The characteristics of the study such as author(s), year of publication, study design, sample size, study setting, regions, and events or cases of PROM were extracted for each article (Table 1).

Outcome measure

The primary outcome of this review was the prevalence of PROM. The secondary outcomes include determinants of PROM such as antenatal care (ANC) visit, history of abor-

tion, history of PROM, UTI, and abnormal or sexually transmitted infections (STIs).

Study quality

The methodological quality of included studies was assessed using the Joanna Briggs Institute (JBI) assessment checklist for cross-sectional and case-control studies.³⁴ The eight criteria were rated for cross-sectional studies, that is, (1) criteria for inclusion, (2) study subjects and the setting described, (3) exposure measured validly and reliably, (4) standard criteria used for measurement, (5) confounding factors identified, (6) strategies to appropriate statistical analysis deal with confounding factors, (7) outcomes measured validly and reliably and (8) appropriate statistical analysis. Similarly, case-control studies were rated using 10 criteria, that is, (1) comparable groups, (2) cases and controls matched, (3) the same criteria used for identification, (4) exposure measured in a standard, valid, and reliable way, (5) exposure measured in the same way for cases and controls, (6) confounding factors identified, (7) strategies to deal with confounding factors, (8) outcomes assessed in a standard, valid, and reliable way for

Table 1. Descriptive summary of studies included in the meta-analysis of prevalence and associated factors of PROM in Ethiopia.

First author	Publication year	Study region	Study design	Sample size	Prevalence	Quality of the study
Tadesse et al. ²⁹	2017	Oromia	Cross-sectional	807	3.8	Low risk
Addisu et al. ³²	2020	Amhara	Cross-sectional	424	13.8	Low risk
Woyessa et al. ³¹	2020	Oromia	Cross-sectional	284	13.4	Low risk
Yadeta et al. ³⁰	2020	Harari	Cross-sectional	1688	23.5	Low risk
Mirkuzie et al. ³⁹	2016	Addis Ababa	Cross-sectional	2820	19.7	Low risk
Endale et al. ⁴¹	2016	SNNPR	Cross-sectional	4525	4.1	Low risk
Diriba et al. ⁵	2017	Oromia	Cross-sectional	2896	14.6	Low risk
Woldegeorges et al. ⁴²	2019	Tigray	Cross-sectional	212	13.7	Low risk
Sirak et al. ⁴⁰	2014	Addis Ababa	Cross-sectional	8283	1.4	Low risk
Workineh et al. ⁷	2017	SNNPR	Case-control	298	–	Low risk
Assefa et al. ¹³	2018	Tigray	Case-control	2440	–	Low risk

PROM: premature rupture of the membrane; SNNPR: South Nations, Nationalities, and People's Republic.

cases and controls, (9) the exposure period of interest long enough, and (10) appropriate statistical analysis. Finally, studies that scored 50% and above in the quality assessment indicators both for cross-sectional and case-control checklist were considered as low risk and included in the analysis (Supplemental file, Table S3).³⁵ Two review authors (G.T. and A.M.) independently rated the quality of the eligible studies. The review authors (K.S., A.K.T., or A.D.) was consulted in case of disagreements.

Statistical analysis

The characteristics of included studies were tabulated. Quantitative synthesis of the pooled estimate was computed using RevMan version 5.3 software. The association between PROM and possible factors was reported using odds ratios with a 95% confidence interval. Random effect models were fitted³⁶ to pool the prevalence of PROM and its associated factors among pregnant women. The level of heterogeneity was determined using the *I*-squared statistic (I^2).³⁷ Egger's regression intercept was used to identify publication bias and its presence was declared at a *p*-value less than 0.³⁸

Results

As shown in Figure 1, a total of 288 articles were identified during the initial search, of which 13 articles were assessed against eligibility criteria. Two articles were excluded, and the prevalence of PROM is merged with other obstetric complications. Finally, 11 articles were included in this systematic review and meta-analysis (Figure 1).

Characteristics of included studies

A total of 11 studies with 24,677 sample sizes were included, of which nine were cross-sectional,^{5,29–32,39–42} and two were case-control studies.^{7,13} The studies included in this

systematic review and meta-analysis were from five regions and one city administration of the country (Table 1).

Prevalence of PROM

We included nine cross-sectional studies that reported the proportion of PROM in the pooled prevalence of PROM among pregnant women in Ethiopia. The total sample size of the included studies was 21,939, of which 1828 pregnancies were complicated by the PROM. Therefore, the pooled prevalence of PROM in this study was 9.2% (95% confidence interval (CI)=5.0, 16.4) among pregnant women in Ethiopia. However, a substantial heterogeneity was observed among the included studies ($I^2=99.3%$, p -value < 0.01).

Sub-group analysis

To identify possible sources of heterogeneity, subgroup analysis was done based on sample size, study region, and study setting. The heterogeneity that was present in the overall meta-analysis was partially explained with stratification by sample size. For example, in a subgroup analysis of sample size <500 (odds ratio (OR)=13.6 (95% CI=11.2, 16.3); p -value=0.90; for heterogeneity test, $I^2=0%$) was not statistically heterogeneous (Table 2).

Factors associated with premature rupture of membrane

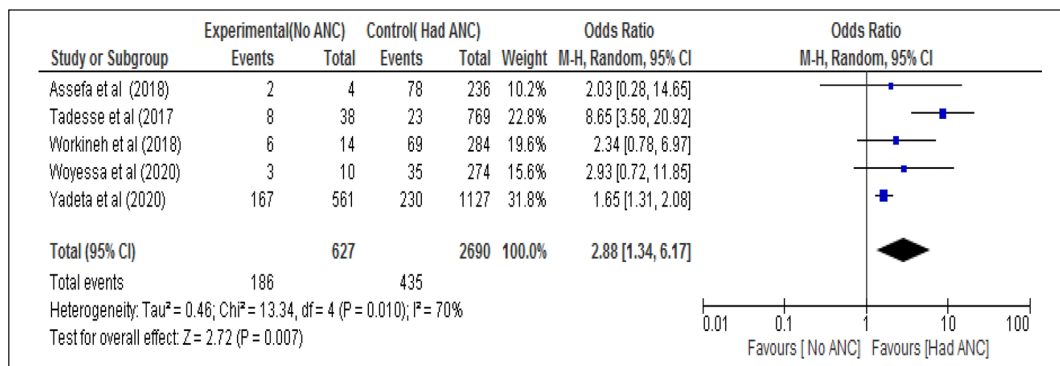
Antenatal care

The association between not receiving ANC and PROM was examined using five studies.^{7,13,29–31} Although statistically significant heterogeneity was observed ($I^2=69.6%$; p -value =0.27), women who did not receive ANC during the current pregnancy had 2.88 times increased odds of developing PROM compared to their counterparts (OR=2.88, 95% CI=1.34, 6.17) (Figure 2).

Table 2. Subgroup analysis of the prevalence of PROM in Ethiopia.

Variable	Characteristics	Number of studies	Sample size	Prevalence (95% CI)	Heterogeneity
By region	Oromia	3	3987	9.3 (4.3, 18.9)	96.5
	Amhara	1	424	13.7 (10.3, 17.3)	–
	Harari	1	1688	23.5 (21.6, 25.6)	–
	Addis Ababa	2	11,103	5.5 (0.3, 49.7)	99.8
	SNNPR	1	4525	4.1 (3.5, 4.7)	–
	Tigray	1	212	13.7 (9.7, 19.0)	–
By sample size	<500	3	708	13.6 (11.5, 16.0)	0.00
	500–1000	1	807	3.8 (2.7, 5.4)	–
	>1000	5	20,212	8.6 (3.6, 19.3)	99.3
Study setting	General Hospital	4	1727	10.1 (5.5, 17.6)	93.1
	Tertiary Hospital	3	15,704	4.4 (1.1, 16.4)	99.6

PROM: premature rupture of the membrane; CI: confidence interval; SNNPR: South Nations, Nationalities, and People's Republic.

**Figure 2.** Forest plot showing the pooled effect of ANC on PROM in Ethiopia.

Previous history of PROM

This group of analyses was conducted using four studies.^{13,30–32} The meta-analysis indicated that women with a history of the previous PROM were at increased odds of developing PROM. Accordingly, women who had a history of PROM were 4.09 times more likely to develop PROM compared to their counterparts. Moderate heterogeneity was detected among the included studies ($I^2 = 57\%$) (Figure 3).

History of abortion

Three studies^{13,30,31} included in this meta-analysis revealed that women who had a history of abortion had 3.13 times increased odds of PROM (OR=3.13, 95% CI=1.63, 6.01) compared to their counterparts. In this review, a statistically significant high heterogeneity was observed among the included studies ($I^2 = 76\%$), but Egger's test showed no evidence of publication bias (p -value=0.106) (Figure 4).

UTIs

As indicated in Figure 5, the pooled effect of two included studies^{31,32} illustrated that women who had UTI had 2.96

times increased odds of developing PROM (OR=2.96, 95% CI=1.08, 8.09) compared to their counterparts (Figure 5).

Abnormal vaginal discharge

The pooled analysis of two studies identified that the odds of developing PROM were 6.78 times more common among pregnant women who had vaginal discharge compared to their counterparts (OR=6.78, CI=4.11, 11.16) (Figure 6).

Publication bias

In the pooled analysis of prevalence studies, Egger's regression test revealed no evidence of publication bias among the included studies (p -value=0.30). Similarly, there was no publication bias among the included studies in the factor analysis. Hence, no major threat to the validity of the review.

Discussion

A disproportionate burden of prematurity due to PROM leads to increased neonatal mortality and morbidity in Sub-Saharan African countries.^{43,44} In Ethiopia, PROM is one of the major causes of prematurity and infection, which in turn

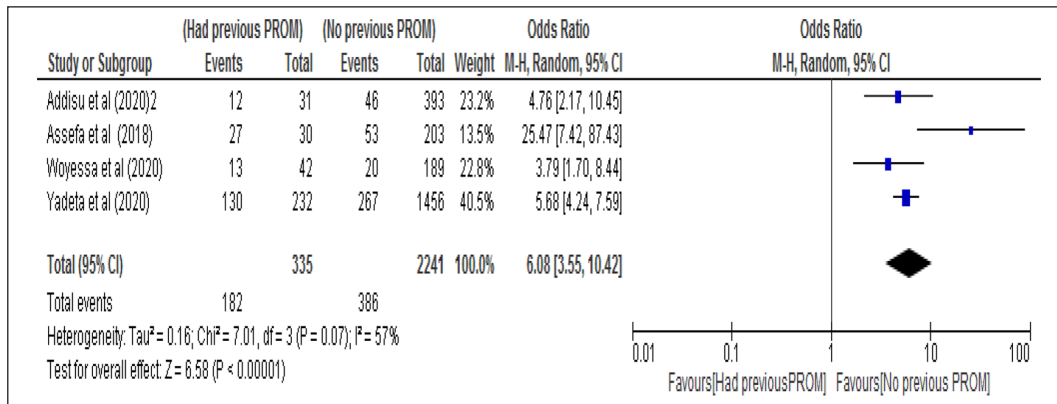


Figure 3. Forest plot showing the pooled effect of the previous PROM on premature rupture of the membrane in Ethiopia.

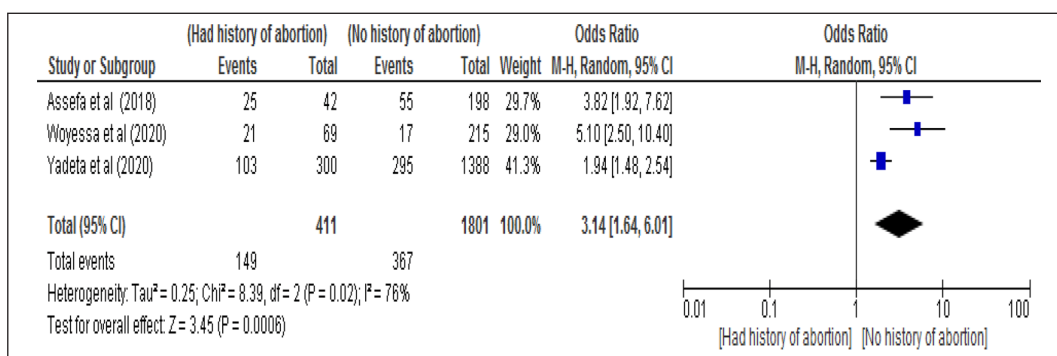


Figure 4. Forest plot showing the pooled effect of abortion history on PROM in Ethiopia.

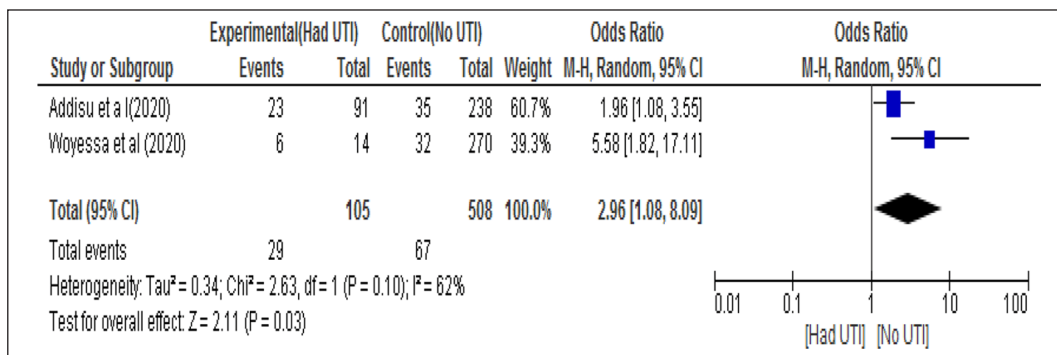


Figure 5. Forest plot showing the pooled effect of UTI on PROM in Ethiopia.

are the leading cause of neonatal death.^{13,28} In addition, puerperal infection, chorioamnionitis, and disseminated intravascular coagulopathy are among the causes of maternal sufferings linked with PROM.⁴⁵ Hence, the impact of PROM on neonatal and maternal mortality indicates a need for pooled data on factors related to PROM in Ethiopia.

In this systematic review and meta-analysis, the estimated pooled prevalence of PROM among pregnant women in Ethiopia was found to be 9.2%. Our finding is in the range of worldwide prevalence of PROM which ranges from 5% to

15%.⁴ A study from Indonesia also reported relatively similar findings (10%).⁴⁶ However, our finding was substantially higher than the global systematic review and meta-analysis report conducted in 2020 (4.33%).⁴⁷ The possible explanation for this discrepancy may be due to the differences in the accessibility and the quality of maternity services they deliver for early screening, preventive measures, and treatments of risk factors for PROM.⁴⁸ It is also important to note that in Ethiopia where the coverage and quality of maternity care services are low,²³ women will not have an adequate

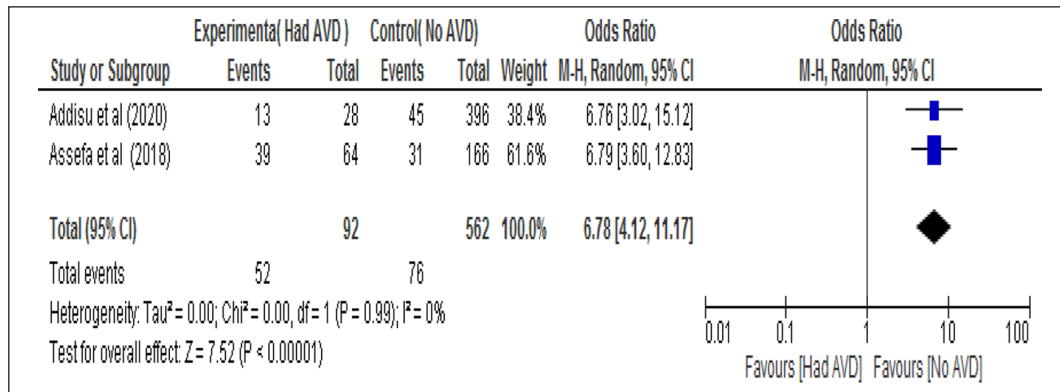


Figure 6. Forest plot showing the pooled effect of abnormal vaginal discharge on PROM in Ethiopia.

opportunity to get counseling and health education about the likely risk factors of PROM and early treatment measures for asymptomatic reproductive and UTI during pregnancy. In addition, sociodemographic differences such as comparatively low socioeconomic status, geographical barriers in accessing health care and cultural differences in health seeking behaviors may further aggravate the occurrence of PROM in Ethiopia.

In congruent with previous studies, women who had ANC follow-up had decreased odds of developing PROM.¹⁵ This is because ANC is a universally accepted strategy to reduce pregnancy complications by promoting and maintaining the optimal health of the woman throughout her pregnancy.⁴⁹ It offers an opportunity for preventive measures and treatments to the causes of genital tract infection which is the likely risk factor for PROM.⁵⁰ In addition, ANC provides an opportunity for health promotion and counseling on risk reduction on the potential predisposing factor of PROM such as nutritional advice, personal hygiene, and avoid behavioral risk factors (i.e. smoking and substance use) during pregnancy.⁵¹

Similarly, women who had a history of abortion had increased odds of developing PROM compared to women with no history. Studies in China⁵² and Uganda⁵³ also reported that women who had a history of abortion were more likely to develop PROM. This could be due to women who had a history of abortion may be predisposed to increase systemic inflammation and stimulation of the infection pathway or increased risk of intra-amniotic infection and intra-partum infection.^{14,31} Cervical trauma from mechanical dilatation during an abortion may increase the risk of cervical incompetence facilitating upper genital tract infection which spread to intra-amniotic infection following pregnancy¹²; or this association is further explained by, women who have had an abortion in the past, especially multiple abortions, are more likely to have a short cervix, which has been linked to an increased risk of PROM.^{54,55}

The history of PROM was the strongest predictor for premature rupture of membranes in this study. Thus, women who had a previous history of PROM have a 6.08-fold increased odds of developing premature rupture of membrane. A similar

association has been noted in past studies.⁵⁶⁻⁵⁸ This may be due to the recurrence of risk factors for PROM in the study participants such as cervical incompetence and connective tissue disorders, and prior untreated genitourinary infection.¹²

The pooled analysis showed that UTI and vaginal discharge were predictors of PROM. The findings of this review bear similarity among studies reported from Uganda⁵³ and Brazil.⁴⁸ Genital tract infection such as UTI and abnormal vaginal discharge, which is a common symptom of genital infections caused by a bacterial infection such as *Chlamydia trachomatis*, bacterial vaginosis, and *Neisseria gonorrhoeae*. These bacteria release inflammatory mediators or produce proteases, and phospholipases enzymes, and these inflammatory mediators or enzymes produced by genital infections are implicated in weakening of the fetal membranes among pregnant women, causing PROM.^{12,14,59} However, it has been suggested that intrauterine infection secondary to ascending genital tract colonization can lead to increased cytokine activity that enhances membrane apoptosis, production of proteases, and dissolution of the membrane's extracellular matrix.^{9,53} Generally, the study highlighted that reinforcing pregnancy care, tackling abortion-related risk factors, and preventing and treating urinary and genital tract infections would have paramount importance in reducing the public health impacts of PROM.

Strength and limitation of the study

The extensive searches of multiple databases without limiting the search to the study period and the inclusion of unpublished work in this meta-analysis that results in capturing more articles that addresses PROM in Ethiopia are the strength of the systematic review and meta-analysis. However, the absence of primary study representation across all regions of the country due to the unavailability of study from some regions was the limitation of this study. Regardless of these limitations, this study provided important information that is helpful to design an intervention for the reduction of PROM and its pregnancy complications among women and newborns in Ethiopia.

Conclusion

Nearly one in ten pregnancies was complicated by PROM in Ethiopia. The incidence of PROM depends on ANC visit, history of PROM, history of abortion, abnormal vaginal discharge, and UTI. Therefore, promoting utilization of ANC visits, early identification, and treatment of urinary and reproductive tract infection, tailored intervention for pregnant women with a history of abortion, and PROM play a substantial role in reducing PROM among pregnant women in Ethiopia.

Author contributions

G.T., A.M., and K.S. contributed to the conceptualization. G.T., A.M., and K.S. contributed to the methodology, software, formal analysis, validation, and data curation. G.T., A.M., A.K.T., K.S., and A.D. contributed to the investigation. G.T., A.M., and K.S. contributed to writing original draft preparation. G.T., A.M., and A.K.T. contributed to writing review and editing. All authors have read and agreed to the published version of the manuscript.

Declaration of conflicting interests

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Supplemental material

Supplemental material for this article is available online.

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