Preterm birth and its associated factors in Ethiopia: a systematic review and meta-analysis

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Abstract

Background: Preterm birth is a public health concern globally. In low- and middle-income countries, like Ethiopia, preterm birth is under reported and underestimated. Therefore, this systematic review and meta-analysis assessed the pooled prevalence and associated risk factors for preterm birth in Ethiopia.

Methods: In this review the databases used were PubMed, Google scholar, EMBASE, HINARI and African journal online. Publication bias was checked using a funnel plot and Eggers test.

Results: A total of 30 studies were included in this systematic review and meta-analysis. The overall pooled prevalence of preterm birth in Ethiopia was 11.4% (95% CI; 9.04, 13.76). On pooled analysis, preterm birth was associated with pregnancy-induced hypertension being HIV-positive, premature rupture of membrane, rural residence, the mother having a history of abortion, multiple pregnancies, and anemia during pregnancy.

Conclusion: The national prevalence of preterm birth in Ethiopia was low. Early identifying those pregnant women who are at risk of the above determinants and proving quality healthcare and counsel them how to prevent preterm births, which decrease the rate of preterm birth and its consequences. So, both governmental and non-governmental health sectors work on the minimization of these risk factors.

Keywords: Prevalence; pre-term birth; determinants; systematic review; meta-analysis; Ethiopia.

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Background

According to WHO definition, preterm birth is a birth that occurs before 37 completed weeks of conception or fewer than 259 days from the first date of a woman’s last menstrual period for singleton pregnancy. Based on gestational age, it is classified as extremely preterm (<28 weeks), very preterm (28 to < 32 wks.), and moderate to (32 to < 34 weeks) and late preterm (34 to 37 weeks). In other ways on the basis of birth weight, preterm can be classified as low birth weight (1500gm to <2500gm), very low birth weight (<1500 to 1000gm) and extremely low birth (<1000gm). In addition, on the basis of initiation of labor preterm birth can be categorized into two spontaneous or induced. Spontaneous preterm birth occurs when a pregnant mother goes into labor without the use of drugs or techniques to induce labor before 37 weeks of gestation. Induced preterm birth is a delivery involving labor induction, where drugs or manual techniques are used to initiate the process of labor before 37 weeks of gestation for maternal and fetal indications.

Globally, different studies reported that more than 15 million (11%) babies are estimated to be PTB each year and about 12 million (more than 81%) of these PTB occur in Sub-Sahara Africa and South Asia. Besides, the burden of pre-term birth ranges between 5% and 18% in the world. In the lower and middle-income countries, on average, 12% of babies are born premature compared with 9% in higher-income countries.
Studies conducted across the world identified risk factors associated with preterm birth, such as having a history of preterm birth, short cervical length, smoking, chronic cough, short inter-pregnancies interval, anemia, urinary tract infection, certain pregnancy-related complications (such as multiple-pregnancy, pregnancy-induced hypertension, vaginal bleeding, PROM, IUFD, IUGR, polyhydramnios, Oligohydramnious, congenital anomalies of the fetus), lack of antenatal care follow-ups, lifestyle factors (such as low pre-pregnancy weight, and substance use during pregnancy) 

Preterm babies can suffer lifelong effects such as cerebral palsy, mental retardation, visual and hearing impairments, poor health, and growth. Their developmental milestones are negatively affected. Preterm babies require prolonged hospital stay after delivery, repeated hospital admissions in the first year of life and increased risk of acute/chronic lung disease and putting their parents in social and financial problems.

**Methods**

**Reporting**
The report was written by using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.

**Searching Strategy and Information sources**
We have searched the following finding Items for this review (PRISMA) which was strictly followed by systematic review and meta-analysis guidelines. The databases used were PubMed, Google scholar, EMBASE, HINARI AJOL (African journal online). There were no restriction articles based on publication period. Searching engines were based on adapted PICO principles to search through the above-listed databases to access all the essential articles. To conduct a search of the literature databases, we have used Boolean logic, connectors “OR,” “AND” in combinations. The search strategy for the PubMed database was done as following: Magnitude of preterm birth “OR” prevalence of preterm birth” OR determinants of preterm birth” OR “risk factors of preterm birth “OR “magnitude of preterm birth “OR” prevalence of premature birth”(MeSH terms) AND birth “OR” parturition “OR” newborn (MeSH terms) “OR” infant AND Ethiopia AND “April 2009(PDat)-April 2020(PDat)”, stated below (Table 1)

| Databases                | Searching terms                                                                 | Number of studies |
|--------------------------|---------------------------------------------------------------------------------|-------------------|
| MEDLINE/PubMed           | “preterm birth” “OR” “premature birth” AND “determinants” “OR” predictors “OR” “risk factors” “OR” associated factors” | 303               |
| Google scholar           | “preterm birth” or” premature birth” and “determinants” or “associated factors” “OR” or “risk factors” and “Ethiopia” | 30                |
| From other databases     | From hand searching using back and front searching and EMBASE                   | 207               |
| Total retrieved articles  |                                                                                  | 540               |
| Number of included studies|                                                                                 | 30                |

**Inclusion and exclusion criteria**
Cross-sectional, cohort, and case–control studies were included. Articles included in this review were reported the prevalence, or magnitude and associated factors, or determining factors among mothers who were giving birth. Articles were included that were published only in English language literature, published from 2009-2020. Articles without full text and inaccessibility of abstract, commentaries, letters, duplicated studies, anonymous reports, and editorials were excluded.

**Data extraction and Risk of bias**
Findings from all databases were exported to Microsoft Excel spreadsheet. Two reviewers (FW, GG) independently extracted the data and reviewed the screened articles. Differences were recon reviewers (FY, SA &AA). Finally, the consensus was reached through a discussion between reviewers. Newcastle-Ottawa Quality Assessment Scale (NOS) for cross-sectional, cohort, and case–control studies were used to assess the methodological quality of a study and to determine the extent to which a study addressed the possibility of bias in its design, conduct, and analysis. All reviewers independently assessed the articles which were included in the review. The average mean score for the cross-sectional studies was 8.91 out of 11, for case–control stud-
ies 10.66 out of 22 and Cohort study 14 out of 22. No study that scored below the cutoff point was excluded from the review. All of the included articles scored (NOS) 7 and more can be considered a “good” study and have a low risk of bias for cross-sectional studies and 9 or more scores for case-control and cohort chosen to indicate a high standard for comparative observational studies, stated (S1 Table given below, S2 Table and S3 Table). The last search date was Apr15,2020.

**Data collection process**
Two independent reviewers (FW, GG) extracted data by using structured data extraction form. The name of the first author, year of study, year of publication, study of region, study area, study design, sample size, the prevalence rate, determinants of preterm birth, and AOR (95% CI) were extracted.

**Outcome of measurement**
The measurement outcome of this study had two main outcome variables. The prevalence of preterm birth was the primary outcome of the study, whereas associated factors/determinant for preterm birth were the second outcome variable. The odds ratio was calculated for the common factors of the reported studies. The most common associated factors included in this systematic review and meta-analysis were pregnancy-induced hypertension, being HIV-positive, premature rupture of membrane, rural residence, mother having a history of abortion, anemia during pregnancy and multiple pregnancy.

**Publication bias and heterogeneity**
Heterogeneity was checked using I² and its corresponding p-value. A value of 25%, 50%, and 75% was used to state the heterogeneity test as low, moderate and marked heterogeneity, respectively. The random effect model of analysis was used with the evidence of heterogeneity. Funnel plot and Egger regression test was used to check the existence of publication bias. Sub-group analysis, trim fill and sensitivity analysis were employed to select the most influential risk factors and avoid evidence of publication bias.

**Data analysis**
Stata 11 software with forest plots were used to report the estimated pooled prevalence and determinants of each study with the 95% confidence interval (CI). We have conducted subgroup analysis by sample size of participants and year of publication of study due to marked heterogeneity I² =96.3%. We have also conducted Trim fill and sensitivity analysis to see the effects of a single study on the prevalence of preterm birth. Finally, the odds ratio with 95% CI of pregnancy induced hypertension, being HIV-positive, premature rupture of membrane, rural residence, mother having a history of abortion, anemia during pregnancy and multiple pregnancy were computed.

**Results**
**Description of eligible studies**
A total of 540 articles were retrieved related to preterm birth through electronic searches. Of those retrieved, 303 papers were from PubMed/MIDLINE, 30 from Google scholars, and 207 from other sources. From the total papers, 88 duplicate and 400 non-eligible papers were identified and excluded during the screening of the titles and abstracts. The remaining 42 articles were given full test review, resulting in 30 papers being considered appropriate and eligible for analysis. Twelve articles were excluded based on the exclusion criteria stated below (Fig. 1).
Characteristics of the included studies

As a result, 30 studies were met the inclusion criteria to undergo the final systematic review and Meta-analysis. This systematic review and Meta-analysis consist of 23 cross-sectional, 6 case-control and 1 cohort studies with total 17,403 study participants in different regions in Ethiopia (Table 2).
### Table 2: Study characteristics included in the systematic review and meta-analysis in Ethiopia (n = 30).

| Authors                    | Year of study | Region       | Study Design      | Sample size | Quality status |
|----------------------------|---------------|--------------|-------------------|-------------|----------------|
| Abebe T et al. (35)        | 2016          | Addis Ababa  | Cross-sectional   | 384         | Low risk       |
| Abebayehu M et al. (36)    | 2018          | Amhara       | case-control      | 405         | Low risk       |
| Mulukn D et al. (37)       | 2017          | Amhara       | case-control      | 417         | Low risk       |
| Gebrekiros A et al. (38)   | 2018          | Tigray       | Cross-sectional   | 472         | Low risk       |
| Dawit G et al (39)         | 2016          | Amhara       | Cross-sectional   | 548         | Low risk       |
| Demelash W et al(40)       | 2017          | Oromia       | Cross-sectional   | 325         | Low risk       |
| Kahsay G et al(41)         | 2016          | Amhara       | Cross-sectional   | 540         | Low risk       |
| Bekele I et al(42)         | 2015          | Oromia       | Cross-sectional   | 220         | Low risk       |
| Hayelom G et al(43)        | 2014          | Tigray       | Cohort            | 1152        | Low risk       |
| Bayew K et al(44)          | 2018          | Tigray       | Cross-sectional   | 325         | Low risk       |
| Tesfaye B et al(45)        | 2018          | Tigray       | Cross-sectional   | 413         | Low risk       |
| Girmay T et al(46)         | 2017/2018     | Tigray       | case-control      | 264         | Low risk       |
| Samuel D et al(47)         | 2018          | SNNPR        | case-control      | 280         | Low risk       |
| Melkamu B et al(48)        | 2014-2016     | Oromia       | Cross-sectional   | 1400        | Low risk       |
| Sheka Shemisi et al(49)    | 2017          | Oromia       | case-control      | 656         | Low risk       |
| Tigist B et al(50)         | 2013          | Amhara       | Cross-sectional   | 422         | Low risk       |
| Ayenew E et al(51)         | 2018          | Amhara       | Cross-sectional   | 325         | Low risk       |
| Akilew A et al(52)         | 2013          | Amhara       | Cross-sectional   | 481         | Low risk       |
| Abdo et al(53)             | 2015          | SNNPR        | Cross-sectional   | 327         | Low risk       |
| Abera H et al(54)          | 2015-2016     | Tigray       | Cross-sectional   | 425         | Low risk       |
| Cherie N et al (55)        | 2017          | Amhara       | Cross-sectional   | 462         | Low risk       |
| Tsegaye and Kassa(56)      | 2017          | SNNPR        | Cross-sectional   | 589         | Low risk       |
| Abdo RA et al(57)          | 2019          | SNNPR        | Cross-sectional   | 313         | Low risk       |
| Abebe E et al(58)          | 2012-2013     | Amhara       | Cross-sectional   | 3003        | Low risk       |
| Tsegaye L et al (59)       | 2017          | SNNPR        | Cross-sectional   | 718         | Low risk       |
| Getachew M et al(60)       | 2018          | Amhara       | Cross-sectional   | 1134        | Low risk       |
| Eshete A et al(61)         | 2009          | Amhara       | Cross-sectional   | 295         | Low risk       |
| Hailemariam Workie(62)     | 2015          | Tigray       | case-control      | 340         | Low risk       |
| Eskeziaw A et al(63)       | 2017          | Amhara       | Cross-sectional   | 462         | Low risk       |

**Prevalence of preterm birth among mothers who gave birth at health institutions in Ethiopia**

The overall pooled prevalence of preterm birth in Ethiopia is presented with a forest plot (Fig.2). Therefore, the pooled estimated prevalence of preterm birth in Ethiopia was 11.4% (95% CI; 9.04, 13.76; I²=96.3%, P≤0.001).
Subgroup analysis
Subgroup analysis was done with the evidence of heterogeneity. Hence, the Cochrane I² statistic =96.3\%, \( P \leq 0.001 \) with evidence of marked heterogeneity. Therefore, subgroup analysis was conducted using the sample size of participants and year of publication of the articles. Based on the subgroup analysis, the prevalence of preterm birth in Ethiopia was 10.73\% (95\% CI: 7.67, 13.79) I²=97.3\%, \( P \leq 0.001 \) in which sample size was \( \geq 400 \) (Table 3).

| Variables            | Subgroup | No of studies | Prevalence\% (95\%CI) | I²(\%) | P-value |
|----------------------|----------|---------------|------------------------|--------|---------|
| Sample size          | \( \geq 400 \) | 15            | 10.73(7.67,13.79)      | 97.3   | \( P \leq 0.001 \) |
|                      | \(< 400 \) | 10            | 12.48(8.56,16.40)      | 93.1   | \( P \leq 0.001 \) |
| Year of publication  | 2014-2018 | 16            | 10.98(8.12,13.85)      | 95.7   | \( P \leq 0.001 \) |
|                      | \( \geq 2019 \) | 9             | 12.15(7.74,16.57)      | 97.2   | \( P \leq 0.001 \) |

Publication bias
A funnel plot was assessed for the asymmetry distribution of preterm birth among mothers who gave birth at health institutions in Ethiopia by visual inspection. Egger's regression test showed with a p-value of 0.003 indicated for the existence of publication bias. Hence, trim and fill analysis was conducted to overcome the publication bias. Eleven studies filled with 25 studies and overall, 36 studies were enrolled and computed through the trim and fill analysis with a pooled prevalence of 6.52\% (95\% CI; 3.97-9.07) using a random effect model (Fig. 3 a & b).
Sensitivity analysis

This review showed that the point estimate of its omitted analysis lies under the confidence interval of the combined analysis (Fig 4).

Figure 3: Funnel plot of publication bias a (before an adjustment)

Figure 3. b (after trim-fill analysis was computed)
Risk factors associated with preterm birth among mothers who gave birth at health institutions in Ethiopia
The most common associated factors included in this systematic review and meta-analysis were pregnancy-induced hypertension, being HIV-positive, premature rupture of membrane, rural residence, mother having a history of abortion, multiple pregnancy, and anemia during pregnancy.

Women who have pregnancy-induced hypertension (AOR: 5.11, 95%CI: 3.73, 7.01) was positively associated with preterm birth. No heterogeneity (I²=0.0%; p-value=0.872) was detected among the included studies; due this reason, the fixed effect model was calculated. Moreover, the possibility of publication bias was not detected using Egger's tests with a p-value of 0.568.

Women who is HIV-positive were the predictors of preterm birth (AOR: 4.74; 95%CI: 2.79, 8.05). No heterogeneity (I²=0.0%; p-value=0.629) was detected among the included studies; for this reason, the fixed effect meta-analysis model was computed. Moreover, no possibility of publication bias was detected using Egger's tests with a p-value of 0.595.

We found that women who had premature rupture of membrane four times (AOR: 5.36, 95%CI: 3.76, 7.64) greater at increased risk the likelihood of having a preterm birth compared to their counterparts. Moderate heterogeneity (I²=56.8%; p-value=0.031) was detected among the studies. Therefore, random effect model meta-analysis was employed. Furthermore, no possibility of publication bias was detected using Egger's tests with a p-value of 0.762.

Being a rural residency was one the significant risk factor for preterm birth (AOR: 2.35, 95%CI: 1.56, 3.55). No heterogeneity (I²=0.0%; p-value=0.839) was detected among the included studies; for this reason, the fixed effect meta-analysis model was computed. Moreover, no existence of publication bias was declared using the Egger's tests with a p-value of 0.314.

Pregnant women who were anemic (AOR: 3.41, 95%CI: 2.1, 5.56) were positively associated with preterm birth. Low heterogeneity (I²=26.9%; p-value=0.251) was detected among the included studies; for this reason, the random effect meta-analysis model was computed. Furthermore, publication bias was not detected using Egger's tests with a p-value of 0.657.

Pregnant women who have two or more fetus intrauterine (AOR: 3.60 95%CI:2.49, 5.19) were positively associated with preterm birth. No heterogeneity (I²=0.0%; p-value=0.429) was detected among the included studies; for this reason, the fixed effect meta-analysis model was computed. Furthermore, publication bias was not detected using Egger's tests with a p-value of 0.835.

Figure 4: Sensitivity analysis of the pooled prevalence of preterm birth in Ethiopia
Women having a history of abortion (AOR: 2.92, 95%CI: 1.91, 4.47) were the determining factor of preterm birth. No heterogeneity (I²=0.0%; p-value=0.726) was detected. Hence, the fixed effect meta-analysis model was computed. Furthermore, the existence of publication bias was not detected using Egger's tests with a p-value of 0.835(Table. 4).

| Variables                  | Model   | Egger test (P-value) | Status of heterogeneity | AOR (95%CI)   | I² (%) | P-value |
|----------------------------|---------|----------------------|-------------------------|---------------|--------|---------|
| PIH                        | Fixed   | 0.568                | No heterogeneity        | 5.11(3.73, 7.01) | 0.0    | 0.872   |
| HIV-Positive               | Fixed   | 0.595                | No heterogeneity        | 4.74(2.79, 8.05) | 0.0    | 0.629   |
| PROM                       | Random  | 0.762                | Moderate heterogeneity  | 5.36(3.76, 7.64) | 56.8   | 0.031   |
| Rural residence            | Fixed   | 0.314                | No heterogeneity        | 2.35(1.56, 3.55) | 0.0    | 0.839   |
| Hx of abortion             | Fixed   | 0.835                | No heterogeneity        | 2.92(1.91, 4.47) | 0.0    | 0.726   |
| Multiple pregnancy         | Fixed   | 0.835                | No heterogeneity        | 3.60(2.49, 5.19) | 0.0    | 0.429   |
| Anemia during pregnancy    | Random  | 0.657                | Low heterogeneity       | 3.41(2.1, 5.56) | 26.9   | 0.251   |

**Discussion**

In this meta-analysis, the overall pooled prevalence of preterm birth among mothers who gave birth at health institutions in Ethiopia was 11.4% (95% CI: 9.04,13.76). This finding agrees with studies conducted in Tanzania 13% 12, India 12.95% 13 and Brazil 13.7%. 14 The possible explanation might be due to the fact that endogenous prostaglandins released after ruptured membrane that initiates the uterine contraction, thereby cause preterm birth.

Abruptio placenta is another complication of pregnancy induced hypertension that may require termination of pregnancy as a lifesaving for both the mother and fetus. The study determined that women who had developed pregnancy-induced hypertension were 5.11-time (AOR: 5.11, 95%CI: 3.73, 7.01) greater risk with preterm birth than the counterpart. The finding is consistent with the study done in East Africa 22, China 21, India 17, Kenya (24), Nigeria 25, Brazil 26, and two different studies in Iran 19,20. The possible explanation might be due to the existing scientific evidence which speculates that Pregnancy induced hypertension is linked to vascular and placental damage, which in turn reduces placental blood flow and leads to uteroplacental insufficiency resulting in obstetric emergencies that require termination of pregnancy as a lifesaving for both the mother and fetus. Abruptio placenta is another complication of pregnancy-induced hypertension that may require termination of pregnancies 27.

This review showed that HIV-positive pregnant mothers were 4.7 times (AOR: 4.74, 95%CI: 2.79, 8.05) more at increased risk of having a preterm birth than negative mothers. This is in agreement with a study conducted in South Africa 28 and Tanzania 29. It could be explained by the effect of ART drugs and have low immunity status of the mother at greater risk for preterm birth.

We found that women who had premature rupture of membrane four times (AOR: 5.36, 95%CI: 3.76, 7.64) greater at increased risk the likelihood of having preterm birth as compared to their counterparts. This is in agreement with a study done in two different studies in Iran 19,20. Kenya 24, Nigeria 25 and India 17. This might be due to the fact that endogenous prostaglandins released after ruptured membrane that initiates the uterine contraction, thereby cause preterm birth.
Pregnant women who are living in rural areas 2.4 times (AOR: 2.35, 95% CI: 1.56, 3.55) more at increased risk for preterm birth than in urban areas, which is consistent with a study conducted in Kenya. This is the fact that pregnant women who are living in rural areas suffer from different risk conditions like face-unbalanced diet, walk a long distance for fulfilling their family’s needs, do extraneous work, and have poor access health care system, thereby distance from health facility that might contribute to preterm birth.

Pregnant women who were anemic (AOR: 3.41, 95% CI: 2.1, 5.56) were positively associated with preterm birth. This is in agreement with a study done in India, Malawi, China, and East Africa. This is because of the biological mechanisms of anemia, iron deficiency or both could cause preterm delivery. In fact, anemia and iron deficiency can induce stress and maternal infections, which in turn stimulate the synthesis of Corticotrophin-Releasing Hormone (CRH) that elevated CRH concentrations to be a known risk factor for preterm birth.

This review showed that multiple gestation has been associated with the increased likelihood of preterm birth (AOR: 3.60 95% CI:2.49, 5.19). This finding agrees with those studies done in Kenya, India, Iran. This might be due to multiple gestation is associated with uterine over-distension, which causes increased gap junction of myometrial muscles and induce the oxytocin receptors. Finally, it can initiate uterine contraction that is resulting preterm birth.

Another risk factor associated with preterm birth had a history of abortion (AOR: 2.92, 95% CI: 1.91, 4.47), which is consistent those studies done in Brazil, Iran and Tanzania. This is because during surgical evacuation of the uterus mechanically stretches the cervix could cause cervical incompetency, which in turn predispose preterm birth for subsequent pregnancies.

**Conclusion**
The national prevalence of preterm birth in Ethiopia was low. The most common associated factors included in this systematic review and meta-analysis were pregnancy-induced hypertension, being HIV-positive, premature rupture of membrane, rural residence, the mother having a history of abortion, multiple pregnancy, and anemia during pregnancy. This review can be used to base line for health policy makers, clinicians, and program officers to design action plan work for prevention and intervention measures on preterm birth. Early identifying those pregnant women who are at risk of the above determinants and proving quality healthcare and counsel them how to prevent preterm birth which may decrease the rate of preterm birth and its consequences.

**Abbreviations**
AOR-Adjusted Odd Ratio, ART-Anti-Retroviral Therapy, CI- Confidence interval, HIV-Human Immuno Deficiency Virus, PIH-Pregnancy Induced Hypertension, PROM-Premature Rupture of membrane.

**Declarations**

**Authors’ contribution**
FW, GG, and FY participated in the design, selection of articles, and data extraction. FW, SA and GG involved in statistical analysis. FW, SA and AA participated in writing the manuscript and all authors critically reviewed the manuscript. All authors read and approved the final version of the paper.

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**Availability of data and materials**
All related data have been presented within the manuscript.

**Ethics approval and consent to participate**
Not applicable

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**Competing interests**
All authors declare that they have no competing interests.
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