

# Prevalence of perinatal asphyxia and its associated factors in Ethiopia; A systematic review and meta-Analysis

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## Research article

**Keywords:** Birth asphyxia, perinatal asphyxia, associated factor, systematic review, Ethiopia

**Posted Date:** November 15th, 2019

**DOI:** <https://doi.org/10.21203/rs.2.17346/v1>

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# Abstract

**Background:** Perinatal asphyxia(PNA) is a severe health problem and main cause of neonatal mortality and morbidity worldwide. In Ethiopia, there are many studies conducted on PNA characterized by replete of inconsistent; unavailability of nation wide study to determines the prevalence of PNA and its determinants is an important gap. The aim of this study is to develop national consensus on pooled prevalence and associated factor key reports to enhance the quality and consistency of the evidence on perinatal asphyxia.

**Method:** Systematic review and meta-analysis using computerized databases; searches were performed to locate all articles on the prevalence of perinatal asphyxia. Databases included were Pub Med, Cochran library, Google Scholar, Scopus and Science Direct systematically between 2014 and April 2019. All identified studies reporting the prevalence of PNA in Ethiopia were pooled. Two independent authors extracted the data using a standardized data extraction tool. The Cochrane Q test statistics and I<sup>2</sup> tests were used to assess the heterogeneity of the studies. Random-effects model was used to calculate pooled estimates and determinant factor of PNA in Stata/se version-14.

**Result:** The prevalence of PNA reported from fifteen studies was in the range of 3.1 to 47.5%. The pooled occurrence of PNA in Ethiopia based on 15 articles with a sample size of 17,091 was 21.1% (95% CI: 14, 28). There was high heterogeneity observed (I<sup>2</sup> = 99.4%, p <0.001). Thus, Subgroup analysis in the study area was computed .Thus, the highest prevalence (40.4%) was observed from Oromia region and the lowest 8% noted from Dire Dawa city administration. Pooled odd ratio estimates from included studies revealed prolonged labour (OR=3.7, 95% CI 2.4, 5.7), low birth weight (OR=6.5, 95% CI 4.0, 10.3), and Meconium stained liquor (OR=6.6, 95% CI: 4.4, 10.1) are significant risk factors of perinatal asphyxia.

**Conclusion:** In this review, prolonged labour, meconium stained liquor and low birth weight are significantly associated with perinatal asphyxia. Therefore, improve facility-based intra partum care and quality neonatal resuscitation service through capacity building for health professionals is needed.

## Background

Perinatal asphyxia(PNA) is a lack of blood flow or gas exchange to or from the fetus in the period immediately before, during, or after the birth process(1, 2). Perinatal asphyxia can result in profound systemic and neurologic sequelae due decreased blood flow and/or oxygen to a fetus or infant during the peripartum period(3). According to World Health Organization in 2017, Worldwide 2.5 million children died in the first month of life that indicate high risk of dying in the first 28 days of life, during the neonatal period(4). The incidence of PNA is higher in developing countries (Sub-Saharan Africa and Southern Asia) where limited access to maternal and neonatal care(4, 5).

Currently, Ethiopia is one of the top five countries contributing more than half of the neonatal deaths globally (6). Perinatal asphyxia is one of the intrapartum related common and serious clinical complications at birth and contributes significantly to most neonatal deaths, which accounts 23%

globally(7, 8) and 34 % in Ethiopia at the top of prematurity (21.8%) and sepsis (18.5%).(5, 9, 10). Perinatal asphyxia could be reduced by facility-based skilled professional intra partum care and neonatal resuscitation service (11, 12). In addition PNA is the cause of short and long lasting morbidity for neonates' which accounts 12.5% of overall morbidity like hypoxic ischemic organ damage followed by severe life-long pathologies, neurodegenerative diseases, mental retardation, epilepsies, and life-long functional psychotic syndromes(9).

There are many studies with inconsistent findings in Ethiopia but there is no national wide study to determine the prevalence and associated factors of birth/perinatal asphyxia is identified as a gap. Therefore, the aim of this study is to develop national consensus on pooled prevalence and associated factor key reports to enhance the quality and consistency of the evidence on perinatal asphyxia. Hence, this review could be a base line for clinicians, stakeholders, and police maker to intervene on neonatal mortality and untreatable long-term morbidity.

## Methods

### *Study design*

Systematic review and Meta-analysis using computerized databases

### *Patient involvement*

Patients were not directly involved in the design of this study.

### *Design settings*

Ethiopia is found in Eastern Africa bounded by Kenya to the south, Eritrea to the north, Djibouti and Somalia to the east, and Sudan to the west. Currently, the Ethiopian population is estimated to be more 106 million and approximately 3 million babies have born every year (13).

### *Search strategy*

To find potentially relevant articles, a comprehensive search was carried out on Pub Med/MEDLINE, Google Scholar, Scopus, and Science Direct databases. We extended our search by retrieving reference lists of eligible articles, hand searches for grey literature and other relevant literature collections. The search of the literature was conducted between January and April 2019 and all studies published from April 2014 to April 2019 were considered. Search protocol was formulated by using common key words 'prevalence AND associated factor OR determinants AND birth asphyxia OR perinatal asphyxia OR neonatal asphyxia OR Neonates OR neonatal intensive care unit OR Hospitals AND Ethiopia. We presented this meta-analysis according to the scientific Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guide line (14)

### *Study population*

### *Inclusion criteria:*

*Study area:* All studies conducted in Ethiopia

*Study design:* All observational study designs reporting the prevalence of perinatal asphyxia

*Population:* Studies involving infants immediately before, during and after birth

*Language:* Only articles reported in English language

*Publication condition:* published articles

*Exclusion criteria:* Articles, which were not fully accessible to assess the quality.

### *Outcome variables*

Perinatal asphyxia and associated factors are the two main outcomes this study. The primary outcome prevalence of perinatal asphyxia was calculated as the total number of PNA divided by the total number of live birth infants in the study multiplied by 100. The second outcome variable associated factors are determinates in the form of the log odds ratio based on binary outcomes from primary studies.

### *Data Extraction*

All identified studies were extracted all necessary data from included articles using a standardized data extraction format adapted from the Joanna Briggs Institute (JBI), by two reviewers (GT and SA) independently. Discussions and mutual consensus were in place when possible points of view were raised. For our outcome, the data extraction format included primary author, publication year, regions of the country, study area, sample size and prevalence with 95% confidence interval.

### *Risk of bias and quality appraisal*

The risk of bias for included studies was assessed using the JBI's critical appraisal checklist for prevalence studies (15). In addition, the included articles were evaluated for quality by two authors (BGL and SA) independently and the reviewers compared their quality appraisal scores and resolved any discrepancy before calculating the final appraisal score by third authors (MAA). Only high quality studies were included in the analysis. To assess the quality of each study, the Newcastle-Ottawa Scale for cross-sectional and cohort studies was adapted (16). The tool has three sections; the first section focuses on the outcome and statistical analysis of each original study with a possibility of two stars to be gained. The second section graded from five stars and considers the credibility on the methodological quality of each original study. The third section of the tool deals with the comparability of the study cases or cohorts, with a possibility of two stars to be given. Articles with a scale of  $\geq 5$  out of 10 scales were considered as high quality. Consequently, all eligible studies had high quality scores.

### *Data processing and analysis*

Data on study design, sample size, and others were extracted in Microsoft Excel format, and then analysis was carried out using STATA/se Version 14 statistical software. Heterogeneity among reported prevalence was assessed by computing p-values of  $I^2$ -statics and Cochrane Q-test (17). The pooled prevalence of perinatal asphyxia was carried out with random effects meta-analysis model, generating the pooled 95% confidence interval by using the Der Simonian and Laird's methods. To minimize the random variations between the point estimates of the primary study; subgroup analysis was done based on study settings, study design and sample size. In addition, to identify the possible source of heterogeneity univariate meta-regression was undertaken. Publication bias was assessed by visually checking for asymmetry in funnel plots and objectively testing using Egger's test at 5% significant level. Point prevalence as well as 95% confidence intervals were presented in the forest plot format. In this plot, the size of each box indicated the weight of the study, while each crossed line refers to 95% confidence interval.

## Results

### *PRISMA flow chart*

We retrieved 384 articles regarding prevalence of asphyxia using Pub Med, Google Scholar, Scopus, and Science Direct. Lastly, 15 studies met the eligibility criteria and included in the final meta-analysis. As shown in the follow chart of study selection process (Fig.1)

### *Explanation for included studies*

As described in *Table 1*, these 15 studies were retrospective cohort and cross-sectional study design published between April 2014 and 2019. In the current meta-analysis, 17,091 study participants were represented. The prevalence of perinatal asphyxia reported was between 3.1% (18) and 47.5% (19) and the sample size of the studies ranged from 154(20) to 3684(21).

### *Prevalence of perinatal asphyxia in Ethiopia*

Prevalence of perinatal asphyxia in Ethiopia was 21.1% (95% CI: 14, 28). A high heterogeneity was observed across the included papers in forest plot ( $I^2 = 99.4\%$ ,  $p < 0.001$ ) (Fig. 2). As a result, a random effect meta-analysis model was computed to estimate the comprehensive prevalence of perinatal asphyxia. As described in *Table 2*, the region of the country where the study conducted, publication year, and sample sizes were investigated by using univariate meta-regression models to identify the possible sources of heterogeneity. However, none of the variables were found to be significant. Publication bias was assessed by funnel plot and slight presence of bias was represented substantial asymmetry (Fig.3). To confirm publication bias, objectivity Egger's test was employed and does not show the presence of small study effect ( $p = 0.26$ ).

### *Subgroup analysis*

In this meta-analysis, we computed subgroup analysis based on the study area/regions. Thus, the highest prevalence was determined in Oromia region 40.4% (95% CI: 26.1, 54.7), followed by the Tigray region

26.7% (95% CI: 18, 35.4) and the lowest was noted in Dire Dawa city administration 8% (95% CI: 2, 17.4) (Table 3).

### *Associated factors of perinatal asphyxia in Ethiopia*

In this meta-analysis, we studied the association between perinatal asphyxia and prolonged labor by using five studies (Fig. 4). The findings from these five studies showed that the prevalence of PNA was significantly associated with long duration labour above 24 hours. Consequently, the probability of PNA was 3.7 times higher among mothers who had long duration of labour as compared to its counter parts (OR = 3.7, 95% CI: 2.4, 5.7).

The association between meconium stained liquor and perinatal asphyxia based on studies (Fig.5) showed that the occurrence of PNA was associated with meconium stained liquor. Subsequently, the probability of PNA was 6.6 times higher among infants who had meconium stained liquor as compared to not having meconium stained liquor (OR = 6.6, 95% CI: 4.4, 10.1).

We have done the association between low birth weight and perinatal asphyxia by using five studies (Fig.6). The findings from these articles revealed that the pooled prevalence of perinatal asphyxia was significantly associated with low birth weight. Thus, the likelihood of PNA was 6.5 times higher among infants who had low birth weight as compared to its counter parts (OR = 6.5, 95% CI 4.0, 10.3).

## **Discussion**

Birth asphyxia is one of the intrapartum-related common and serious clinical complications at birth. To the best of our knowledge; this meta-analysis is the first of its kind to estimate the pooled prevalence of perinatal asphyxia and determinant factor in Ethiopia.

This study revealed that, overall prevalence of perinatal asphyxia is 21% (95% CI: 14, 28) in Ethiopia. The result of this meta-analysis is in line with a studies conducted in Gusau Nigeria (21.1%) (33), and Dare Salaam Tanzania (21.1%) (33). However, our finding is higher than reported by studies in Malawi (6.1%) (34), Cameroon (8.1%), and Iran (1%) (16). The possible explanation for the observed variations could be attributed to methodological difference of the study, maternal and child health service, and the sample size each study used had a great impact on the prevalence of perinatal asphyxia.

We did subgroup analysis by study area/region due to a significant heterogeneity finding. Thus, highest prevalence of perinatal asphyxia was determined in Oromia region 40.4%, followed by the Tigray region 26.7% and the lowest was noted in Dire Dawa city administration 8%. This variation could be the differences in accessibility of delivery institution, health seeking behavior, skill of health professionals, and behavioral characteristics of caregivers.

Meconium stained liquor was found statistically associated factor with perinatal asphyxia. This finding is in line with those of studies conducted in Nigeria, England, and Thailand (35–37). In healthy, well oxygenated fetuses, this diluted meconium is readily cleared from the lungs by normal physiological

mechanism. However, the Presence of meconium in the amniotic fluid might be lead to aspiration of meconium into the lung or air way obstruction that could eventually result in perinatal asphyxia.

In addition, prolonged labor was a risk factor for perinatal asphyxia. This result is consistent with the findings in India, Cameron, Pakistan, Nigeria, and Thailand (35, 38–41). This could be due to the prolonged labor can associated with fetal and maternal exhaustion and fetal distress and/or will be exposed to Pitocin, forceps/vacuum extractors which could be a cause for the baby to have PNA.

The other determinant factor of perinatal asphyxia is low birth weight. This study is congruent to the studies reported in Nepal, Thailand, Uganda and England (35, 37, 39, 42). The possible justification could be low-birth-weight infants often have pulmonary immaturity and limited respiratory muscle strength which will cause difficulty of birthing and cardiopulmonary transition(43). In contrary, high birth weight at birth (a proxy for birth weight) had been found an associated factor for birth asphyxia (44)

### *Strength and Limitations of the study*

Critical appraisal by three authors is the strength of the study. While the first limitation of the study was only English reports were considered to conduct this study. Some of the studies included in this review had a relatively small sample size. Besides, this meta-analysis represented only studies reported from five regions and two administrative town of the country.

## **Conclusion**

In this review, pooled perinatal asphyxia in Ethiopia was found high. Low birth weight, prolonged labor and meconium stained liquor are risk factor for PNA. Improve facility-based intra partum care and neonatal resuscitation service quality through capacity building for health professionals.

## **Abbreviations**

APGAR

Appearance Pulls Grimes Activity Respiration

CI

Confidence Interval

EDHS

Ethiopian Demography and Health Survey

JB

Joanna Briggs Institute

OR

Odd Ratio

PNA

Perinatal Asphyxia

## **Declarations**

### **Ethics approval and consent to participate**

Not applicable

### **Consent for publication**

Not applicable

### **Availability of data and material**

Minimal data could be accessed upon request from first author (MAA)

### **Competing interests**

The authors declare that they have no competing interests

### **Funding**

Not applicable

### **Author contributions**

MAA: Conception of research protocol, study design, literature review, data extraction, data analysis, interpretation and drafting the manuscript.

GT: Study design and contribute on data extraction, quality assessment, data analysis and manuscript review

BGL: contribute on data extraction, quality assessment, data analysis and manuscript review



SA: Study design, literature review, data extraction, data analysis, interpretation and manuscript review. All authors have read and approved the manuscript

## Acknowledgements

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## Tables

**Table1:** descriptive summary of studies included in the systematic review and meta-analysis in the prevalence of perinatal asphyxia in Ethiopia, 2019

Authorship (Reference)	Publication(yr)	Study Area/ Region	Study design	Mid- Study period	Sample	Prevalence at 95%CI
Ahmed et al. (8)	2017	Dire Dawa	Retrospective	2015.5	302	3.1(1.2,5.1)
Ahmed et al. (12)	2018	Somalia	Retrospective	2017	792	3.4(2.1,4.7)
Ahmed et al. (13)	2019	SNNP*	Retrospective	2016	964	26.2(23.5,29.0)
Ahmed et al. (21)	2015	Addis Ababa	Retrospective	2011	3684	13.8(12.7,14.9)
Ahmed et al. (24)	2017	Dire Dawa	Retrospective	2015	3418	12.7(11.6,13.9)
Ahmed et al. (30)	2018	Amhara	Cross sectional	2017	154	29.9(22.7,37.1)
Ahmed et al. (25)	2018	Tigray	Cross sectional	2018	423	22.1(18.2,26.1)
Ahmed et al. (26)	2018	Oromiya	Cross sectional	2015	371	32.9(28.1,37.7)
Ahmed et al. (27)	2017	Tigray	Cross sectional	2014	1152	31(28.3,33.7)
Ahmed et al. (28)	2017	Amhara	Cross sectional	2015.5	769	12.5(10.5,14.8)
Ahmed et al. (29)	2014	Oromiya	Cross sectional	2012.5	3604	47.5(45.9,49.1)
Ahmed et al. (29)	2017	Amhara	Cross sectional	2013	261	16(11.6,20.5)
Ahmed et al. (30)	2016	Amhara	Cross sectional	2014	325	16.6(12.6,20.7)
Ahmed et al. (31)	2018	Amhara	Cross sectional	2017	516	26.6(22.7,30.4)
Ahmed et al. (32)	2018	Addis Ababa	Cross sectional	2016	356	23.6(19.2,28.0)

**SNNP\*=Southern Nation, Nationality and People**

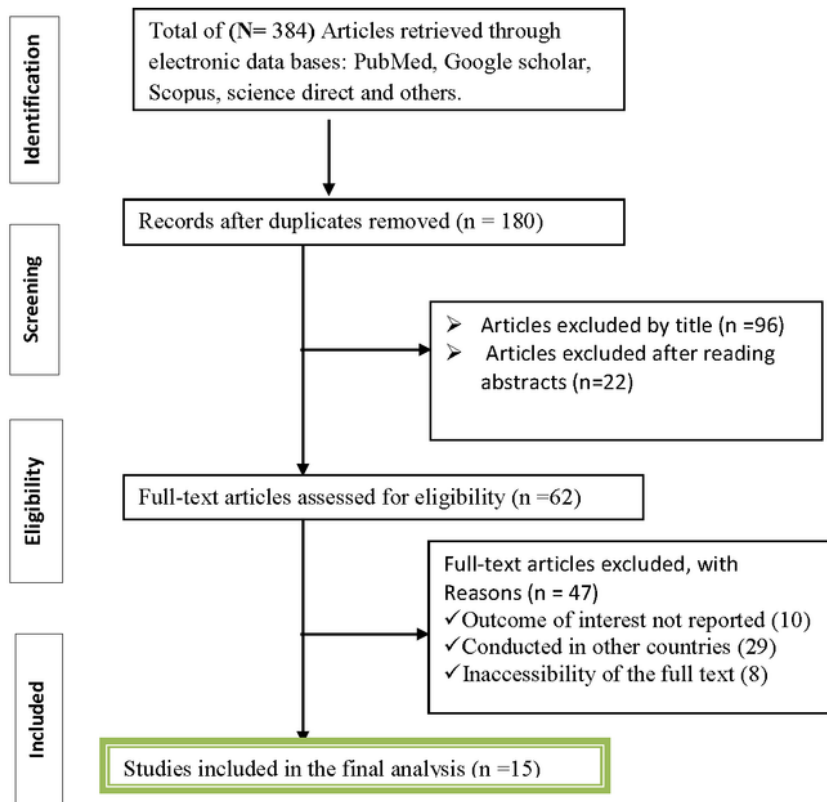
Table 2: Related factors with heterogeneity of perinatal asphyxia prevalence (based on univariate meta-regression)

Variables	Coefficient	P-value
Publication year	-0.23	0.51
Sample size	0.005	0.32
<b>Region</b>		
Amhara	-4.1	0.61
Addis Ababa	-0.011	0.88
Oromia	-5.2	0.24
Dire Dawa	-5.3	0.51
SNNP & Somalia	-3.2	0.6
Tigray	-0.032	0.79

**Table 3.**Subgroup analysis of perinatal asphyxia in Ethiopia, 2019 (n=15)

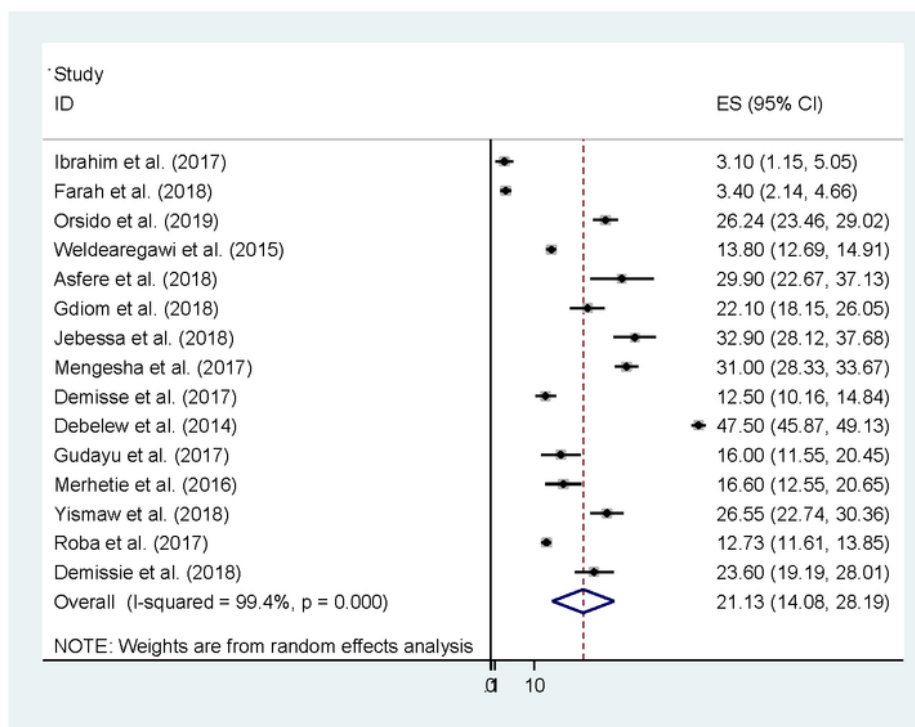
Variables	Characteristics	No-articles included	Sample size	Prevalence with (95% CI)	p-value
By region	Amahra	5	2025	19.9(13.7,26.2)	<0.001
	Addis Ababa	2	4040	18.5(8.9,20.1)	<0.001
	Oromia	2	3975	40.4(26.1, 54.7)	<0.001
	SNNP&Somalia	2	1756	14.8(7.6,37.1)	<0.001
	Dire Dawa	2	3720	8(2, 17.4)	<0.001
	Tigray	2	1575	26.7(8, 35.4)	<0.001
Study design	Retrospective	5	9160	11.8(5.8, 17.8)	<0.001
	Cross sectional	10	7931	25.6(16.4, 35.4)	0.004
Sample mean	Above mean(1139)	4	4558	26%(10.4, 42.1)	0.008
	Below mean(1139)	11	12532	19.2(12.6,25.7)	<0.001

# Figures



**Figure 1**

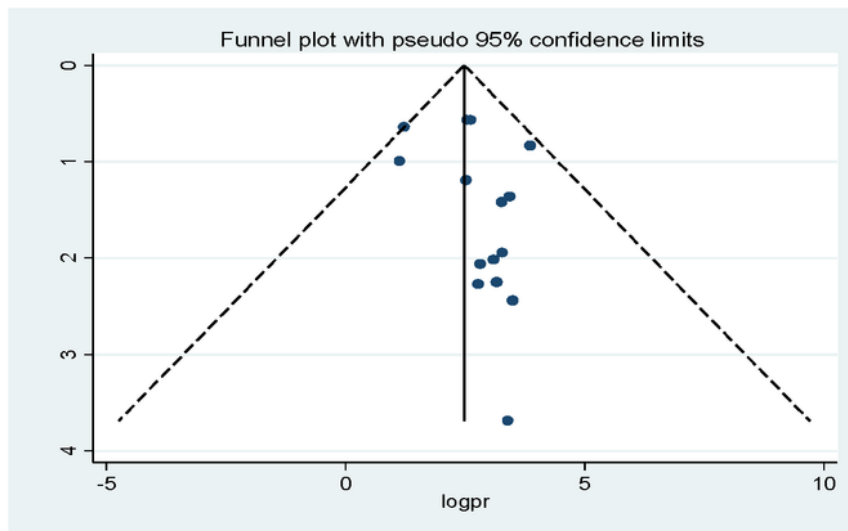
PRISMA study selection flow diagram for systematic review and meta-analysis on perinatal asphyxia in Ethiopia.



**Figure 2**

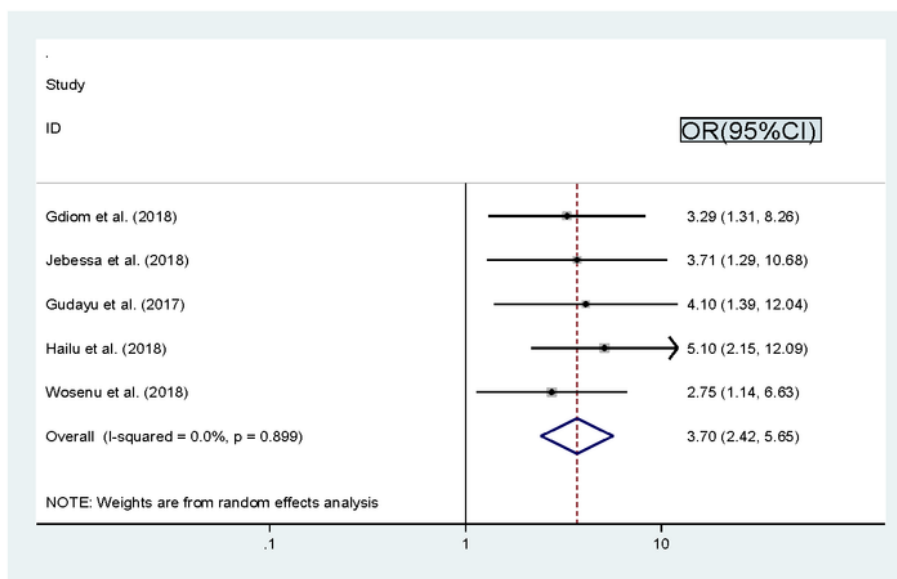
Forest plot of the pooled prevalence of perinatal asphyxia in Ethiopia.





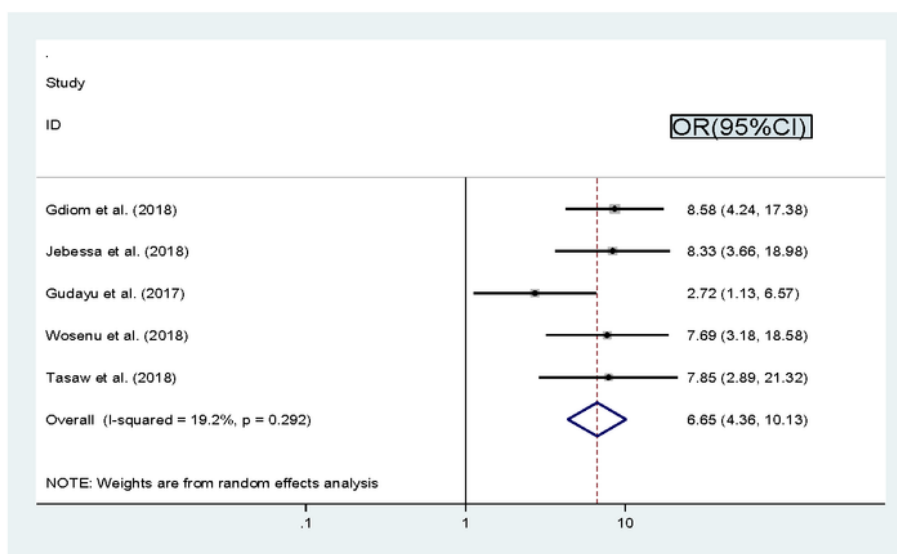
**Figure 3**

Funnel plot with 95% confidence limits of the pooled prevalence of perinatal asphyxia in Ethio-pia.



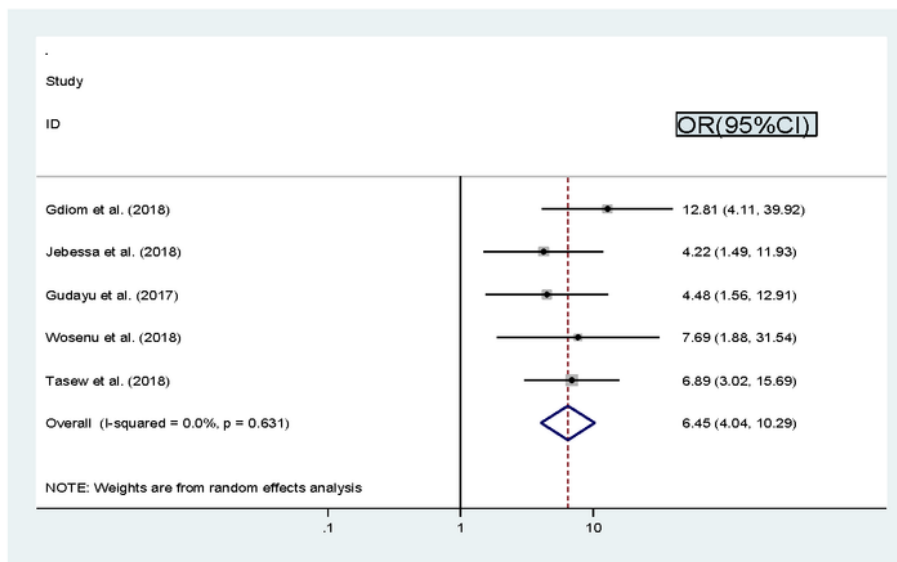
**Figure 4**

pooled odd ratio between perinatal asphyxia and prolonged labour



**Figure 5**

pooled odd ratio between perinatal asphyxia and meconium stained liquor



**Figure 6**

pooled odd ratio between perinatal asphyxia and low birth weight