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; neonatal mortality and morbidity; associated factors; Ethiopia

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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 2 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 2 = 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.

Keywords: Birth asphyxia; perinatal asphyxia; associated factor; systematic review; Ethiopia

Background

Perinatal asphyxia 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). It 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, globally 2.5 million children died in the first month of life predictive of a high risk of dying in the first 28 days of life referred as the neonatal period(4). The incidence of PNA is higher in developing countries (most notably sub-Saharan Africa and southern Asia contexts) where there is limited access to maternal and neonatal care (4, 5).

Currently, Ethiopia is amongst the top five countries contributing more than half of the neonatal deaths globally (6). Perinatal asphyxia is a common and serious intrapartum related complication at birth, accounting for 23% of neonatal death globally (7) and 34% in Ethiopia surpassing both prematurity (21.8%) and sepsis (18.5%)(8, 9). It could be significantly reduced by facility-based skilled professional intrapartum care and neonatal resuscitation capacities (10, 11). In addition, PNA results in both short and long lasting neonatal morbidities accounting for 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(8).

Despite many studies being conducted in Ethiopia, there is no systematic review and meta-analysis done to estimate the pooled prevalence and associated factors of PNA. Therefore, the aim of this study is to estimate the prevalence of national PNA and its associated factors to enhance the quality and consistency of the evidence. Hence, this review could serve as a base-line for clinicians, stakeholders, and policy makers to intervene on neonatal mortality and morbidities related to PNA.

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

Search strategy

To identify potentially relevant articles, a comprehensive search was carried out on Pub Med/MEDLINE, Google Scholar, Scopus, and Science Direct databases. Our search extended by hand searches for grey literature and other relevant literature collections also done by retrieving reference lists of eligible articles. The search of the literature was conducted between January and April 2019 and considered all relevant publications from January 2016 to April 2019. The 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 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guide line(12)(**Additional file 1**).

Eligibility

Inclusion criteria:

Study area: All studies conducted in Ethiopia

Study design: All observational study designs reporting the prevalence of PNA

Population: Studies involving infants immediately before, during and after birth within seven days of postpartum

Language: Only articles reported in English language

Publication condition: published and unpublished articles

Exclusion criteria: case reports, national reports, clinical studies, reviews, and articles which have not defined criteria for PNA and unable to assess the quality of articles due to the absence of full text.

Outcome variables

Primary outcome (PNA) was diagnosed by persistently low APGAR (Appearance, Pulse, Grimace, Activity, and Respiration score at 5th min less or equal to 6(less than 7) and it 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 is the associated factors which influence the primary outcome PNA in the form of the log odds ratio. For key associated factors, the odds ratio determined based on binary outcomes; prolonged labor (<24hours vs. >24hours), birth weight (<2500 grams vs. >2500 grams), and meconium stained (yes vs. no) from primary studies.

Data Extraction

All relevant data were extracted by two reviewers (DB and SA) independently from included articles; discussions and mutual consensus were in place when divergent points of view were raised with third author (GT). 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 Joanna Briggs Institute's(JBI) critical appraisal checklist for prevalence studies(13). In addition, included articles were evaluated for quality by two authors (BG and AM) independently and the reviewers compared their quality appraisal scores and resolved any discrepancy before calculating the final appraisal score by the third author (MA). To assess the quality of each study, the Newcastle-Ottawa Scale for cross-sectional and cohort studies was adopted(14). 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 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 rating of ≥ 5 out of 10 stars were considered as high quality. In our case, all eligible studies met this standard.

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. Heterogeneity among reported prevalence was assessed by computing p-values of I^2-statics. Higgins's I^2 statistic measures the percentage of variation between the sample estimates that is due to heterogeneity rather than to sampling error (15). The pooled prevalence of PNA was carried out with a random effects meta-analysis model, generating the pooled 95% confidence interval 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 for study settings/region, study design, and sample size. To identify the possible sources of heterogeneity, univariate meta-regression was undertaken for sample size and publication year, and regions. 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. Twelve studies met the eligibility criteria and were included in the final meta-analysis as shown in the following chart of study selection process (**Figure 1**)

Explanation for included studies

As described in **Table 1**, the 12 qualified observational studies published between January 2016 and 2019 with the sample size of 8,651 study participants were represented in this meta-analysis. The prevalence of PNA reported was between 3.1% (16) and 30% (17) with the sample sizes ranging from 154(17) to 3684(18).

Prevalence of perinatal asphyxia in Ethiopia

Prevalence of PNA was 17% (95% CI: 12, 22). A high heterogeneity was observed across the included papers as reflected in forest plot (I^2 = 97.7%, p<0.001) (**Figure 2**).

As a result, a random effect meta-analysis model was computed to estimate the comprehensive prevalence of PNA. As described in **Table 2**, the region of the country where the study conducted, publication year, and sample sizes were investigated 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 (**Figure 3**). To confirm publication bias, objectivity Egger's test was employed and did not show the presence of small study effect (p=0.138).

Subgroup analysis

In this meta-analysis, we computed subgroup analysis based on the study area/regions. The highest PNA prevalence was found in Amhara region at 20% (95% CI: 14, 28), followed by the Dire Dawa city administration at 10% (95% CI: 9, 11) (**Table 3**).

Associated factors of perinatal asphyxia

In this meta-analysis, we studied the association between PNA and prolonged labour with five included studies (**Figure 4**). The findings from these five studies showed prevalence of PNA was significantly associated with labour exceeding 24 hours. The probability of PNA was 3.7 times higher among mothers who had long duration of labour as compared to less than 24-hours counter-parts (OR=3.7, 95% CI: 2.4, 5.7).

The association between meconium stained liquor and PNA based on relevant studies showed a strong association. The probability of PNA was 6.6 times higher among infants who had meconium stained liquor as compared to those not having meconium stained liquor (OR=6.6, 95% CI: 4.4, 10.1) (**Figure 5**).

Association between low birth weight and PNA was reflected in five included studies. The findings revealed that the pooled prevalence of PNA 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 non-low birth weight (OR=6.5, 95% CI 4.0, 10.3) (**Figure 6**).

Discussion

Birth/perinatal asphyxia is one of the most common and serious intrapartal-related clinical complications at birth. To the best of our knowledge, this meta-analysis is the first to estimate the pooled prevalence and associated factors of PNA in Ethiopia.

This study revealed an overall prevalence of PNA of 17% (95% CI: 12, 22) in Ethiopia. The result of this meta-analysis is lower than the studies in Gusau, Nigeria (30.1%)(28), Dar es Salaam, Tanzania(30.9%)(29), and North-Tanzania (26.6%)(30). However, our finding is higher than reported by studies in Malawi (6.1%) (31) and Thailand (11.7%)(32). The possible explanation for the observed variations could be attributed to criteria for PNA identification, gestational age of neonates, methodological difference of the studies, maternal and child health service levels, and the sample size.

We did subgroup analysis by study area/region due to a significant heterogeneity finding. Thus, highest prevalence of PNA was in Amhara region at 20% followed by Dire Dawa city administration at 10%. This regional variation could be the related to gestational age of neonates, differences in accessibility to delivery institutions, culture of the study area, health seeking behaviors, and behavioral characteristics of caregivers.

Meconium stained liquor was a statistically associated with PNA. This finding is similar to those of studies conducted in Nigeria, England, and Thailand (33-35). In healthy, well oxygenated fetuses, diluted meconium is readily cleared from the lungs by normal physiological mechanism. However, the presence of meconium in the amniotic fluid often leads to aspiration of meconium into the lungs or airway obstruction that could eventually result in PNA.

In addition, prolonged labor was a risk factor for PNA in our findings. This result is consistent with the findings in India, Cameron, Pakistan, Nigeria, and Thailand (33, 36-38). This finding could be due to prolonged labour being associated with fetal and maternal exhaustion, fetal distress, and/or exposure to Pitocin and/or forceps/vacuum extractors.

Another identified associated factor of PNA in our review was low birth weight. This finding is also reflected in studies reported from in Nepal, Thailand, Uganda, and England (33, 34, 37, 39).The possible rationale could be low-birth-weight infants often have pulmonary immaturity and limited respiratory muscle strength which will cause difficulty of birthing and cardiopulmonary transition(40). In contrary, high birth weight at birth had been found an associated factor for PNA(41).

In general this high PNA needs emphasis to expansion of quality neonatal health service to decreases neonatal mortality and permanent neonatal illnesses like hypoxic ischemic organ damage followed by severe life-long pathologies, neurodegenerative diseases, mental retardation, epilepsies, and life-long functional psychotic syndromes.

Limitations of the study

The first limitation of this study is gestational age of newborns which could biases the estimates. The other limitation was only English reports were considered in this study which may have restricted inclusion of some relevant articles. Some of the studies included in this review had a relatively small sample size. This meta-analysis also solely represented only studies reported from five regions and two administrative town of the country. In addition, this study is not registered in PROSPERO which might compromise the credibility of the study.

Conclusion

In this review, pooled PNA in Ethiopia was found high and low birth weight, prolonged labour and meconium stained liquor are risk factors for PNA. This information may be useful in guiding improvement of facility-based intra partum care and neonatal resuscitation service quality for health professionals and decision makers to minimize PNA.

Abbreviations

APGAR	Appearance Pulse Grimace Activity Respiration
CI	Confidence Interval
EDHS	Ethiopian Demography and Health Survey
JBI	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

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Author contributions

MA: 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

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

SA: Study design, literature review, data extraction, data analysis, interpretation and manuscript review.

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

AM: data extraction, criteria setting and quality assessment. All authors have read and approved the manuscript

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Authors of primary study

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Tables

Table1: Descriptive summary of studies included in the systematic review and meta-analysis of PNA in Ethiopia

uthorship Reference)	Publication year	Mid-year of study period	Study Area/Region	Study design	Sample	Prevalence (95%CI)
orahim et . (16)	2017	2015.5	Dire Dawa	Retrospective	302	0.03(0.02,0.06)
arah et al. 19)	2018	2017	Somalia	Retrospective	792	0.03(0.02,0.05)
rsido et . (20)	2019	2016	SNNP*	Retrospective	964	0.26(0.24,0.29)
oba et . (21)	2017	2015	Dire Dawa	Retrospective	3418	0.13(0.12,0.14)
sfere et . (17)	2018	2017	Amhara	Cross sectional	154	0.30(0.23,0.38)
ebreheat : al.(22)	2018	2018	Tigray	Cross sectional	423	0.22(0.18,0.26)
elachew : al. (23)	2018	2015	Oromia	Cross sectional	371	0.12(0.09,0.16)
emisse et . (8)	2017	2015.5	Amhara	Cross sectional	769	0.12(0.10,0.15)
udayu et . (24)	2017	2013	Amhara	Cross sectional	261	0.16(0.12,0.21)
okeb et . (25)	2016	2014	Amhara	Cross sectional	325	0.17(0.13,0.21)
smaw et .(26)	2018	2017	Amhara	Cross sectional	516	0.27(0.23,0.31)
emissie et .(27)	2018	2016	Addis Ababa	Cross sectional	356	0.24(0.19,0.28)

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
Region		
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

Additional File

PRISMA 2009 check list

Figures

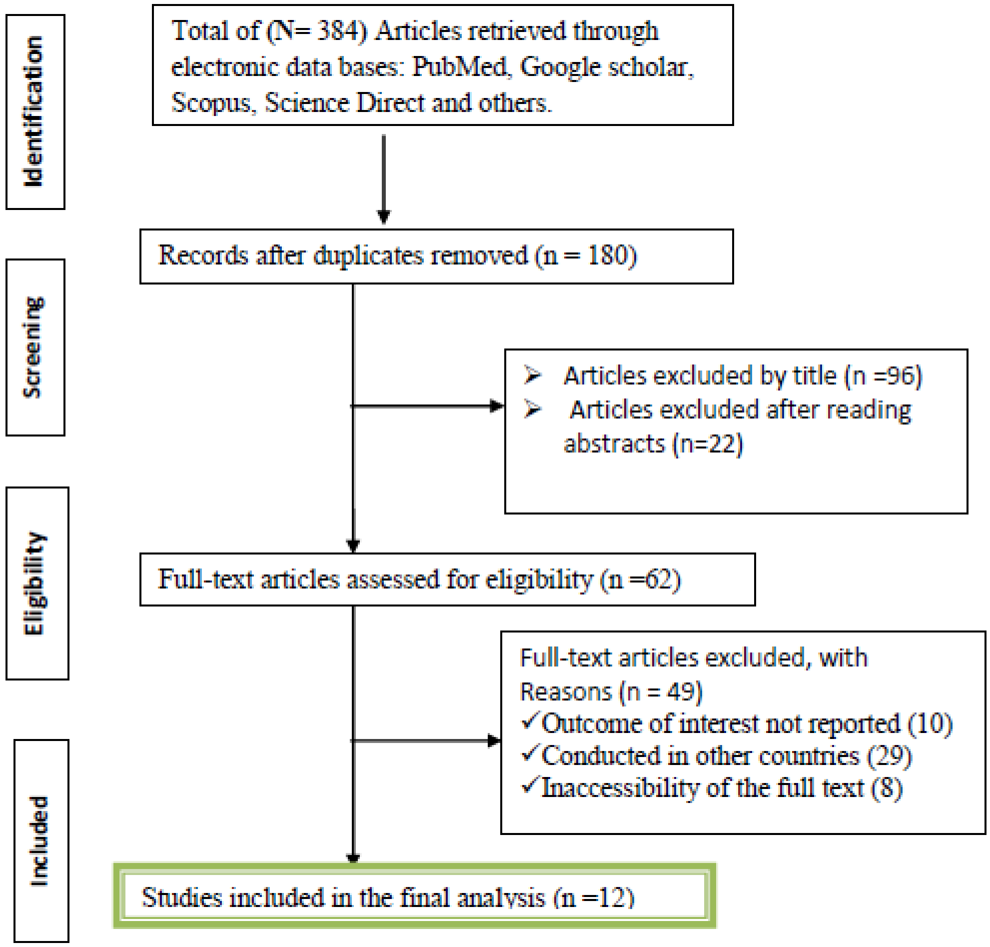

Figure 1

PRISMA study selection flow diagram for systematic review and meta-analysis.

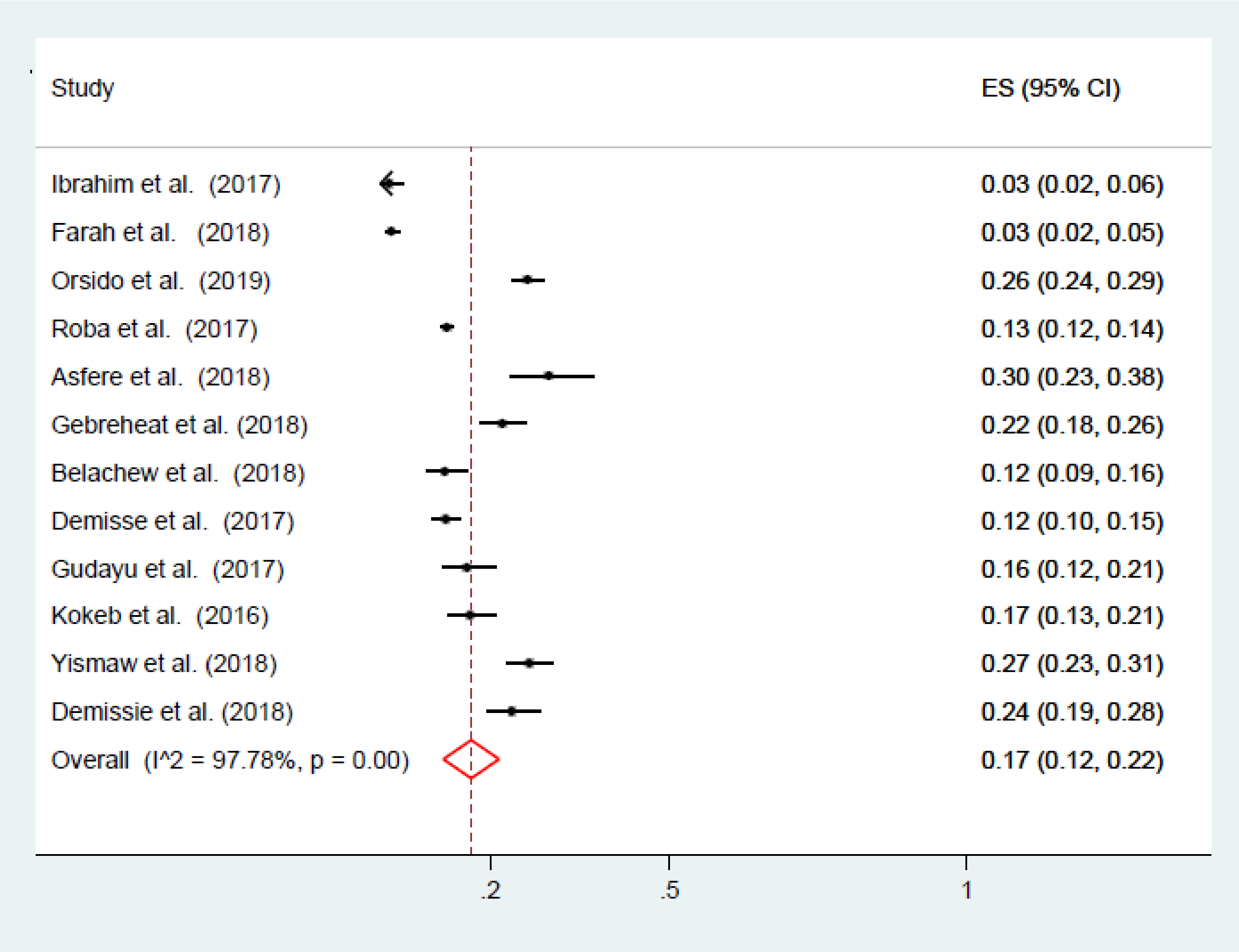

Figure 2

Forest plot of the pooled prevalence of PNA

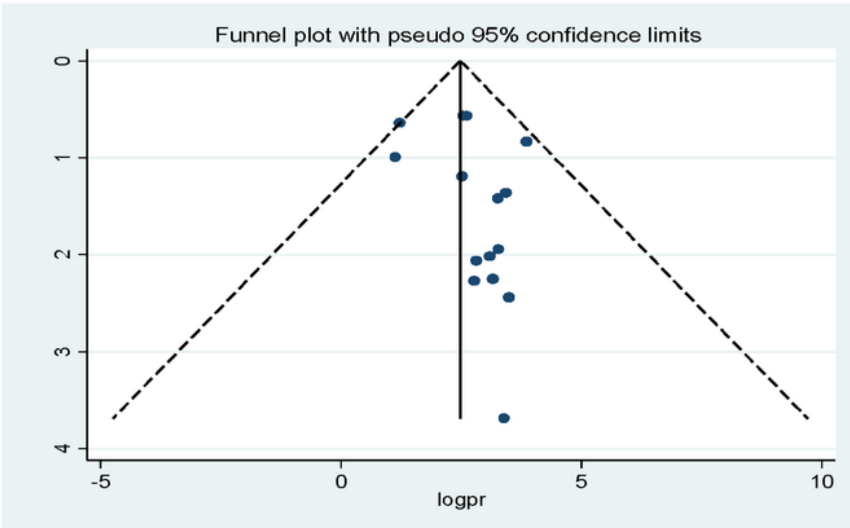

Figure 3

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

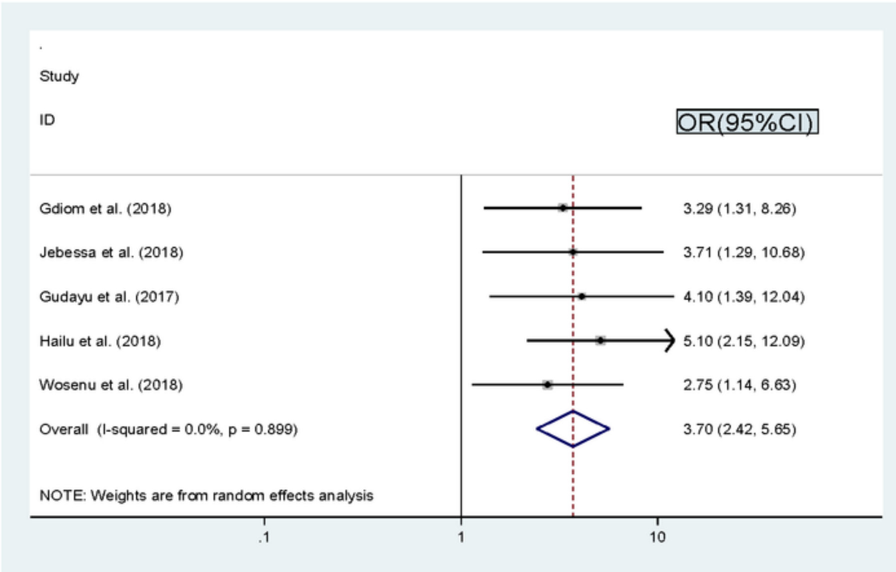

Figure 4

pooled odd ratio between perinatal asphyxia and prolonged labour

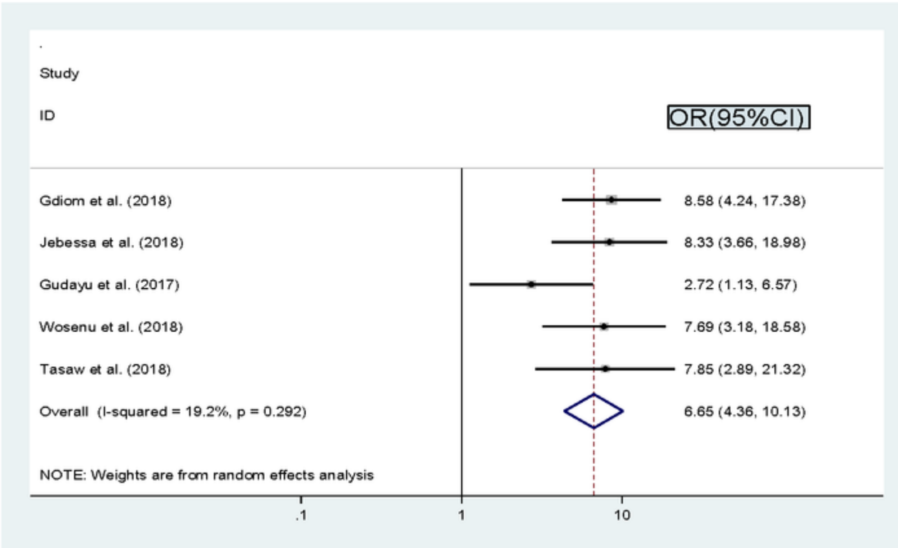

Figure 5

pooled odd ratio between perinatal asphyxia and meconium stained liquor

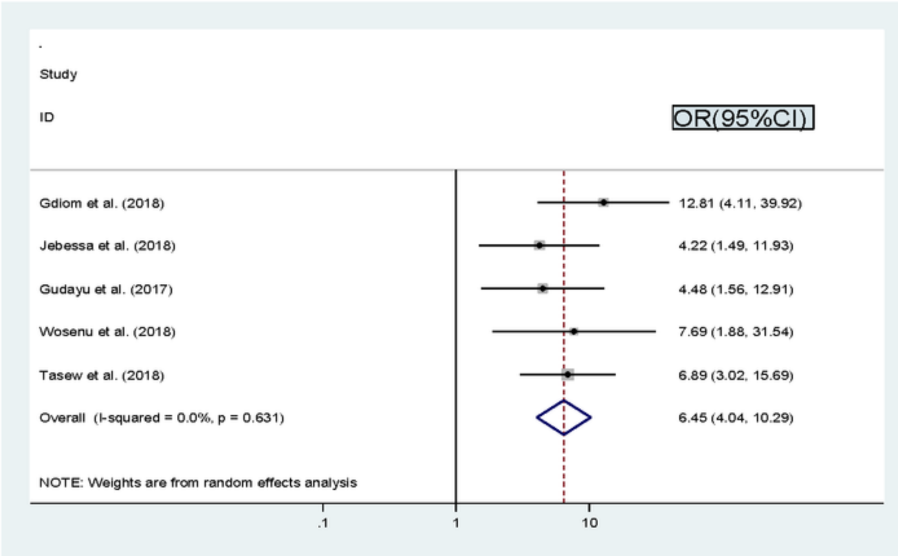

Figure 6

pooled odd ratio between perinatal asphyxia and low birth weight

Supplementary Files

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- AdditionalFile1.doc