Determinants of Perinatal birth Asphyxia among Newborns in Ethiopia: A Systematic Review and Meta-analysis of Observational Studies Protocol

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Abstract

Background: Birth asphyxia among newborns accounted for nearly fifty percent of neonatal mortality in sub-Saharan African countries. This scenario has been worst in Ethiopia where every two out of three deaths attributed to birth asphyxia among these babies. Moreover, studies conducted in Ethiopia are highly variable and inconclusive to estimate the pooled prevalence and risk factors of birth asphyxia.

Objective: This study aims to analyses collectively and systematically the prevalence of birth asphyxia and associated factors among newborns in Ethiopia.

Methods: The protocol for this review is registered at PROSPERO with registration number CRD42020158224. A comprehensive online databases (PubMed, HINARI, Scopus, EMBASE, Science direct, and Cochrane library database), Google Scholar, African Journals online, other gray and online repository accessed studies will be searched using different search engines. In addition, maternity & infant care databases uploaded at Ethiopian Health Development Journal and Ethiopian Journal of Health Sciences will be searched until June 30, 2020. Newcastle-Ottawa Quality Assessment Scale (NOS) will be used for critical appraisal of studies.. Three reviewers will screen all retrieved articles, conduct data extraction, and then critically appraise all identified studies. All identified observational studies reporting the prevalence of birth asphyxia and associated factors among neonates in Ethiopia will be considered. The analysis of data will be done using STATA 11.0 statistical software. We will demonstrate pooled estimates and determinants of birth asphyxia with effect size and 95% confidence interval. Heterogeneity among the included studies will be assessed through the Cochrane Q-test statistics and I^2 test. Publication bias will be checked using funnel plot and egger's test. Finally, statistical significance level will be declared at a p-value of less than 0.05.

Discussion: the result from this systematic review will inform and guide health policy planners to invest limited resources on maternal and neonatal health. Furthermore, it will be a stimulus for future cumulative meta-analysis researchers in developing nations.

1. Background

The World Health Organization (WHO) defines birth asphyxia as failure to initiate and sustain normal breathing at the first and fifth minute of birth [1]. Although more than two-thirds of newborns death are preventable, most of the neonatal deaths occur at home, uncounted, and invisible to national and regional policies and programs [2]. The prevalence of birth asphyxia varies across the globe and African countries contributes nearly fifty percent of the total magnitude of birth asphyxia [3-6]. Similarly, in Sub-Saharan countries, the prevalence of birth asphyxia is still unacceptably high which ranges from 21.3% to 56.9% [4, 7-11]. In Ethiopia, the magnitude of birth asphyxia varies between 3.1% and 56.9% in Ethiopia [10-13].

Globally, 2.5 million children and more than a million African babies are estimated to die in the first month of life, annually [14]. Worldwide, 25% of all neonatal deaths are attributed to birth asphyxia [15]. In

Ethiopia, two-thirds of neonatal deaths are attributed to birth asphyxia [16]. Furthermore, birth asphyxia is the first cause of neonatal deaths (31.6%) followed by prematurity (21.8%) and sepsis (18.5%) in developing countries, like, Ethiopia [17].

Studies conducted across the globe have identified factors associated with birth asphyxia. These include; antepartum risk factors (i.e. maternal age, maternal education, pre-eclampsia, primi-gravidity) intrapartum risk factors (i.e. prolonged labor, premature rupture of membrane, non-cephalic presentation, mode of delivery and maternal fever), and fetal risk factors (i.e. pre-term babies, fetal distress and baby weight) [18-22].

Globally and regionally various strategies and interventions have been implemented to decline neonatal mortality rates because of birth asphyxia [14, 15, 23]. For instance, one of the main objective in the Sustainable Development Goals of 2030 (SDG-3) is to reduce the neonatal mortality rate below 12 deaths per 1,000 live births [24]. Similarly, Ethiopia has made remarkable progress in achieving many of the national child health indicators [25] and it has designed the National Child Survival Strategy to reduce child mortality [26]. However, the burden of birth asphyxia is still unacceptably high in the country. Besides, the previous studies conducted in the country were highly variable and inconclusive to draw conclusion regarding the pooled prevalence of birth asphyxia and its determinants among newborns [27]..

Therefore, this study intended to determine the pooled estimate of birth asphyxia prevalence and its determinants among newborns in Ethiopia.

2. Objective

2.1 General objective

To estimate the pooled prevalence and associated factors of birth asphyxia among newborns in Ethiopia.

2.2 Specific objectives:

- To determine the pooled prevalence of birth asphyxia among newborns in Ethiopia
- To identify factors associated with birth asphyxia among newborns

3. Research Questions

1. What is the estimated pooled prevalence of birth asphyxia among newborns in Ethiopia?
2. What are the risk factors of birth asphyxia?

4. Methods And Materials

4.1 Search Strategy

The protocol for this review was registered at PROSPERO with registration number CRD42020158224 [https://www.crd.york.ac.uk/prospero/#recordDetails]. We used the Preferred Reporting Items for Systematic review and Meta-analyses (PRISMA-2015) to screen the included studies (*Additional file 1*) [28]. Different Online databases (PubMed, HINARI, Scopus, EMBASE, Science direct, Cochrane library database, and African Journals online), Google Scholar and other gray literatures were used to search articles on birth asphyxia. Searching terms were developed based on the formulated research questions during protocol development. We have developed different Boolean operators to have comprehensive database searches on birth asphyxia. Thus, the international online electronic database repositories include; "perinatal asphyxia" OR "birth asphyxia," OR "breathing difficulty at birth," OR "neonatal asphyxia," OR "low APGAR score," OR "hypoxic-ischemic encephalopathy" OR "Neonatal Encephalopathy" AND "determinants" OR "predictors," OR "risk factors," OR associated factors," OR causes," AND "newborn," OR neonate," AND "Ethiopia" [*additional file 2*).

Moreover, we will utilize snowballing to screen the references of identified articles for potentially relevant studies. Furthermore, Studies identified by our database searching strategy will be retrieved and managed using Endnote X8 (Thomson Reuters, Philadelphia, PA, USA) software.

4.2 Eligibility Criteria

4.2.1 Inclusion criteria:

Setting/context: This review will include studies conducted in Ethiopia.

Population: the review will include studies involving newborns (preterm, near-term, term and post-term newborns) immediately after birth (1-5 minutes of birth) and the babies who were born after 28 weeks of completed gestations (after the age of viability).

Study design: All observational studies (i.e. cross-sectional, case-control, and cohort) that have reported the prevalence of birth asphyxia and its determinants among newborns.

Language: studies reported in the English language will be considered.

Publication year: no restriction on year of publication

4.2.2 Exclusion criteria:

We will exclude studies published in languages other than English. . In addition, we will exclude studies other than observational studies like, case reports, conference reports, national survey reports and expert opinions that has not addressed the determinants of birth asphyxia among newborns.

4.3 Outcome measurement

This systematic review and meta-analysis had two main outcomes. The first outcome was the prevalence of birth asphyxia among the neonates. In this study, birth asphyxia was defined as newborn with Apgar score less than 7 at the 1st or 5th minutes of birth. The pooled prevalence was calculated by dividing the number of neonates with birth asphyxia to the total number of neonates who have been included in the study (total sample size) multiplied by 100. The second outcome of the study was to identify maternal and neonatal factors associated with birth asphyxia that was determined in the form of pooled odds ratio. Moreover, the outcomes of this study were to focus on single studies estimating the prevalence and associated factors of birth asphyxia among live newborns in Ethiopia.

4.4 selection of studies

Two authors (AWT and GBW) will review the studies based on inclusion and exclusion criteria. The review will follow two stages. In the first stage, reviewers will assess both the titles and abstracts of the studies identified from the search. In the second stage, full-text screening will done to screen the full texts selected in the previous stage. If the articles are not open access, we will contact the corresponding author at least for three times. If the authors are not willing to provide the full text, we will exclude that specific article.

We will provide reason for exclusion for all excluded studies in the PRISMA-2009 flow diagram. Finally, we will prepare a final list of articles for data extraction

4.7 Data extraction

Three authors (AW, SE and GB) will independently extracted all necessary data using a standardized data extraction format (additional file 3). We will pretest the data extraction form on three studies of each type, to ensure that it adequately facilitates the collection of all necessary data required for an effective systematic review and meta-analysis. Discrepancies between data extractors will be discussed to reach consensus. If a consensus cannot be reached, the authors will consult a third reviewer (KU). For each included articles, we will record the first author's last name, year of publication, the setting where the study was conducted, study design, study period, sample size, the response rate, the population, outcome definition, comparison groups, and the effect estimate.

4.8 Quality assessments

Four authors (AWT, SB, KU and GB) will independently conduct quality assessment of included studies, by using the checklist of the NOS appraisal tool for cross-sectional, cohort and case-control studies (*Additional file 4*). In customising the scale to fit this study, we will took into account the study sampling methods and similarities between the study groups regarding adjustment for confounding factors, the ascertainment of exposure and outcomes, and study design. The abstracting tool will include different questions based on the study designs. The four investigators independently will perform the quality assessment while abstracting the data for the meta-analysis. The quality scores of the four abstractors will be averaged. Finally, the studies with NOS score of six and more were considered a "good" quality

study (low risk) while studies scored less than six will be considered as "poor" quality study (high risk) [29]..

4.9 Data synthesis and analysis

The extracted data will be entered into a Microsoft Excel Database and then imported into STATA version 14.0 (Stata Corp LLC, Texas, USA) software with packages of Meta-analysis for further analysis. The researchers will perform a narrative description of the study population, the studies included, the risk factors identified, and the cause for birth asphyxia as well as the outcome characteristics. We will use tables and figures to summarize the selected studies and results.

The pooled prevalence of birth asphyxia in Ethiopia will be demonstrated. We will use fixed effect model if the studies have similar methodology, same population, and study design. If not, we will utilize the random effect model [30]. Then, the "metaprop" command with random-effects models at 95% confidence intervals will be used to calculate the pooled prevalence of birth asphyxia at national level [31]. The Freeman Tuckey variant of the arcsine square root transformation of proportions will be fitted to avoid variance instability when handling proportions close to one [32]. We will assess heterogeneity by using chi-squared test on Cochran's Q statistic with a 5% level of statistical significance [26] and I^2 statistic test [33], assuming that I^2 value of 25%, 50%, and 75% being representative of low, moderate, and high heterogeneity, respectively [33]. If the heterogeneity is significant ($I^2 > 75\%$), then, we will conduct subgroup analyses and meta-regression to investigate sources of heterogeneity.

Publication bias will be examined by the visual inspection of funnel plots [34] and Egger's test [35]. A p value < 0.10 will be considered indicative of statistically significant publication bias. Thus, if there is evidence of publication bias, we will use Duval and Tweedie's trim-and-fill method [36].

For factors associated with birth asphyxia; two-by-two tables will be constructed (if possible), the odds ratio with 95% confidence interval will be calculated. Then, the statistically significance level will be declared at a p-value less than 0.05. However, if the meta-analysis is not possible, we will conduct narrative synthesis.

4.10 Subgroup and sensitivity analyses

Sub-group analysis will be performed based on sample size, regions, year of publication, and quality of studies. Finally, to conduct sensitivity analysis, we will assess the stability or robustness of the pooled estimates to outliers and the impact of individual studies [36].

4.11 Discussion

This review will provide a detailed summary of the evidence on prevalence and factors of birth asphyxia in Ethiopia. This review will be the first to synthesis available data on birth asphyxia. Findings of the review will fill an evidence gap in understanding the burden, risk factors, and causes of birth asphyxia in the country. The result from this review will inform health policy planners and researchers up-to-date data

on birth asphyxia and provide direction in which risk factors the policy should focus to reduce burden of birth asphyxia in the country.

4.12 Dissemination of results

The results of this systematic review and meta-analysis will be published in a peer-reviewed journal and presented at national and international research conferences.

Abbreviation

EDHS   Ethiopian Demographic and Health Survey.

JBI   Joanna Briggs Institute.

LMICs   Low and Middle Income Countries.

MeSH   Medical Subject Headings.

PECO   Population, Exposure, Comparison, and Outcome.

PRISMA   Preferred Reporting Items for Systematic Review and Meta-Analysis.

WHO   World Health Organization.

Declarations

Ethics approval and consent to participate

Not applicable

Availability of data and materials

All materials and data related to this article are included in the main document of the manuscript. However, if anyone has interested to have raw data, he/she can contact the corresponding author.

Consent for publication

Not applicable

Competing interests

The authors have declared that there are no competing interests.

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