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The effect of antenatal care on low birth weight and neonatal mortality: protocol for umbrella review of meta-analysis

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Abstract

Background The World Health Organization defines low birth weight as a birth weight of less than 2500 g, regardless of the gestational age. It is regarded as the most significant predictor of infant mortality overall, particularly for deaths that occur in the first few months of life. Among all the months of a person's existence, the neonatal period, the first month of life, has one of the highest death rates. The necessity for an umbrella review is highlighted by the lack of a comprehensive synthesis of collective meta-analytic evidence connecting antenatal care as a factor of low birth weight and newborn death. Thus, this umbrella review's main goal is to thoroughly synthesize the existing meta-analytic evidence, with a focus on assessing the relationship between antenatal care with low birth weight and neonatal mortality.

Methods All English-language meta-analyses of cohort, case-control, and cross-sectional studies that looked at the relationship between antenatal care with low birth weight and neonatal mortality will be included, regardless of the time and location of publication. To find pertinent literature for review, major medical electronic databases including Embase, CINAHL, Cochrane database, and PubMed will be used. Two reviewers will screen the eligible articles, extract data, and evaluate their quality independently. The reviewers will work together to reach a consensus on any disagreements. If there are still issues, a third reviewer will be consulted in order to fix them. The meta-umbrella R package will be used for all statistical analysis. The random-effects model and 95% prediction interval for the summary estimate will be used for both outcomes. Q and I^2 test statistics will be calculated to determine the degree of heterogeneity. We will use Egger's regression asymmetry test to assess publication bias, the Ioannidis test for excess significance bias, and Hedges' g value for each risk factor.

Discussion This is the first comprehensive analysis of the effect of antenatal care on low birth weight and neonatal mortality that we are aware of. For clinicians and researchers seeking to lower low birth weight and neonatal mortality, summarizing this evidence is helpful.

Trial registration PROSPERO-CRD42024567150.

Keywords Antenatal care, Low birth weight, Neonatal mortality, Meta-analyses

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Background

The World Health Organization (WHO) defines low birth weight (LBW) as a birth weight of less than 2500 g, regardless of the gestational age [1]. Every year, more than 20 million newborns are born underweight. This accounts for approximately 15–20% of all births globally. The vast majority of these occurrences, around 96.5%, happen in developing countries [2].Children born LBW risk a number of serious health issues. These include an increased risk of infant mortality, learning challenges caused by stunted growth and impaired neurodevelopment, cognitive and motor skill impairments, and chronic health disorders such as heart disease and diabetes [3]. The long-term effects of LBW go far beyond childhood and infancy [4]. Additionally, it is regarded as the most significant predictor of infant mortality overall, particularly for deaths that occur in the first few months of life [5]. This indicates Poor maternal health can encompass a range of issues, such as chronic illnesses, infections, complications during pregnancy, and also inadequate maternal nutrition can lead to deficiencies in essential nutrients needed for fetal growth and development, potentially resulting in low birth weight, preterm birth, or weakened immunity in infants [6].

Annually, an estimated 15 million babies are born preterm, while more than 20 million are born with low birth weight [7]. LBW babies have a mortality rate of 40 times higher than normal-weight babies [8].The World Health Assembly established a policy goal to minimize LBW by 30% [9]. Various interventions have been implemented to reduce babies with LBW through packages of care offered during the prenatal, antenatal, intranatal, and postnatal periods [10]. The birth weight of a child is determined by the amount of growth during pregnancy and gestational age, which are related to the mother's lifestyle, genetic makeup, and general health, according to the WHO technical consultation report on promoting optimal fetal development [11].

Infants' LBW could be avoided by recognizing and managing the risk factors that are mostly influenced by living and social environments [12]. At a global rate of 19 deaths per 1000 live births, neonatal mortality, which is defined as death within the first 28 days of life, is a key indicator for neonatal health and well-being and is increasingly contributing to overall under-five mortality. It is also the period of time in which the child is most vulnerable to death [13, 14]. Among all the months of a person's existence, the neonatal period, the first month of life, has one of the highest death rates [15].

Almost one million neonatal deaths occur on the day of birth, and during the first seven days of life, nearly two million neonates die [16]. It is a serious public health issue that puts children's lives in jeopardy, with notable differences between developed (4 to 46%) and developing (0.2 to 64.4%) nations [17].

Worldwide, there are about 3 million neonatal deaths, or roughly 43% of children under the age of five [18]. Additionally, it was noted that of the 8.8 million fatalities of children under five worldwide, 40% and 30% happen in the early neonatal and neonatal periods, respectively [19].

Multi-sector approaches are needed to provide for the health of mothers and newborns, and strong maternal autonomy in making decisions is essential to reversing barriers at the household level. This is because women with limited decision-making power are less likely to give birth at health facilities, postnatal care centers, and antenatal care centers [20]. Antenatal care (ANC) is one of the most cost-effective and crucial components of maternal health care services. In developing countries where access to care, empowerment, and decision making power of women is low, ANC service is vital [21]. ANC is one of the mother and child health preventive interventions that can be provided at the lowest possible cost. Neonatal mortality and LBW can be decreased by following the guidelines of starting ANC in the first trimester of pregnancy [22]. The World Health Organization (WHO) recommends at least eight ANC visits to provide effective ANC services [23]. Regular ANC attendance provide an opportunity for early detection and management of pregnancy-related complications, nutritional supplementation, health education, and timely interventions, which collectively contribute to improved neonatal survival and birth weight outcomes [24]. Studies have shown that inadequate ANC attendance is associated with an increased risk of LBW due to poor maternal nutrition, undiagnosed infections, and hypertensive disorders during pregnancy [25].

By lowering neonatal deaths, and LBW, ANC directly and indirectly increases baby survival and health. It also serves as a gateway for medical interactions with mothers at a critical juncture in the continuum of care [26]. The effects of ANC on LBW and neonatal mortality have been extensively studied, however the results of the research that have been done so far have been conflicting or unclear. The necessity for an umbrella review is highlighted by the lack of a comprehensive synthesis of collective meta-analytic evidence connecting ANC as a factor of LBW and newborn death. This novel project has the potential to shed light on the relationship between ANC, LBW, and newborn mortality. Clarifying the exposure to prenatal care that lowers the risk of low birth weight and neonatal mortality makes it significant. This information can then be used to inform targeted clinical and public health interventions to address this pressing global health concern. Thus, this umbrella review's main goal is to thoroughly synthesize the existing meta-analytic evidence,

Table 1 Search strategy of pubmed database for effect of antenatal care on low birth weight and neonatal mortality. Protocol for umbrella review of meta-analysis

S.no		Searching
1.	#1	"Antenatal care"[All Fields] OR "prenatal care"[MeSH Terms] OR "maternity care"[All Fields] OR "maternal health care"[All Fields] OR "Maternal Health Services"[MeSH Terms] OR "pregnancy care"[All Fields]
	#2	"neonatal mortality"[All Fields] OR "Infant mortality"[MeSH Terms] OR "perinatal mortality"[All Fields] OR "perinatal death"[MeSH Terms] OR "Newborn mortality"[All Fields] OR "Neonatal death"[All Fields] OR "Newborn death"[All Fields]
	#3	"meta-analysis"[Title/Abstract]OR"meta-analyses"[Title/Abstract]OR"systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR "overview*"[Title/Abstract] OR "review*"[Title/Abstract]) AND "English"[Language]
		#1 AND #2 AND #3
2.	#1	"Antenatal care"[All Fields] OR "prenatal care"[MeSH Terms] OR "maternity care"[All Fields] OR "maternal health care"[All Fields] OR "Maternal Health Services"[MeSH Terms] OR "pregnancy care"[All Fields]
	#2	"infant, newborn"[MeSH Terms] OR "child"[MeSH Terms]) AND "Birth Weight"[MeSH Terms]) OR "low birth weight"[All Fields] OR "very low birth weight"[All Fields] OR "underweight"[All Fields] OR "abnormal birth weight"[All Fields]
	#3	"meta-analysis"[Title/Abstract]OR"meta-analyses"[Title/Abstract]OR"systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR "overview*"[Title/Abstract] OR "review*"[Title/Abstract]) AND "English"[Language]
		#1 AND #2 AND #3

with a focus on assessing the relationship between ANC with low birth weight and neonatal mortality.

Objectives

- To summarize the effect of antenatal care on low birth weight.
- To summarize the effect of antenatal care on neonatal mortality.

Methods

This umbrella review procedure adheres to the umbrella review methodology developed by the Joanna Briggs Institute [27]. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols 2015 (PRISMA-P 2015) statement is followed in reporting this protocol(supportive file 1) [28]. Our umbrella review procedure was registered and assigned a registration number (CRD42024567150) by the International Prospective Register of Systematic Reviews (PROSPERO) in compliance with the standards. Ethical approval was not necessary for this review, as we simply reviewed the published literature.

Eligibility criteria

All English-language meta-analyses of randomized control trial (RCT), cohort, case-control, and cross-sectional studies that looked at the relationship between antenatal care with low birth weight and neonatal mortality will be included, regardless of the time and location of publication. Studies not published in English and journals with no full text will not include in our analysis. Studies that merely detailed the meta-analysis's design or methodology will be disregarded. Excluded from consideration will made on meta-analyses that lacked specific study data, such as the number of study populations with odds ratios, relative risks, and 95% confidence intervals, or in which the missing data could not be obtained from the original research.

The inclusion of studies will be based on how comprehensively they provide their results. Duplicate publications, meaning the same meta-analysis reported in many articles, will be ruled out. We shall note the rationale behind these research exclusion.

Searching strategy

Two authors will perform search for relevant systematic reviews with meta-analysis (FA and WF). The search is restricted to English-language publications only, with no location or date limitations. To find research in the databases, we will use MeSH terms, Emtree, CINAHL headings, and combined keywords. To find pertinent literature for review, major medical electronic databases including Embase, CINAHL, Cochrane database, and PubMed will be used.

To cover gray literature, we manually searched literature using the Google search engines and Google Scholar. The search strings or terms stemmed from the following keywords: effect of ANC, effect of prenatal care, low birth weight, neonatal mortality, perinatal mortality, adverse birth outcomes, Meta-analysis, and Synthesis. "OR" or "AND" will be used separately and in combination as Boolean operators (Table 1). All newborns weighing less than 2500 g at birth and all neonatal deaths that occur within the first 28 days of life comprise the population of this evidence synthesis, with the effect of ANC(attendance of ANC) being identified as the exposure of interest. While women who have not been exposed are specified as comparison groups, low birth weight and neonatal mortality are the outcomes of interest.

Study selection

Electronic search results will be downloaded into the Endnote software, and duplicates will be eliminated both automatically and manually. Using the aforementioned inclusion criteria, two impartial reviewers (FA and AA) will go through the titles and abstracts to find reviews that might be of interest. When exclusion cannot be ascertained from the study title or abstract for the final selection, full texts will be retrieved. The reviewers will work together to reach a consensus on any disagreements. If there are still issues, a third reviewer (FY) will be consulted in order to fix them. A PRISMA flow diagram will be used to summarize the study selection.

Data extraction

Two reviewers (FA and FY) will independently extract data from each eligible systematic review using standardized abstraction forms created in Microsoft Excel. If a consensus cannot be reached, ambiguities pertaining to data extraction will be settled through discussion or by a third reviewer (WF).

First author, year of publication, number and type of studies in each meta-analysis, total sample size, heterogeneity test findings, P-values for fixed or random effects, and the measure of association (risk ratio, odds ratio, etc.) with 95% confidence interval will all be retrieved. When there are only plots available for the data, we will utilize Ycasd to calculate the effect size and its 95% confidence interval [29]. If the relevant data were not included in the paper, we will get in touch with the appropriate authors to request the information.

Quality assessment

Pairs of reviewers (FA and WF) will independently assess the quality of the meta-analysis using the AMSTAR-2 tool [30]. The instrument has 16 items. It is not intended to generate an overall score but provides a categorical rating based on critical domains: protocol register, adequacy of the literature search, justification for excluding individual studies, risk of bias from individual studies being included, appropriateness of meta-analytical methods, consideration of risk of bias when interpreting the results, and assessment of publication bias. The overall quality or confidence in the review results can be rated as moderate "high" (no or one non-critical weakness), "moderate" (more than one non-critical weakness), "low" (one critical flaw with or without non-critical weaknesses), and "critically low" (more than one critical flaw with or without non-critical weaknesses). Any differences of opinion amongst the reviewers will be settled by discussion and, if necessary, by a third reviewer. The outcomes of the risk of bias evaluation will be summarized narratively and organized into tables, adhering to the recommendations provided by Shea, B.J.and collaborators [30].

Data synthesis and statistical analysis

The meta-umbrella R package will be used for all statistical analysis [31]. It is one tool that enables users to conduct umbrella reviews with the stratification of evidence is the meta-umbrella R program. If the random model had already been used for both outcomes (LBW and neonatal mortality), we derived the pooled effect size (odds ratio or relative risk) from the included meta-analysis.

If not, the pooled effect size and associated 95% confidence interval will be obtained by extracting the original data and reanalyzing it using random effects techniques. In order to depict the range in where the impact estimates of further research will lie, we will additionally estimate the 95% prediction interval for the summary estimate based on the random-effect model [32]. The Q and I^2 test statistics will be calculated to determine the degree of heterogeneity [33].

For the Q statistic < 0.05 will be considered significant. The degree of heterogeneity will be classified into substantial ($I^2 > 50\%$) and considerable ($I^2 > 75\%$). Egger's regression asymmetry test to assess publication bias [34].

Publication bias will be evaluated using Egger's test, a statistical tool that can be used to identify it in meta-analyses. If Egger's test yields a result of $P < 0.05$, publication bias will be presumed to be present. The Ioannidis test for excess significant bias will be employed to evaluate the overall bias present in the meta-analyses [35]. A statistical technique called Ioannidis can be used to identify bias in meta-analyses, including publication bias and selective reporting bias. An Ioannidis test P-value of less than 0.05 will be regarded as proof of general bias. The Hedges' g values for every risk factor are also provided. Hedges' g is a measure of effect size that indicates the degree of difference between two groups [36].Cohen suggested using the following rule of thumb for interpreting results: Small effect (cannot be discerned by the naked eye) = 0.2, Medium Effect = 0.5, Large Effect (can be seen by the naked eye) = 0.8 [37].

Discussion

In order to conduct this comprehensive analysis, we will (1) locate and summarize previous systematic reviews with meta-analyses, and (2) assess the available quantitative data critically. We will compile a thorough summary of the literature's knowledge on the effects of ANC on LBW and neonatal mortality, including summary of findings tables and reports summarizing findings from all included reviews based on data synthesis.

For clinicians and researchers seeking to lower LBW and neonatal mortality, summarizing this evidence is helpful. The quality and variability of the collected reviews will be among the study's weaknesses. We will reanalyze each result using a random-effects model and assess the caliber of the included studies in order to overcome these constraints.

The most recent systematic methodologies available will be used to undertake this umbrella review.

Abbreviations

CI	Confidence interval
LBW	Low birth weight
ANC	Antenatal care
PRISMA-P	Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols
AMSTAR	A Measurement Tool to Assess Systematic Review
WHO	World Health Organization

Supplementary Information

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Supplementary Material 1

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Author contributions
FA: carried on the conception and constructed this protocol, developed the search strategy, compared, and found the best tools for assessing possible bias and evaluating the quality of the included reviews, wrote the protocol, and read and approved the final manuscript. AA: carried out the conception and construction of this protocol, compared and found the best tools for assessing possible bias, evaluating the quality of the included reviews, added grammar editing and conceptual clarification, and read and approved the final manuscript. FY: carried on the conception and constructed this protocol, compared, and found the best tools for assessing possible bias and evaluating the quality of the included reviews, added grammar editing and conceptual clarification, and read and approved the final manuscript. WF: carried on the conception and constructed this protocol, developed the search strategy, compared and found the best tools for assessing possible bias and evaluating the quality of the included reviews, wrote the protocol, and read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethical approval and dissemination plan
Ethical approval was not required for this study. This umbrella review has been submitted to a peer-reviewed journal for publication.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Organization WH. UNICEF-WHO low birthweight estimates: levels and trends 2000–2015. World Health Organization; 2019.
2. Defilipo ÉC, et al. Factors associated with low birthweight: a case-control study in a City of Minas Gerais. Rev Saude Publica. 2020;54:71.
3. Ngo N, Bhowmik J, Biswas RK. Factors associated with low birthweight in low-and-Middle income countries in South Asia. Int J Environ Res Public Health. 2022;19(21):14139.
4. Mulatu H, et al. Magnitude and factors associated with low birth weight among new born in selected public hospitals of addis Ababa, Ethiopia, 2016. Glob J Med Res. 2017;17(5):27–34.
5. Dilnessa T, Belete E, Tefera M. Prevalence of low birth weight and associated factors among new born babies in Ataye primary hospital, North Shoa, Ethiopia, 2018. Asian J Health Sci Med. 2020;18(3):1–1.
6. Ghimire R, et al. Determinants of low birth weight: a case control study in Pravara rural hospital in Western Maharashtra, India. Int J Sci Res. 2014;3:243–5.
7. Organization WH. Preterm and low birth weight infants. Newborn Health. Available online: https://www.who.int/teams/maternal-newborn-child-adolescent-health-and-ageing/newborn-health/preterm-and-low-birth-weight (accessed on 3 February 2023).
8. Zenebe K, Awoke T, Birhan N. Low birth weight & associated factors among newborns in Gondar town, North West Ethiopia: institutional based cross-sectional study. Indo Global J Pharm Sci. 2014;4(2):74–80.
9. Targets WGN. Low birth weight policy brief: World Health Organization; 2014. 2025.
10. Sema A, et al. Associated factors with low birth weight in dire Dawa City, Eastern Ethiopia: A cross-sectional study. Biomed Res Int. 2019;2019(1):2965094.
11. Organization WH. Promoting optimal fetal development: report of a technical consultation. 2006.
12. Safari M, et al. The prevalence and related factors of low birth weight. Epidemiol Health Syst J. 2016;3(3):214–21.
13. You D, et al. Global, regional, and National levels and trends in under-5 mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Inter-agency group for child mortality Estimation. Lancet. 2015;386(10010):2275–86.
14. Tolossa T, et al. Impact of antenatal care on neonatal mortality among neonates in Ethiopia: a systematic review and meta-analysis. Archives Public Health. 2020;78:1–11.
15. Wakgari N, Wencheko E. Risk factors of neonatal mortality in Ethiopia. Ethiop J Health Dev. 2013;27(3):192–9.
16. Tekelab T, et al. The impact of antenatal care on neonatal mortality in sub-Saharan Africa: A systematic review and meta-analysis. PLoS ONE. 2019;14(9):e0222566.
17. Bitew ZW, et al. Incidence density rate of neonatal mortality and predictors in Sub-Saharan Africa: A systematic review and Meta-Analysis. Int J Pediatr. 2020;2020(1):3894026.
18. Zhang B, et al. Neonatal mortality in hospitalized Chinese population: a meta-analysis. Biomed Res Int. 2019;2019(1):7919501.
19. Berhan Y, Berhan A. Meta-analysis of selected maternal and fetal factors for perinatal mortality. Ethiop J Health Sci. 2014;24:55–68.
20. Mitiku HD. Neonatal mortality and associated factors in Ethiopia: a cross-sectional population-based study. BMC Womens Health. 2021;21:1–9.
21. Tufa G, Tsegaye R, Seyoum D. Factors associated with timely antenatal care booking among pregnant women in remote area of bule hora district, Southern Ethiopia. International journal of women's health; 2020. pp. 657–66.
22. Neupane S, Doku DT. Association of the quality of antenatal care with neonatal mortality: meta-analysis of individual participant data from 60 low-and middle-income countries. Int Health. 2019;11(6):596–604.
23. Organization WH. WHO recommendations on antenatal care for a positive pregnancy experience. World Health Organization; 2016.
24. Kozuki N, et al. The associations of parity and maternal age with small-for-gestational-age, preterm, and neonatal and infant mortality: a meta-analysis. BMC Public Health. 2013;13:1–10.
25. Engdaw GT, et al. Effect of antenatal care on low birth weight: a systematic review and meta-analysis in Africa, 2022. Front Public Health. 2023;11:1158809.
26. Amsalu T, Wondemagegn ATW et al. The effect of antenatal care follow-up on neonatal health outcomes: a systematic review and meta-analysis. 2018.
27. Aromataris E, et al. Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. JBI Evid Implement. 2015;13(3):132–40.

28. Shamseer L et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ, 2015. 349.
29. Gross A, Schirm S, Scholz M. Ycasd–a tool for capturing and scaling data from graphical representations. BMC Bioinformatics. 2014;15:1–10.
30. Shea BJ et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ, 2017. 358.
31. Gosling CJ et al. Metaumbrella: the first comprehensive suite to perform data analysis in umbrella reviews with stratification of the evidence. BMJ Ment Health, 2023. 26(1).
32. Riley RD, Higgins JP, Deeks JJ. Interpretation of random effects meta-analyses. BMJ, 2011. 342.
33. Cochran WG. The combination of estimates from different experiments. Biometrics. 1954;10(1):101–29.
34. Egger M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629–34.
35. Ioannidis JP, Trikalinos TA. An exploratory test for an excess of significant findings. Clin Trails. 2007;4(3):245–53.
36. Hedges LV, Olkin I. Statistical methods for meta-analysis. Academic; 2014.
37. Cohen J. Statistical power analysis for the behavioral sciences. routledge; 2013.

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