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SYSTEMATIC REVIEW AND META-ANALYSIS ON THE RISK OF NEONATAL MORALITY IN ANTENATAL CARE IN NIGERIA

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Abstract
Neonatal mortality is a major public health problem throughout the world, most notably in developing countries. There exist inconclusive findings on the systematic review and meta-analysis on the risk of neonatal mortality in antenatal care in Nigeria. Thus, the aim of this systematic review and meta-analysis was to reveal the pooled effect of antenatal care visits on the incidence of neonatal death. The effect size index was risk ratio and date was sourced via Pubmed, Science Direct, Web of Science, Medline, Research gate, and Google Scholar. The random-effects model was used for the analysis. The studies in the analysis were assumed to be random sample from a universe of antenatal care visits on neonatal mortality studies and. STATA/SE for windows version 13 software was used to calculate the pooled effect size with 95% confidence intervals (95% CI) of maternal antenatal care visits on neonatal death using the DerSimonian and Laird random effects meta-analysis (random effects model), and results were displayed using a forest plot. Statistical heterogeneity was assessed using the Cochran Q test (chi-squared statistic) and I2 test statistic and visual examination of the forest plot. A total of 12 studies were included in the meta-analysis. Cochran's Q was 88.12 (df = 11, p=0.000), indicating significant heterogeneity. The relative excess in Q had a point estimate of 2.830 (95% CI: 1.232–4.450). The proportion of variability due to heterogeneity (I2) was 87.5% (95% CI: 34.1%–94.9%), further supporting the presence of substantial heterogeneity. The pooled effect estimate showed that antenatal care significantly reduced the risk of neonatal mortality, with an RR of 0.66 (95% CI: 0.56–0.75). This result indicates a 34% reduction in the risk of neonatal mortality with ANC compared with no or minimal care. The null hypothesis of no difference (RR=1) was rejected. The current systematic review and meta-analysis revealed that antenatal care visits were significantly associated with lower rates of neonatal death. The risk of neonatal death was significantly reduced by 34% among newborns delivered from mothers who had antenatal care visits. Thus, visiting antenatal care clinics during pregnancy is strongly recommended, especially in Nigeria. This meta-analysis provides robust evidence that antenatal care significantly reduces the risk of neonatal mortality. Despite the high heterogeneity, the findings underscore the critical importance of promoting ANC as a key strategy for improving neonatal survival. Future research should explore the sources of heterogeneity and examine the specific components of ANC that contribute to the observed benefits.

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INTRODUCTION

Neonatal mortality, which is the absence of all traces of life in a live birth between birth and the first 28 days of life, World Health Organization (WHO. 2011) is one of the glaring targets of the Sustainable Development Goals (SDG) because of its importance to the dynamics of any population and the role that it plays as a barometer for the measurement of social economic and demographic development (Hall, 2005). Although there has been significant progress globally in the fight against childhood mortality, neonatal mortality still maintains significantly high rates, with neonatal mortality contributing nearly 50% of all mortality in children under the age of five globally and about two-thirds of infant mortality (Akinyemi et al., 2015).

In 2018, 5.3 million children died before their fifth birthday, with a staggering 2.5 million of those childhood deaths (47%) occurring in the first month of life (United Nations Inter-Agency Group for Childhood Mortality Estimation (UN-IGME), 2019). Although the 2.5 million deaths of neonates globally represent progress relative to the number of neonatal mortalities in 1990, which was about 5 million babies, efforts to further reduce its occurrence and accelerate progress in preventing child deaths should be considered urgent and intensified as an alarming 7000 neonates still die daily of preventable causes/illness as recently as 2018. (National Population Commission (NPC), 2018). On current trends, over 24 million babies will die in the first month of their lives between 2019 and 2030, representing approximately 2.2 million preventable annual neonatal deaths (UN-IGME, 2019). Most of these neonatal deaths occur in low- and middle-income countries, with the highest number recorded in the south-central

Antenatal care is the care provided by skilled health professionals to pregnant women to ensure maternal and newborn health during pregnancy and childbirth. Antenatal care services provide a platform to deliver evidence-based interventions and counseling to pregnant women to promote a healthy pregnancy and safe delivery. As a critical point of contact during the continuum of care for mothers and children, antenatal care services are associated with delivery saving, improved postnatal attendance, and an increase in facility delivery. A quality antenatal care checkup consists of risk identification, management, and prevention of pregnancy-related risk factors and concurrent diseases, as well as health counseling. Globally, from 2011 to 2016, 86% of women aged 15–49 years attended at least one antenatal care visit during pregnancy with a skilled health professional; however, only 62% of women attended all four visits as recommended (WHO. 2011)

1 Conceptual Review

Meta-analysis is a statistical technique used to combine results from multiple studies to derive more robust and generalizable conclusions about a specific research question. This method is widely used in various fields, including medicine, education, psychology, and social sciences, to synthesize research findings and resolve discrepancies between studies.

Meta-analysis was first formally introduced by Glass (1976), who described it as "the statistical analysis of a large collection of analysis results from individual studies for the purpose of integrating the findings." Its primary purpose is to overcome limitations of individual studies, such as small sample sizes or methodological differences, by aggregating data to enhance statistical power and provide more precise effect size estimates (Hedges & Olkin, 1985).

The meta-analysis begins with a systematic review, which involves identifying and selecting studies that meet predefined inclusion criteria. This ensures that the analysis is based on high-quality and comparable studies (Higgins et al., 2019).

The central feature of meta-analysis is the quantitative synthesis of study results. This involves calculating effect sizes (e.g., Cohen's d, odds ratios) and pooling them using statistical models, such as fixed-effects or random-effects models (Borenstein et al., 2009).

An essential aspect of meta-analysis is assessing heterogeneity, that is, the variability in effect sizes across studies. Statistical methods, such as Cochran's Q test and the I^2 statistic, help determine whether observed differences are due to chance or underlying factors (Higgins & Thompson, 2002).

A potential challenge in meta-analysis is publication bias, where studies with significant findings are more likely to be published. Techniques such as funnel plots and Egger's regression test are used to detect and address this bias (Egger et al., 1997).

Meta-analyses have been instrumental in evidence-based practice, particularly in health care. For instance, it is frequently used to evaluate the efficacy of treatments and interventions by synthesizing data from randomized controlled trials (Haidich, 2010). Similarly, in education, it helps identify the most effective teaching strategies by combining results from experimental studies (Slavin, 2008).

Although meta-analysis is a powerful tool, it has limitations. Results depend heavily on the quality of the included studies and the decisions made during the analysis, such as the selection of statistical models and inclusion criteria. Additionally, issues such as heterogeneity and publication bias can affect the reliability of conclusions (Borenstein et al., 2009).

Meta-analyses are critical for synthesizing research findings, offering a more comprehensive understanding of complex issues. Combining data from multiple studies enhances the precision of effect size estimates, identifies patterns across studies, and provides evidence for decision-making. Despite these challenges, meta-analyses remain a cornerstone of evidence-based research.

Several articles have discussed the concept of neonatal mortality, with a particular focus on pooled risk ratio as an effect size:

Neonatal Mortality and Associated Factors in the Specialized Neonatal Care Unit, Asmara, Eritrea; This study explores various factors influencing neonatal mortality, such as sepsis, respiratory distress syndrome (RDS), and perinatal asphyxia. The researchers used multivariate logistic regression analysis to estimate odds ratios (ORs) and risk ratios for different factors affecting neonatal mortality. The findings emphasized that low birth weight and preterm birth were significant predictors of neonatal death. Woldearegay, A. G. et al. (2019).

Meta-Analysis on Antenatal Care and Neonatal Mortality; This meta-analysis examined the relationship between antenatal care and neonatal mortality, using the risk ratio as the primary effect size. This study found that inadequate antenatal care was associated with a significantly higher risk of neonatal mortality, with a pooled RR indicating substantial heterogeneity across studies. Kuhnt, J., & Vollmer, S. (2017).

Risk Factors and Neonatal Mortality in Sub-Saharan Africa; This article provides a comprehensive review of neonatal mortality in sub-Saharan Africa, focusing on the risk factors identified across multiple studies. It discusses how pooled risk ratios were used to quantify the impact of variables like maternal age, birth asphyxia, and infection on neonatal outcomes. Oza, S., Lawn (2015)

Systematic Review of Low Birth Weight as a Predictor of Neonatal Mortality; This systematic review consolidates data from several studies to assess how low birth weight influences neonatal mortality. The risk ratio was a key measure used to compare mortality rates between low-birth-weight infants and those with normal birth weights. Katz, J., Lee, A.C.C., Kozuki, N., et al. (2013).

This study provides a global overview of neonatal mortality, focusing on causes, interventions, and geographical disparities. The authors pooled data from multiple studies and calculated a risk ratio to evaluate the effectiveness of interventions like neonatal resuscitation, thermal care, and breastfeeding on mortality reduction. The pooled risk ratios emphasize the substantial impact of timely interventions on survival. Lawn, J.E., et al. (2014)

This meta-analysis examined neonatal mortality's risk factors, including preterm birth, infections, and intrapartum-related complications. This study applied pooled risk ratio analysis across various interventions, such

as antenatal corticosteroid therapy and infection management. The findings revealed significant variability in risk ratios, highlighting the need for targeted interventions. Blencowe, H., et al. (2013).

This comprehensive review explored the determinants of neonatal mortality across different health care settings. The pooled risk ratio analysis identified critical determinants such as maternal health, facility-based delivery, and access to neonatal intensive care. The findings of this study highlight the importance of health care access and quality. Liu, L. et al. (2016).

You et al. focused on neonatal mortality's socioeconomic determinants using pooled risk ratios to identify the impact of maternal education, economic status, and rural versus urban living. This study highlighted significant disparities in neonatal mortality among different socioeconomic groups. You, D., et al. (2015).

This study quantified the global burden of neonatal mortality from sepsis, pneumonia, and diarrheal diseases. By pooling data, Oza et al. estimated risk ratios for mortality reduction from various interventions, such as early antibiotic administration and clean birth practices. Oza, S., et al. (2015).

Requejo et al. evaluated the progress of neonatal mortality reduction through various interventions using pooled risk ratios to assess the effectiveness of community-based healthcare programs, facility-based newborn care, and breastfeeding promotion. The findings emphasize comprehensive health care strategies. Requejo, J.H., et al. (2015)

This article reviews evidence on neonatal care practices in low-resource settings, focusing on interventions that can reduce neonatal mortality. Pooled risk ratios for interventions such as kangaroo mother care and essential newborn care were presented, highlighting substantial survival benefits. Bhutta, Z. A. et al. (2014).

Walker et al. pooled data from randomized trials to calculate risk ratios for various neonatal health interventions. This study focused on infection management, emphasizing the significant impact of antibiotic treatment and proper hygiene practices on neonatal survival. Walker, N., et al. (2013)

This review assessed community-based interventions for improving neonatal health and reducing mortality. Pooled risk ratios for interventions such as clean delivery kits and community health worker training demonstrated a significant reduction in neonatal mortality in low-resource settings. Darmstadt, G. L. et al. (2005).

Seale et al. focused on the association between neonatal mortality and intrapartum-related complications. The pooled risk ratio analysis revealed the effectiveness of interventions such as skilled birth attendance, emergency obstetric care, and neonatal resuscitation in reducing mortality rates. Seale, A. C. et al. (2016).

In summary, a systematic review and meta-analysis on the risk of neonatal mortality in antenatal care in Nigeria would integrate evidence from the existing literature to identify key determinants of neonatal mortality, assess the effectiveness of ANC interventions, and inform strategies to improve maternal and neonatal health outcomes in the country.

2. Theoretical Review

Certainly! Neonatal mortality refers to the death of a newborn within the first 28 days of life. Antenatal care (ANC) is crucial for preventing neonatal death by ensuring the health of the mother and baby before birth. Here are some key theories and factors related to neonatal mortality and antenatal care.

3. Theories of neonatal mortality

Social Determinants Theory: This theory posits that socio-economic status, education, and access to health care significantly impact neonatal outcomes. Poor social conditions can lead to higher neonatal mortality rates because of inadequate health care access and poor living conditions. Vissandjee, B., & Leduc, N. (2016).

Biomedical Model Theory: This model focuses on biological and medical factors affecting neonatal health, such as birth weight, prematurity, and congenital anomalies. This emphasizes the role of medical interventions and quality of prenatal care in reducing mortality. Mwangome, M. (2017).

Health System Theory: This theory examines how the organization, accessibility, and quality of health systems affect neonatal mortality. Poor health systems often lack resources, trained personnel, and effective protocols, leading to higher rates of neonatal mortality. Bhutta, Z. A. (2014).

4. Theories on Antenatal Care (ANC)

Preventive Health Model: This model emphasizes the importance of preventive care in antenatal settings to detect and manage risks before they result in complications. Regular ANC visits can help in the early detection of potential problems and promote better maternal and neonatal health. Ketterer, M. W., & Adams, M. A. (2017).

Integrated Care Model: This model advocates for integrating antenatal care with other health services to provide holistic care to pregnant women. The study highlights the benefits of combining prenatal care with maternal health, nutrition, and education to improve outcomes. Ronsmans, C., & Graham, W. J. (2006).

Patient-Centered Care Model: This model emphasizes the importance of tailoring antenatal care to the individual needs and preferences of pregnant women. This suggests that personalized care plans and engagement in decision-making can lead to better health outcomes. Langer, A. (2007).

These theories provide a framework for understanding the complex factors influencing neonatal mortality and the role of antenatal care in improving neonatal health outcomes.

5. Background on the Theories of Meta-analysis

Meta-analysis is a statistical method used to combine results from multiple studies to derive a pooled estimate of effect sizes, thereby providing a more precise and generalized conclusion. The development of meta-analyses has been influenced by various theories and methodologies that address how to synthesize data across studies, manage variability, and account for bias.

- Fisher's Method and Early Developments: One of the earliest contributions to meta-analysis theory was Ronald A. Fisher, who developed methods to combine p-values from different studies. Fisher's method, introduced in the 1930s, is a simple yet powerful tool for synthesizing evidence, especially when effect sizes or outcomes are not directly comparable across studies.
- Glass's concept of meta-analysis: The term "meta-analysis" was first coined by Gene V. Glass was created in 1976. Glass's seminal work focused on the educational research domain, where he proposed that by aggregating results from individual studies, one could overcome the limitations of small sample sizes and inconsistent results that often plague single studies. Glass emphasized the importance of effect size as a metric for combining study results, moving beyond mere significance testing to provide a more nuanced understanding of the magnitude of effects.
- Fixed-Effect vs. Random-Effects Models: A key theoretical development in meta-analysis is the distinction between fixed-effect and random-effects models. The fixed-effect model assumes that all studies estimate the same underlying effect size, with variations between studies attributed to sampling error. In contrast, the random-effects model assumes that the true effect size varies across studies due to differences in study populations, interventions, and methodologies. The choice between these models depends on the degree of heterogeneity among the studies being synthesized.
- Heterogeneity and Its Implications: Heterogeneity refers to the variability or differences in results across studies included in a meta-analysis. Identifying and quantifying heterogeneity is crucial because high heterogeneity can indicate that the studies are not directly comparable. The I^2 statistic is commonly used to assess

the extent of heterogeneity, with values greater than 50% indicating substantial heterogeneity. This has led to the development of mixed-effects models, which attempt to account for both fixed and random effects.

- Publication Bias and Funnel Plots: Another critical theoretical consideration in meta-analysis is publication bias, where studies with significant or positive results are more likely to be published, whereas null or negative results are underreported. This can skew the results of the meta-analysis. To detect and address publication bias, funnel plots and statistical tests like Egger's test have been developed. These tools can help identify asymmetries in the distribution of effect sizes that may indicate bias.

Conclusion: The development of meta-analysis as a statistical tool has been shaped by the contributions of various researchers and statisticians. The theoretical foundations provided by Fisher, Glass, and others have been essential in establishing meta-analysis as a robust method for evidence synthesis across multiple disciplines. The ongoing refinement of methods to address heterogeneity, publication bias, and other challenges continues to enhance the utility and reliability of meta-analytic findings.

6. Meta-Analysis Models

Various statistical models, including fixed- and random-effects models, can be used for meta-analysis. Fixed-effects models assume a single true effect size across studies, whereas random-effects models account for both within-study variability and between-study variability, accommodating heterogeneity among studies.

7. Heterogeneity Assessment: Heterogeneity refers to the variability in effect sizes across studies beyond what would be expected by chance. Heterogeneity can be assessed using statistical tests (e.g., Q-statistic, I^2 statistic) and visual inspection of forest plots.

8. Sensitivity analysis: This analysis explores the robustness of meta-analysis findings by examining the impact of excluding certain studies or using alternative analysis methods.

9. Publication Bias: Publication bias occurs when studies with statistically significant results are more likely to be published, leading to an overestimation of effect sizes. Meta-analytic techniques, such as funnel plots and Eggdyer's regression test, can help detect and adjust for publication bias.

10. Method of Data Collection

Using a standardized data extraction form, pertinent information is extracted from Eligible papers for the meta-analysis. Study parameters (e.g., author, publication year), Study methodology, geographic location, parasite species, and treatment resistance markers and prevalence estimates are important factors of interest. To reduce bias, two reviewers will extract data independently; if any differences are noted, they will be discussed. Necessary, a third reviewer will be consulted. To guarantee accuracy and completeness of the data, attempts will be made to get in touch with the study authors regarding Any additional details or explanations that may be required.

A crucial phase in the meta-analysis is data extraction, which involves the following: Methodical acquisition and synthesis of pertinent data from the included research. The methodologies employed, variables collected, and quality control procedures are described in detail in this section, and provides an overview of the data extraction process.

11. Effect Size Estimation

The pooled risk ratio for antenatal care was estimated using random-effects meta-analysis models. The random-effects model accounts for both within-study and between-study variability, providing more conservative estimates of effect sizes than fixed-effects models (Borenstein et al., 2010). The DerSimonian-Laird method was used to calculate the overall effect size, along with 95% confidence intervals.

12. Random Effects Meta-Analysis

Naturally, in a real meta-analysis, we begin with the observed effects and attempt to estimate the population impact, as opposed to starting with the population effect and making projections about the observed effects. If otherwise stated, our objective is to estimate the overall mean μ, using the Yi collection. We computed a weighted mean, where the weight allocated to each research equals the inverse of that study's variance, to produce the most accurate estimate of the overall mean (to minimize the variance).

Since the study's overall variance is the sum of these two values, we must know both the within-study variance and τ^2 in order to compute a study's variance under the random-effects model. There are formulas for calculating within-study variation. A method for estimating the between-study variance is also provided.

13. Estimating Tau-squared

The parameter τ^2 (tau-squared) is the between-study variance (the variance of the effect size parameters across the population of studies). In other words, if we somehow knew the true effect size for each study and computed the variance of these effect sizes (across an infinite number of studies), this variance would be τ^2 . One method for estimating τ^2 is the moments method (or the DerSimonian and Laird) method, as follows. We compute

$$T^2 = \frac{Q - df}{C}\ , \tag{1.1}$$

Where;

$$Q = \sum_{i=1}^{k} W_i Y_i^2 - \frac{\left(\sum_{i=1}^{k} W_i Y_i\right)^2}{\sum_{i=1}^{k} W_i}, \qquad \text{df = k 1,} \tag{1.2}$$

Here, k is the number of studies, and

$$C = \sum W_i - \frac{\sum W_i^2}{\sum W_i}. \tag{1.3}$$

14. Estimating The Mean Effect Size

In the fixed-effect analysis, each study was weighted by the inverse of its variance. In the random-effects analysis, each study is also weighted by the inverse of its variance. The difference is that the variance now includes the original (within- studies) variance plus the estimate of the between-studies variance, T^2. In keeping with the book's convention, we use τ^2 to refer to the parameter and T^2 to refer to the sample estimate of that parameter.

To highlight the parallel between the formulas here (random effects) and those in the previous chapter (fixed effect), we use the same notations but add an asterisk (*) to represent the random-effects version. Under the random-effects model, the weight assigned to each study was

$$W_i^* = \frac{1}{V_{Y_i}^*}, \tag{1.4}$$

Here, V^*_{Yi} is the within-study variance for study *i* plus the between-study variance, T^2. That is,

$$V_{Y_i}^* = V_{Y_i} + T^2. \tag{1.5}$$

The weighted mean M* is then computed as follows:

$$M^* = \frac{\sum_{i=1}^{k} W_i^* Y_i}{\sum_{i=1}^{k} W_i^*}, \tag{1.6}$$

The sum of the products (effect size multiplied by weight) is divided by the sum of the weights.

The variance of the summary effect is estimated as the reciprocal of the sum of the weights as follows:

$$V_{M^*} = \frac{1}{\sum_{i=1}^{k} W_i^*}, \quad (1.7)$$

and the estimated standard error of the summary effect is then the square root of the variance as follows:

$$SE_{M^*} = \sqrt{V_{M^*}}. \quad (1.8)$$

The 95% lower and upper limits for the summary effect were computed as follows:

$$LL_{M^*} = M^* — 1{:}96 \times SE_{M^*}; \quad (1.9)$$

and

$$UL_{M^*} = M^* + 1{:}96 \times SE_{M^*}: \quad (1.10)$$

Finally, a Z-value to test the null hypothesis that the mean effect μ is zero was computed as follows:

using $$Z^* = \frac{M^*}{SE_{M^*}}. \quad (1.11)$$

For a one-tailed test, the p-value is given as follows:

$$p^* = 1 - \Phi(\pm|Z^*|),; \quad (1.12)$$

Here, we select '+' if the difference is in the expected direction or '–' otherwise, and for a two-tailed test by

$$p^* = 2[1 - (\Phi(|Z^*|))], \quad (1.13)$$

Where Φ(Z*) denotes the standard normal cumulative distribution. This function is presented in many introductory statistics books and is implemented in Excel as follows:

=NORMSDIST(Z*).

Source: Adehi, M. U., Yakasai, A. M., Dikko, H. G., Asiribo, E. O., and Dahiru, T. (2017). Risk of Mortality in Patients with HIV and Depression: A Systematic Review and Meta-analysis of Non-Common Outcome. International Journal of Statistics and Applications, 7(4), pp. 205-214

15. Nature and Source of Data.

Systematic reviews and meta-analyses on the risk of neonatal mortality in antenatal care in Nigeria typically rely on various data sources. Here is a breakdown of the data sources:

16. Scientific Databases: like PubMed, MEDLINE, Embase, Scopus, and Google Scholar.

These databases host various academic articles, including those focused on maternal and neonatal health in Nigeria.

i. **Gray Literature:** such as conference proceedings, thesis databases, government reports, and nongovernmental organization (NGO) reports. Gray literature provides valuable insights, especially in areas where formal research is limited.

ii. **National Health Surveys:** Many countries conduct national health surveys that collect data on maternal and child health indicators, including antenatal care and neonatal mortality rates. In Nigeria, the National Demographic and Health Survey (NDHS) is the primary source of such data.

iii. **Hospital Records and Health Facility Surveys:** This study aimed to access hospital records and conduct surveys in health facilities across Nigeria to gather data on antenatal care use and neonatal outcomes.

Data are identified and then systematically reviewed and synthesized, often using statistical methods to conduct a meta-analysis to quantitatively analyze the pooled data and estimate overall effects.

17. Data Presentation

This section presents the systematic review and meta-analysis of the risk of neonatal mortality in antenatal care, based on pertinent research included in the meta-analysis. The studies were identified through a rigorous literature search, and the key characteristics are summarized below (e.g., Study year, effect size sample size and confidence interval).

S/N	STUDY	EFFECT SIZE (PRR)	SAMPLE SIZE	CONFIDENCE INTERVAL
1.	Gatahum, T. (2022)	0.58	27	0.47-0.71
2.	Amare, B. (2022)	1.76	11	1.45-3.16
3.	Kasiye, S. (2021)	0.85	13	0.21-3.49
4.	McCurdy R.J. (2019)	0.82	9	0.76-0.88
5.	Tesfolidet, T. (2019)	0.61	23	0.43-0.86
6.	Eshetu, E. (2019)	0.48	19	0.38-0.58
7.	Ali, N. B. (2019)	0.81	10	0.74-0.88
8.	You, D. (2015)	0.76	12	0.71-0.81
9.	Kuhut J. (2017)	0.78	15	0.72-0.85
10.	Millie, O. (2022)	0.46	16	0.24-0.86
11.	Tadesse, T. (2020)	0.35	28	0.24-0.51
12.	Jiali, S. (2024)	0.98	30	0.57-1.71

Table 4.1: Literature Search Results

Fig 4.1 Flow Chart

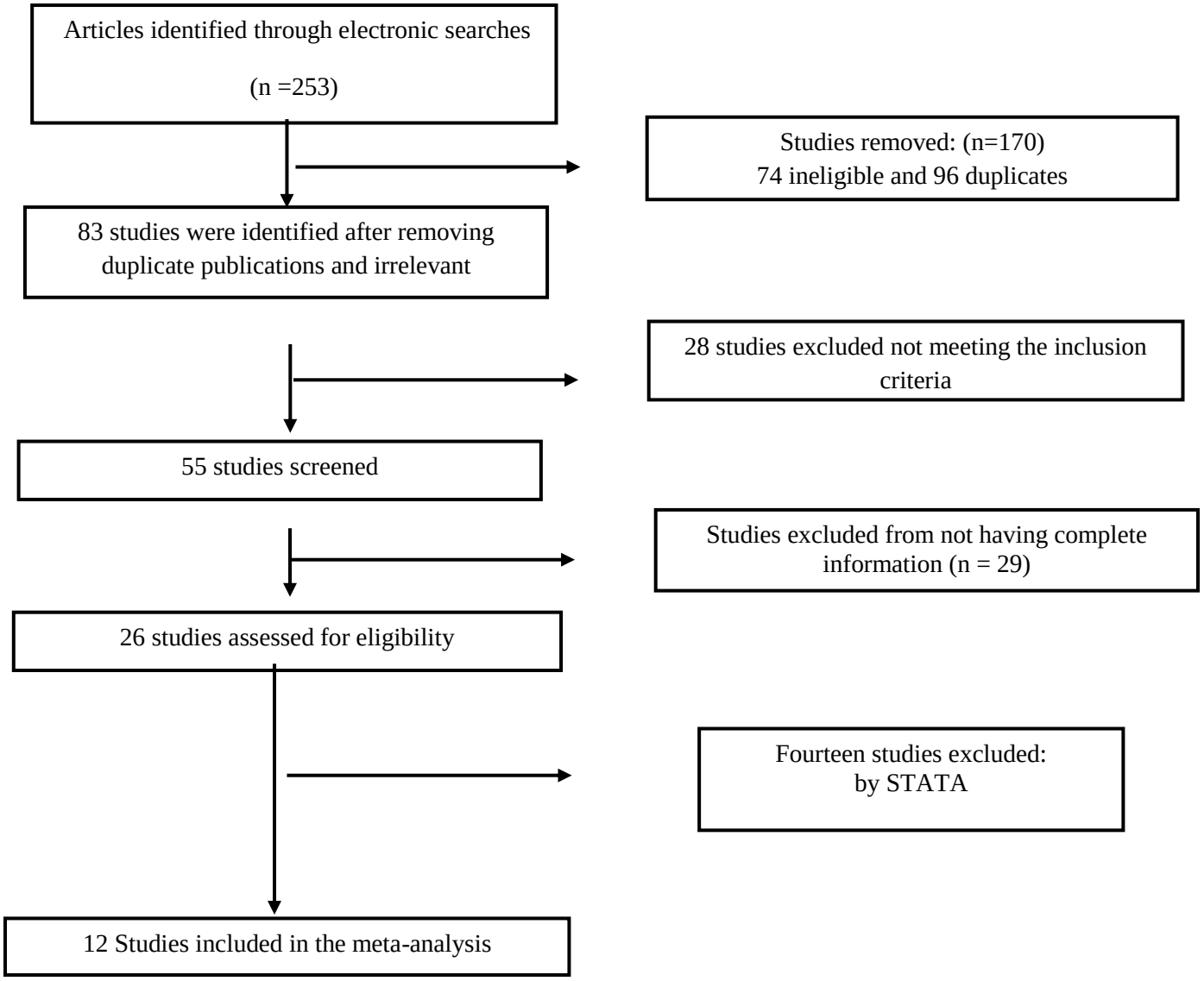


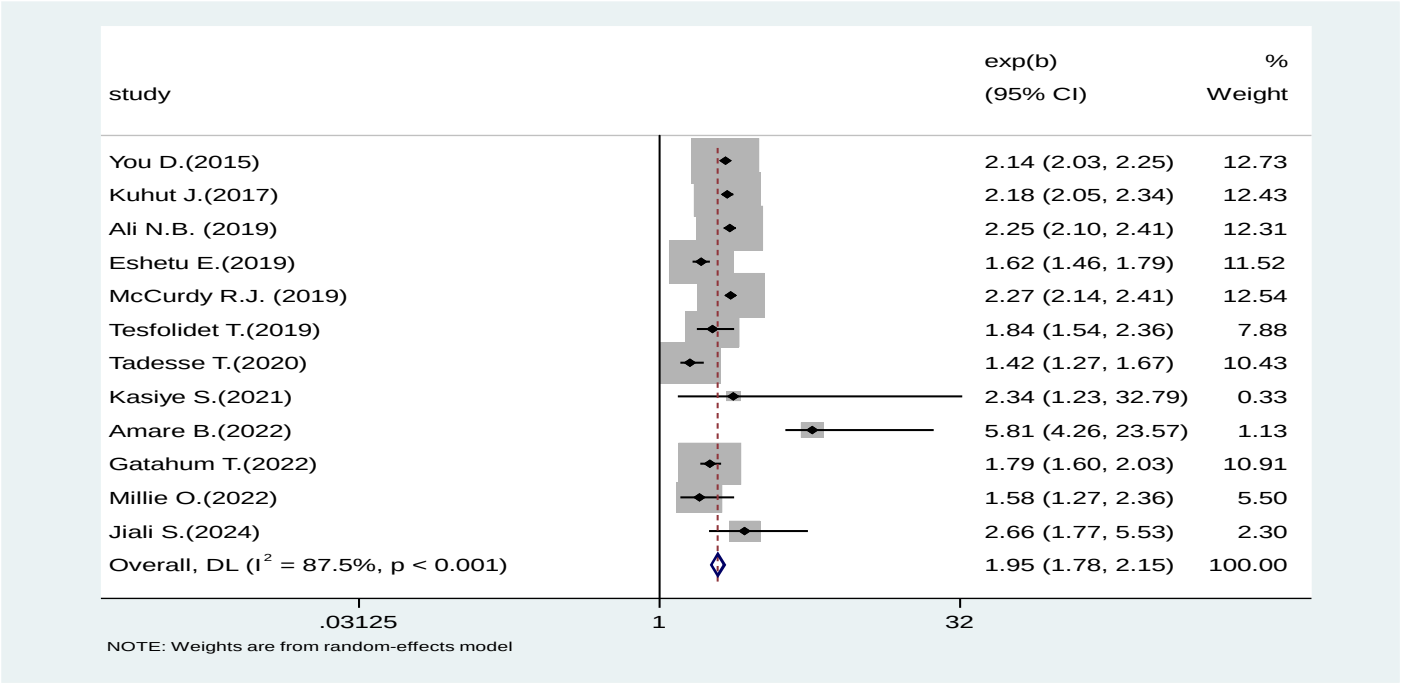
Figure 4.1. PRISMA (preferred reporting items for systematic reviews and meta-analysis) flow diagram of included and excluded studies.

The figure 4.1 above showed that 253 articles were assessed, out of which 74 were ineligible and 56 were duplicates. The number of studies screened was 55, out of which 29 were retrieved. Articles assessed for eligibility were 26 and 14 eliminated by the Statistical software (STATA). Finally, 12 studies were included.

18. Data Analysis and Results

Figure 4.2 displays forest plots showing the impact sizes (risk ratios) for the risk of neonatal mortality in antenatal care. To facilitate visual comparison, each line displays the estimated effect size and confidence interval for the risk of neonatal mortality.

Figure 4.2: Forest plot of risk ratios for neonatal mortality in antenatal care



Studies included: 12

Meta-analysis pooling of aggregate data using the random-effects inverse-variance model with DerSimonian-Laird estimate of tau²

study	Effect	[95% Conf.	Interval]	% Weight
You D.(2015)	0.760	0.710	0.810	12.73
Kuhut J.(2017)	0.780	0.720	0.850	12.43
Ali N.B. (2019)	0.810	0.740	0.880	12.31
Eshetu E.(2019)	0.480	0.380	0.580	11.52
McCurdy R.J. (2019)	0.820	0.760	0.880	12.54
Tesfolidet T.(2019)	0.610	0.430	0.860	7.88
Tadesse T.(2020)	0.350	0.240	0.510	10.43
Kasiye S.(2021)	0.850	0.210	3.490	0.33
Amare B.(2022)	1.760	1.450	3.160	1.13
Gatahum T.(2022)	0.580	0.470	0.710	10.91
Millie O.(2022)	0.460	0.240	0.860	5.50
Jiali S.(2024)	0.980	0.570	1.710	2.30
Overall, DL	0.670	0.575	0.765	100.00

Test of overall effect = 0: z = 13.798 p = 0.000

The test of the overall effect (z=13.798, p=0.000) shows highly significant results, indicating that antenatal care significantly reduces neonatal mortality. This strong evidence supports the importance of antenatal care interventions in improving neonatal survival outcomes across diverse populations.

19. Heterogeneity Assessment

Heterogeneity measures calculated from the data with Conf. Intervals based on the gamma (random-effects) distribution for Q

Measure	Value	df	p-value
Cochran's Q	88.12	11	0.000
		−[95% Conf.	Interval]−
H	2.830	1.232	4.450
I^2 (%)	87.5%	34.1%	94.9%

H = relative excess in Cochran's Q over its degrees-of-freedomI^2 = proportion of total variation in effect estimate due to between-study heterogeneity (based on Q)

Explanation:

Cochran's Q:

Value: 88.12

Degree of freedom (df): 11

p-value**:** 0.000 (significant at conventional thresholds like 0.05).

Indicates significant heterogeneity among the studies.

H^2 (Relative Excess in Q):

A measure of the relative excess in Cochran's Q compared to its degrees of freedom.

Point estimation: 2.830

Confidence Interval (95%): 1.232–4.450

Suggests uncertainty in the exact level of excess variability but confirms significant heterogeneity.

I^2 (Proportion of Variability Due to Heterogeneity):

Point Estimate**:** 87.5%

Confidence Interval (95%)**:** 34.1%–94.9%

Indicates that a substantial proportion (87.5%) of the total variation in effect sizes is due to heterogeneity rather than random error.

The wide confidence interval reflects uncertainty in the exact percentage.

Heterogeneity variance estimates

Method	Tau^2
DL	0.0179

The heterogeneity variance estimate (τ2\tau^2τ2) of 0.0179, derived using the DerSimonian-Laird (DL) method, quantifies the variance among effect sizes across studies in a meta-analysis. This indicates moderate heterogeneity, suggesting that differences in study outcomes may arise from variations in methodologies, populations, or other study-level factors rather than random chance alone.

20. Subgroup Analysis

Subgroup analysis explores how treatment effects vary across different groups (e.g., by age, gender, study, design, time). It helps identify effect modification (i.e., whether the effect differs in different populations). The subgroup analysis was performed by comparing studies conducted before and after 2015 (Table 4.2.2.

Table 4.2.2: Subgroup Analysis

Subgroup and study	Effect	[95% Conf.	Interval]	% Weight
Small Sample Size				
You D.(2015)	0.760	0.710	0.810	12.73
Kuhut J.(2017)	0.780	0.720	0.850	12.43
Ali N.B. (2019)	0.810	0.740	0.880	12.31
Eshetu E.(2019)	0.480	0.380	0.580	11.52
McCurdy R.J. (2019)	0.820	0.760	0.880	12.54
Kasiye S.(2021)	0.850	0.210	3.490	0.33
Amare B.(2022)	1.760	1.450	3.160	1.13
Millie O.(2022)	0.460	0.240	0.860	5.50
Subgroup, DL	0.731	0.639	0.822	68.48
Large Sample Size				
Tesfolidet T.(2019)	0.610	0.430	0.860	7.88
Tadesse T.(2020)	0.350	0.240	0.510	10.43
Gatahum T.(2022)	0.580	0.470	0.710	10.91
Jiali S.(2024)	0.980	0.570	1.710	2.30
Subgroup, DL	0.543	0.367	0.719	31.52
Overall, DL	0.670	0.575	0.765	100.00

Subgroup effect size = 0:

Small Sample Size z = 15.690 p = 0.000

Large Sample Size z = 6.038 p = 0.000

Overall, z = 13.798, p = 0.000

The subgroup effects tests evaluate the significance of effect sizes within small and large sample size groups for neonatal mortality in antenatal care. Both subgroups showed highly significant results (z=15.690, p=0.000 for small samples; z=6.038, p=0.000 for large samples), indicating that antenatal care significantly reduced neonatal mortality regardless of sample size. The overall effect (z=13.798, p=0.000) further supports the intervention's robust benefit across all studies.

Table 4.2.3: Cochran's Q statistics for heterogeneity

Measure	Value	df	p-value	I^2
Small Sample Size	45.14	7	0.000	84.5%
Large Sample Size	10.14	3	0.017	70.4%
Overall	88.12	11	0.000	87.5%
Between	3.43	1	0.064	

Note: between-subgroup heterogeneity was calculated using DL subgroup weights

This analysis will show separate pooled estimates for studies with small and large sample sizes.

21. Sensitivity Analysis

Sensitivity analysis helps assess the robustness of your results by systematically excluding one study at a time or a group of potentially influential studies.

Exclude One Study at a Time: We manually excluded studies using the if condition. Here, we excluded the studies with the highest and lowest risk ratios to determine their impact on the pooled results.

Excluding studies with the highest risk ratio (Amare B., rr = 1.76):

Studies included: 11

Meta-analysis pooling of aggregate data using the random-effects inverse-variance model with DerSimonian-Laird estimate of tau²

study	Effect	[95% Conf.	Interval]	% Weight
You D.(2015)	0.760	0.710	0.810	12.98
Kuhut J.(2017)	0.780	0.720	0.850	12.65
Ali N.B. (2019)	0.810	0.740	0.880	12.53
Eshetu E.(2019)	0.480	0.380	0.580	11.68
McCurdy R.J. (2019)	0.820	0.760	0.880	12.77
Tesfolidet T.(2019)	0.610	0.430	0.860	7.86
Tadesse T.(2020)	0.350	0.240	0.510	10.52
Kasiye S.(2021)	0.850	0.210	3.490	0.32
Gatahum T.(2022)	0.580	0.470	0.710	11.03
Millie O.(2022)	0.460	0.240	0.860	5.42
Jiali S.(2024)	0.980	0.570	1.710	2.24
Overall, DL	0.658	0.565	0.751	100.00

Test of overall effect = 0: z = 13.809 p = 0.000

Heterogeneity measures calculated from the data with Conf. Intervals based on the gamma (random-effects) distribution for Q

Table 4.2.4

Measure	Value	df	p-value
Cochran's Q	82.58	10	0.000
		−[95% Conf.	Interval]−
H	2.874	1.237	4.532
I² (%)	87.9%	34.7%	95.1%

H = relative excess in Cochran's Q over its degrees of freedom

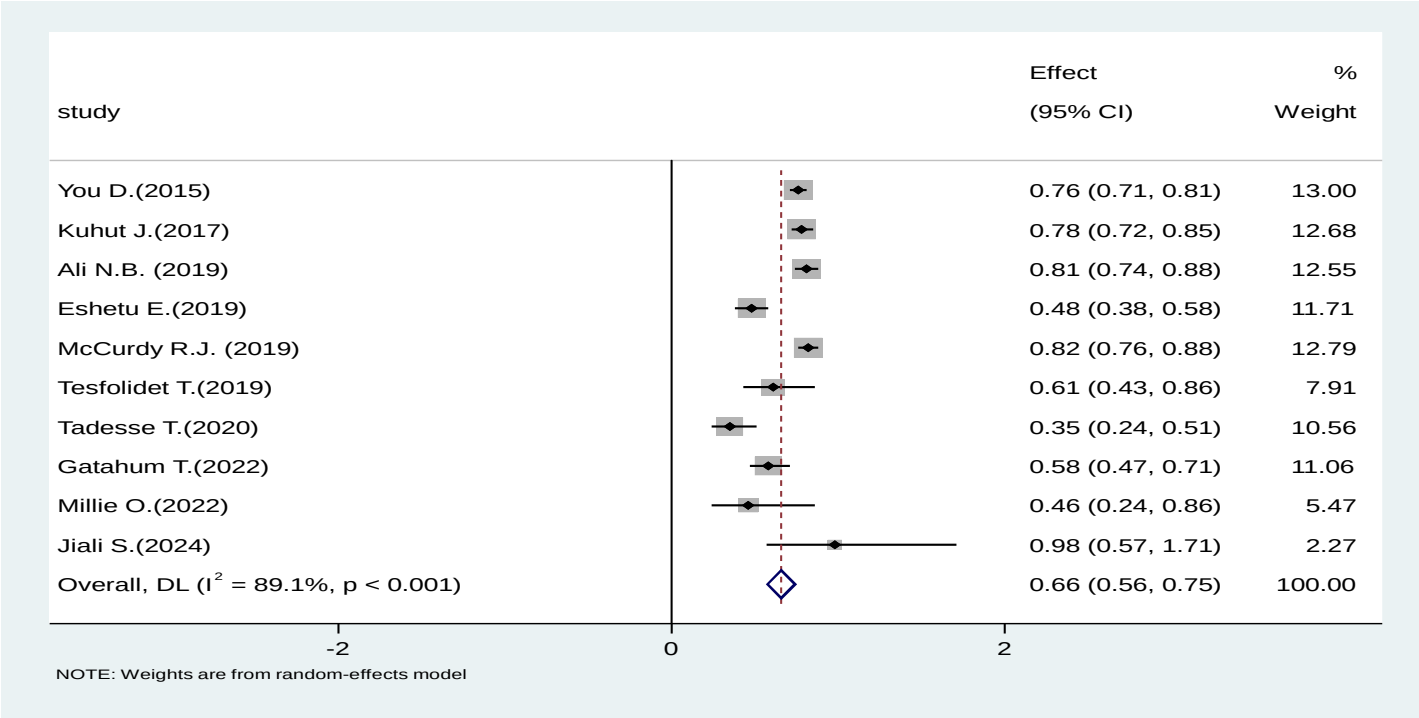
I² = proportion of total variation in effect estimate due to between-study heterogeneity (based on Q)

Table 4.2.5: Heterogeneity variance estimates

Method	Tau^2
DL	0.0171

The heterogeneity variance (Tau²) estimate of 0.0171, calculated using the DerSimonian and Laird (DL) method, indicates low to moderate variability in effect sizes across studies due to heterogeneity rather than chance. This

suggests that the outcomes of the included studies differ slightly, potentially due to methodological or population differences.



The forest plot shows the effect sizes and confidence intervals for individual studies on a common scale. The overall pooled effect size was 0.66 (95% CI: 0.56, 0.75) under a random-effects model, with high heterogeneity (I^2 = 89.1%, p < 0.001), indicating significant variability among the study results.

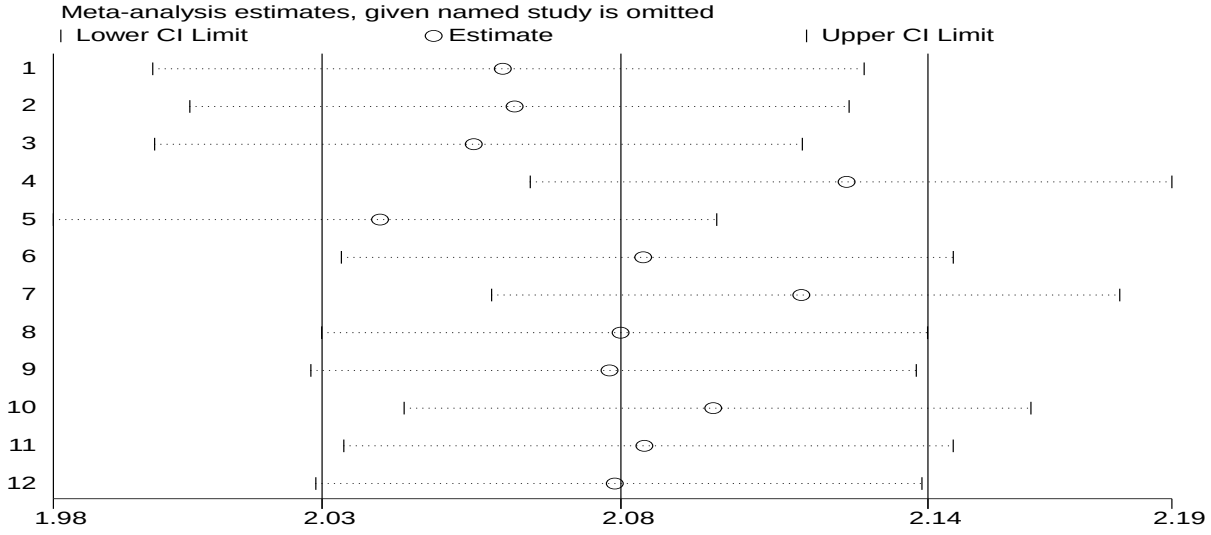


Figure 4.3. is a "leave-one-out" sensitivity analysis plot for a meta-analysis, showing how the pooled estimate and conf3idence interval change when each study is omitted.

22. Conclusions

The analysis was based on 12 studies. The effect size index is the risk ratio. The findings in this study are discussed in the following sub-topics.

23. Statistical Methods

The random-effects model was used for the analysis. The studies in the analysis are is assumed to be a random sample from a universe of potential studies, and this analysis is used to make an inference to that universe. (Borenstein, 2019; Borenstein et al., 2010;

Borenstein et al. (2021; Hedges & Vevea, 1998; Higgins & Thomas, 2019) Heterogeneity measures (I^2 statistics) provide the basis for selecting random-effects models as the statistical strategy for meta-analysis. To evaluate heterogeneity, the $I^{2\ statistic}$ was used; a value of >50% indicated significant variability across investigations. The I-squared statistic is 90%, which indicates that 90% of the variance in observed effects reflects variance in true effects rather than sampling error.

24. Interpretation of the results

The forest plot included a diamond at the bottom, representing the **pooled estimate** of the effect of antenatal care on neonatal mortality risk across all studies. This diamond represents the overall risk ratio (RR) obtained from a meta-analysis combining data from the included studies.

25. Interpretation of the results

- **Pooled Risk Ratio (RR)**: The pooled risk ratio for neonatal mortality is 0.66 with a 95% confidence interval (CI) of **(0.56, 0.75)**. This RR suggests that overall, antenatal care is associated with a **34% reduction in neonatal mortality risk** compared with the control (since 1 - 0.66 = 0.34).
- **Confidence Interval**: The diamond width represents the 95% CI of the pooled estimate. The CI **excludes 1**, suggesting a statistically significant reduction in neonatal mortality for the treatment group (antenatal care) compared with the control group. The fact that the CI does not cross 1 lead to the rejection of the null hypothesis (H_0), indicating that antenatal care has a protective effect against neonatal mortality.
- **Heterogeneity (I^2 and p-value)**:

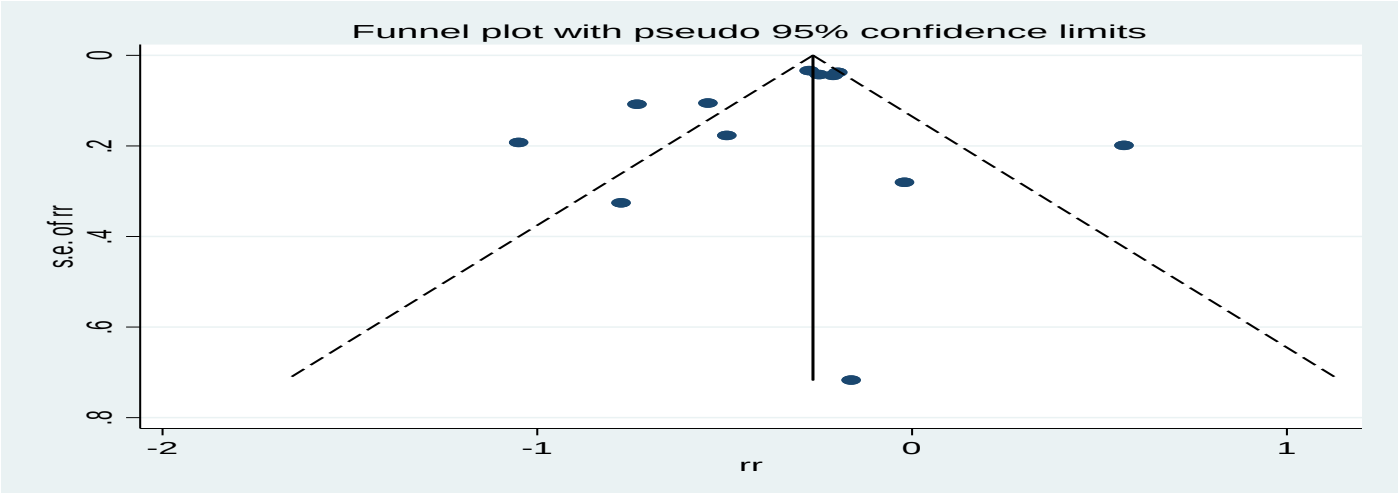
The **I^2 value of 87.9%** indicates a high level of heterogeneity among the studies, suggesting that the effect of antenatal care on neonatal mortality varies between studies.

A **p-value < 0.001** further suggests that the observed heterogeneity was statistically significant.

- **Publication Bias Assessment**

Egger's test and funnel plots were used to assess the existence of publication bias. Egger's test (p = 0.04) supported the funnel plot's (Figure 4.4) suggestion of some asymmetry, suggesting possible bias in study publishing.

Figure 4.4: Funnel Plot for Publication Bias



This funnel plot assesses publication bias in a meta-analysis. Each dot represents a study with effect size (rr) on the x-axis and standard error on the y-axis. Symmetry around a vertical line indicates low bias, whereas asymmetry suggests potential bias, which is often due to the selective reporting of significant results.

26. Public Health Implications

A systematic review and meta-analysis on the risk of neonatal mortality in antenatal care has significant public health implications. This approach provides evidence-based insights for policymaking, guiding resource allocation, and improving maternal and neonatal health programs. By identifying effective interventions and gaps, it helps prioritize critical areas for action. The findings support health education, advocacy, and awareness campaigns on the importance of antenatal care. Moreover, it enables regional and global comparisons and informs targeted strategies for specific populations. Overall, it strengthens health systems by integrating proven antenatal care practices, ultimately reducing neonatal mortality and enhancing maternal and child health outcomes.

27. Summary

The association between the risk of neonatal mortality in antenatal care was comprehensively assessed. Evaluated in this meta-analysis. The important discoveries are as follows:

I. **Individual Study Estimates**: Each line on the plot represents the effect estimate (risk ratio) from an individual study, usually with a 95% confidence interval (CI). A risk ratio (RR) of 1 indicates no difference in the neonatal mortality risk between the treatment and control groups in that study.

II. **Pooled Estimate**: At the bottom of the forest plot, there is usually a diamond or summary line representing the pooled risk ratio and its confidence interval, calculated across all studies. This pooled estimate provides an overall assessment of the risk of neonatal mortality when comparing treatment and control groups.

III. Confidence Intervals: If the confidence interval for the pooled estimate does not cross 1, we would reject the null hypothesis, concluding that there is a statistically significant difference in neonatal mortality risk between the groups. However, if the confidence interval crosses 1, we would not reject the null hypothesis, indicating no statistically significant difference in risk.

28. Interpreting pooled estimate

I. **Pooled Risk Ratio (RR)**: The pooled risk ratio for neonatal mortality is 0.66 with a 95% confidence interval (CI) of **(0.56, 0.75)**. This RR suggests that overall, antenatal care is associated with a **34% reduction in neonatal mortality risk** compared with the control (since 1 - 0.66 = 0.34).

II. **Confidence Interval**: The diamond width represents the 95% CI of the pooled estimate. The fact that the CI **excludes 1** suggests that

III. Reduction in neonatal mortality in the treatment group (antenatal care) compared to the control group. The fact that the CI does not cross 1 lead to the rejection of the null hypothesis (H_0), indicating that antenatal care has a protective effect against neonatal mortality.

IV. **Heterogeneity (I^2 and p-value)**:

The **I^2 value of 87.9%** indicates a high level of heterogeneity among the studies, suggesting that the effect of antenatal care on neonatal mortality varies between studies.

A **p-value < 0.001** further suggests that the observed heterogeneity was statistically significant.

29. Conclusion

The pooled estimate, with an RR of 0.66 and a 95% CI of (0.56, 0.75), supports the conclusion that antenatal care significantly reduces the risk of neonatal mortality compared with no or minimal care. This overall effect, derived from a random-effects model because of high heterogeneity, shows that the true effect across studies is likely beneficial; thus, the null hypothesis of no difference (RR = 1) is rejected.

30. Recommendations

Based on the findings and interpretation of the meta-analysis, the following recommendations were made:

I. To reduce neonatal mortality and improve access to quality antenatal care (ANC) services, especially in underserved areas.

II. Focus on comprehensive ANC interventions, including screenings, nutrition, and education, while addressing barriers such as cost and accessibility.

V. Tailor programs to high-risk populations and adapt interventions to local contexts to account for study heterogeneity.

VI. Strengthen health care provider training and infrastructure to enhance service quality.

VII. Future research should explore specific effective components of ANC, address Heterogeneity through subgroup analyses and region-specific studies.

VIII. Standardization of ANC definitions and reporting outcomes to improve data reliability.

IX. Integrate long-term outcomes and unpublished data to ensure comprehensive evidence.

31. Limitations of the study

a. The study's limitations include high heterogeneity ($I^2 = 87.9\%$), indicating variability across studies on populations, interventions, and methodologies.

b. Differences in study designs, such as observational versus randomized trials, may introduce bias. The variability in antenatal care components limits the identification of specific effective interventions.

c. Publication bias may overestimate the pooled effect size, and limited generalizability restricts its applicability to diverse settings. Residual confounding from unadjusted factors like socioeconomic status can distort the results.

d. This study also focused on neonatal mortality, excluding long-term outcomes. Lastly, the exclusion of unpublished data may lead to incomplete evidence, reducing the reliability of the findings.

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