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Meta Analysis
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Associations between Prematurity, Low Birth Weight, and Residence on the Risk of Newborn Death: A Meta Analysis

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ABSTRACT

Background: Newborn mortality is a global issue that requires serious attention from the world of public health. This study aims to analyze the influence of place of residence, premature birth and low birth weight on the incidence of newborn deaths.
Subjects and Method: This research is a meta-analysis research using the PRISMA diagram and PICO format. Population: Newborns died. Intervention: Village residence, premature birth, low birth weight. Comparison: City residence, normal birth, normal birth weight. Outcome: Newborn death. Articles were searched using online databases such as PubMed, Google Scholar, Elsevier, Science Direct. Search for articles using the keywords: "Neonates Mortality" AND "Residence" AND "Gestational age" OR "Premature" AND "Low birth weight". Using articles published in 2013-2023. Data analysis using RevMan 5.4.
Results: Meta-analysis was carried out using 15 articles with cross-sectional studies from African countries and Ethiopia with a total sample of 17,116 samples. The risk of newborn death increased in newborns living in a village (aOR= 4.17; 95% CI= 2.30 to 7.58; p<0.001), premature birth (aOR= 5.17; 95% CI= 2.87 to 9.33; p< 0.001), and low birth weight (aOR= 2.50; 95% CI= 1.63 to 3.85; p<0.001).
Conclusion: Rural residence, premature birth, and low birth weight increase the risk of newborn death.

Keywords: rural residence, prematurity, low birth weight, newborn death.

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BACKGROUND

Newborn mortality is a global issue that continues to be challenging, requiring serious attention from the world of public health. According to the World Health Organization (WHO), in 2020, around 2.4 million newborn babies died, and almost half (47%) occurred in the neonatal period, which covers the first 28 days of life. Although there has been a decline in the overall newborn mortality rate, from 65 deaths per 1000 live births in 1990 to 29 deaths per 1000 live births in 2018, the neonatal mortality rate has declined more slowly than the mortality rate for children under five years of age. The highest neonatal mortality rate was recorded in Sub-Saharan Africa (27 deaths per 1000 live births), followed by Central and South Asia (23 deaths per 1000 live births) (WHO, 2019).

Causes of neonatal death involve factors such as premature birth, birth-related complications (such as birth asphyxia or inability to breathe at birth), infections, and congenital defects. access to adequate health services, maternal education, family socio-economic status, and environmental quality (WHO, 2018).

A number of studies have been conducted to explore factors that can influence newborn mortality rates. Womack et al. (2020) highlighted disparities in infant mortality between urban and rural areas, with an emphasis on differences based on race, ethnicity, and various causes of death. De Visme et al. (2020) also explain how to understand national variations in infant mortality trends in Western Europe. This study opens up a rich understanding of the complexity of factors influencing newborn mortality.

Zhang et al. (2023) contributed to a method for predicting infant mortality using machine learning, offering an innovative approach to understanding and anticipating the risk of infant mortality. Studies such as Matoba and Collins (2017), Driscoll and Ely (2019), Ranjan et al. (2022), and others have explored disparities in racial, ethnic, and maternal characteristics as factors influencing newborn mortality.

In this context, a meta-analysis that includes findings from these studies can provide a holistic view of the combined influence of the variables of place of residence, baby weight at birth, and gestational age on infant mortality rates. By summarizing these findings, it is hoped that consistent and reliable findings can emerge that can guide health policy planning and preventive interventions that are more effective in reducing infant mortality rates, especially newborns, at the global level.

SUBJECTS AND METHOD

1. Study Design

This study is a systematic review and meta-analysis study using primary data obtained from previous research results. Article searches used 4 online databases, namely: PubMed, Google Scholar, Elsevier, and Science Direct. The keywords used in this research are "Neonates mortality" AND "Residence" AND "Gestational age" OR "Premature" AND "Low birth weight". This study used 15 primary research articles that met the inclusion criteria for this study.

2. Steps of Meta-Analysis

Meta analysis was carried out in the following 5 steps:

1) Formulate research questions using the PICO format (Population, Intervention, Comparison, Outcome)
2) Search for primary article studies from various electronic and non-electronic databases.
3) Screening articles with critical appraisal of primary research.
4) Extract data and synthesize effect estimates using the RevMan 5.4 application
5) Interpret and conclude research results.

3. Inclusion Criteria

The complete article uses a cross-sectional study design, the research subjects are newborn babies (Neonates), the research intervention is babies born in rural areas, babies born with low weight, and babies born prematurely. The outcome of this study is newborn death.

4. Exclusion Criteria
Articles are those that do not use English, articles that carry out bivariate analysis only and do not include Adjusted Odds Ratio values, and the year of publication of the article is less than 2013.

5. Operational Definition of Variable
Newborn death is the death of a newborn before the baby is 30 days old.
Rural residence is the area where babies live and are born when they die as newborns
Low Birth Weight is the condition of a baby born with a body weight of less than 2,500 grams or 2.5 kilograms
Premature is a birth that occurs before the pregnancy reaches 37 weeks or earlier than the expected time.

6. Instrument
Quality assessment in this study used a critical appraisal sheet for cross-sectional studies published by Murti in 2023.

7. Data Analysis
The collected data is then processed using the Review Manager application (RevMan 5.4). Variations in this research data are grouped into two, Fixed Effect Model (FEM) or Random Effect Model (REM) and presented in forest plots and funnel plots.

RESULTS

Searching for articles in this research used online databases such as PubMed, Google Scholar, Elsevier, and Science Direct. The selection process uses the PRISMA diagram. The initial search process obtained 3,254 articles, then article selection was carried out so that the final results for articles that met the requirements were 15 articles and could be included in the meta-analysis (Figure 1)

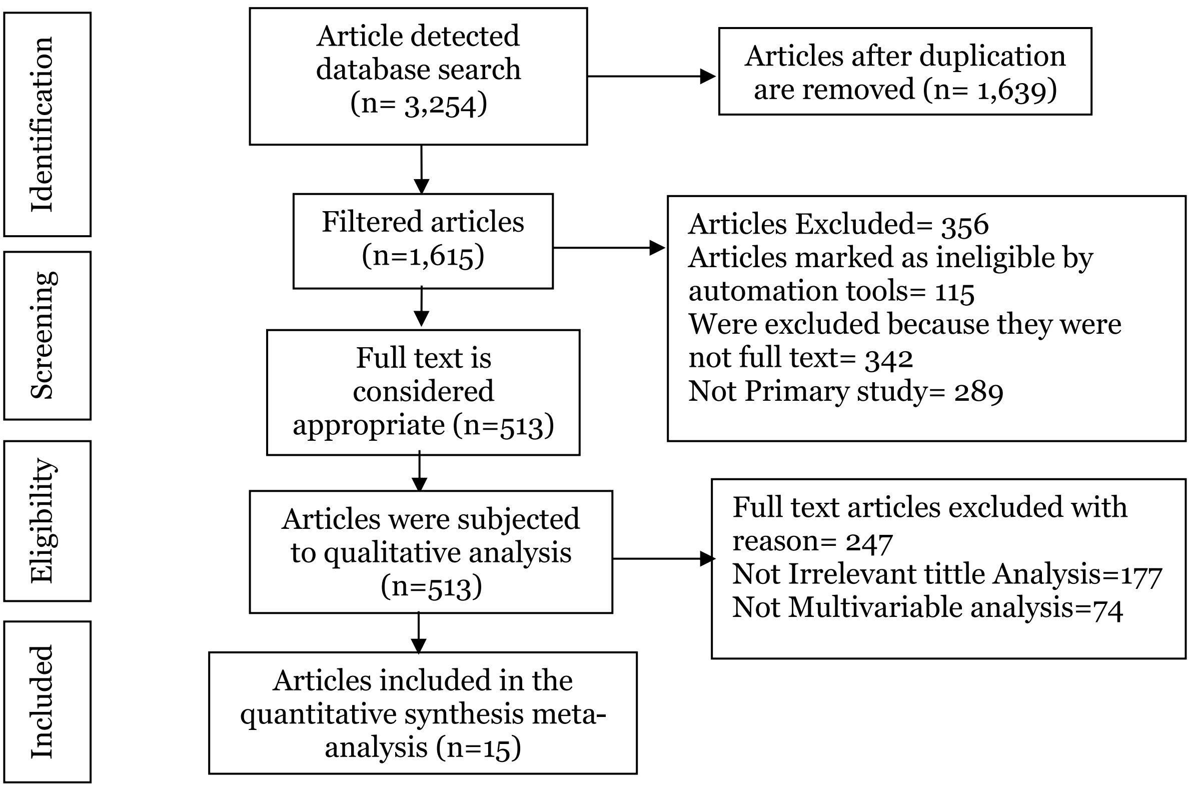

Figure 1. Results of PRISMA flow diagrams of rural residence, low birth weight, and premature with neonates mortality

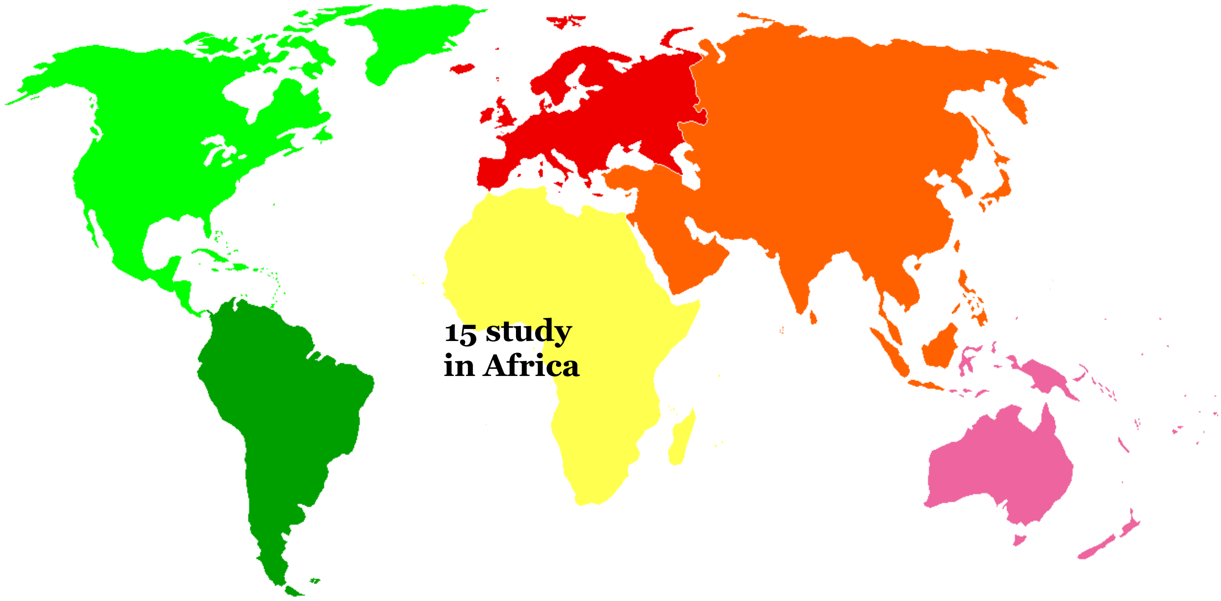

Figure 2. Research distribution map of rural residence, low birth weight, and premature with neonates mortality

Table 1. The results of the quality assessment study of the effect of hepatitis B in pregnancy on preterm birth

Author (year)	1a	1b	1c	1d	2a	2b	3a	3b	4	5	6a	6b	7	Total
Alemu et al. (2017)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Eyeberu et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Kassie et al. (2023)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Andegiorgish et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Seid et al. (2019)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Akalu et al. (2023)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Abera et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Mohammed et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Tadesse et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Thomas et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Atichew et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Hadgu et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Mitiku et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Girma et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Getaneh et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	2	26

Description of question criteria:

1a. Is the population in the primary study the same as the population in the PICO meta-analysis?

1b. Is the operational definition of intervention, namely the exposed status in the primary study, the same as the definition intended in the meta-analysis?

1c. Is the comparison, namely the unexposed status used by the primary study, the same as the definition intended in the meta-analysis?

1d. Are the outcome variables examined in the primary studies the same as the definitions intended in the meta-analysis?

2a. In analytical cross-sectional studies, do researchers choose samples from the population randomly (random sampling)?

2b. As an alternative, if in a cross-sectional analytical study, the sample is not selected randomly, does the researcher select the sample based on outcome status or based on intervention status?

3a. Are the exposure and outcome variables measured with the same instruments (measuring tools) in all primary studies?

3b. If the variable is measured on a categorical scale, are the cutoffs or categories used the same across primary studies?

4. If the sample was not chosen randomly, has the researcher made efforts to prevent bias in selecting research subjects? For example, selecting subjects based on outcome status is not influenced by exposure status (intervention), or selecting subjects based on exposure status (intervention) is not influenced by outcome status.

5. Whether the primary study researcher has made efforts to control the influence of confounding (for example, conducting a multivariate analysis to control for the influence of a number of confounding factors)

6a. Did the researcher analyze the data in this primary study with a multivariate analysis model (e.g., multiple linear regression analysis, multiple logistic regression analysis)

6b. Does the primary study report effect sizes or associations resulting from multivariate analysis (e.g., adjusted OR, adjusted regression coefficient)

7. Is there no possibility of a conflict of interest with the research sponsor, which could cause bias in concluding the research results?

Assessment guide:

1. Total number of questions = 13 questions. Answer "Yes" to each question gives a score of "2". The answer "Undecided" gives a score of "1". The answer "No" gives a score of "0".
2. Maximum total score= 13 questions x 2= 26.
3. Minimum total score = 13 questions x 0 = 0. So the range of total scores for a primary study is between 0 and 26.
4. If the total score of a primary study is >= 24, then the study can be included in the meta-analysis. If the total score of a primary study was <22, then the study was excluded from the meta-analysis.

Table 1. Description of the study cross-sectional of rural residence, low birth weight, and premature in neonatal mortality

Author (Years)	Country	Sample	P	I	C	O
Alemu et al. (2017)	Ethiopia	769	Neonates admitted to the NICU	Rural, Gestational age <34 weeks, Birth weight <2,500 g	Urban, Gestational age >42 weeks, Birth weight >4,000 g	Neonatal mortality
Kassie et al. (2023)	Ethiopia	870	Neonates at the NICU of FHCSH	Residence Rural, preterm, Weight <2,500 g	Urban, term, Weight 2,500-4,000 g	Neonatal mortality
Andegiorgish et al. (2020)	Africa	1,204	Neonates admitted to the SNCU	Gestational age <37 weeks, LBW	Gestational age >37 weeks, normal birth weight	Neonatal mortality
Eyeberu et al. (2021)	Ethiopia	834	Neonates admitted to NICU of HFSUH	LBW, premature	Normal birth weight, Mature gestational age	Neonatal mortality

Author (Years)	Country	Sample	P	I	C	O
Seid et al. (2019)	Ethiopia	3,276	Neonates admitted to NICU of JUMC	Prematurity, LBW	Mature gestational age, Normal birth weight	Neonatal mortality
Akalu et. al (2023)	Ethiopia	368	Newborns admitted NICUs	Gestational age 32-37 weeks	Gestational age >42 weeks	Neonatal mortality
Abera et al. (2021)	Ethiopia	289	Neonates admitted to NICU of WURH	Rural, preterm	Residance urban, Gestational age term	Neonatal death
Mohamed et al. (2022)	Ethiopia	510	Neonates aged 0-28 days	LBW, Preterm birth, rural	Normal birth weight, aterm birth, urban	Neonatal mortality
Tadesse et al. (2021)	Ethiopia	403	Neonates aged 0-28 admitted to NICU	Aterm (<37 weeks)	Gestational age at birth term and above	Neonatal mortality
Thomas et al. (2022)	Ethiopia	376	Neonates admitted to NICU of the Dil Chora Referral Hospital	Rural, Birth weight <2,500 g	Residency urban, Birth weight >2,500	Neonatal mortality
Ayichew et al. (2022)	Ethiopia	570	Neonates have mothers	Birth weight <2,500 g, preterm birth	Birth weight >2,500 g and aterm birth	Neonatal mortality
Hadgu et al. (2020)	Ethiopia	1,785	Neonates admitted to NICU of Ayder Compre-hensive	Rural, Birth weight <1,500, Gestational age <28 weeks	urban, Birth weight >4,000 g, Gestational age >42 weeks	Neonatal death
Mitiku et al. (2021)	Ethiopia	5,128	Neonates born 5 years	Rural	Urban	Neonate death
Girma et al. (2021)	Ethiopia	336	Preterm neonates	Rural, Birth weight less than 2,500 g	Urban, Birth weight ≥2,500 g	Neonatal mortality
Getaneh et al. (2022)	Ethiopia	398	Neonates aged <36 weeks	Birth weight <1,500 g, Gestational age <32 weeks	Birth weight >2500 g, Gestational age >36 weeks	Neonatal mortality

Table 2 is a description of 15 articles with cross-sectional studies selected based on predetermined criteria. The total sample size was 17,116 samples from African countries and Ethiopia. The articles used in this research were articles published from 2017 to 2023. The populations determined were "Neonates born", "Rural Residential", "Premature" or "Gestational Age", and "Low birth Weight" interventions. Comparison of

"Residence urban", "Normal born", and "Normal birth weight". The outcome determined in this study is "Neonatal Mortality".

Table 3 show that aOR and 95% CI data of rural residence and neonatal mortality.

Table 2. aOR and 95% CI data of rural residence and neonatal mortality

Author (Years)	aOR	CI 95%	
		Lower Limit	Upper Limit
Alemu et al. (2017)	1.56	0.88	2.77
Kassie et al. (2023)	1.96	1.26	3.06
Abera et al. (2021)	1.13	0.40	3.13
Mohammed et al. (2022)	0.26	0.04	2.07
Thomas et al. (2022)	2.18	0.92	5.21
Hadgu et al. (2020)	1.30	0.90	1.70
Mitiku et al. (2021)	1.92	0.83	4.34
Girma et al. (2021)	1.68	0.85	3.34

Table 4. aOR and 95% CI data of premature and neonatal mortality

Author (Years)	aOR	CI 95%	
		Lower Limit	Upper Limit
Alemu et al. (2017)	1.04	0.11	10.06
Kassie et al. (2023)	0.58	0.23	1.14
Andegiorgish et al. (2020)	1.46	0.65	3.26
Eyeberu et al. (2021)	0.39	0.12	1.24
Seid et al. (2019)	2.20	1.41	3.42
Akalu et al. (2023)	3.20	1.20	8.50
Abera et al. (2021)	4.15	1.67	10.33
Mohammed et al. (2022)	2.20	1.02	4.29
Tadesse et al. (2021)	1.77	0.78	4.04
Ayichew et al. (2022)	1.74	0.33	9.03
Hadgu et al. (2020)	25.64	2.53	250
Getaneh et al. (2022)	6.64	1.87	13.6

Table 3. aOR and 95% CI data of low birth weight and neonatal mortality

Author (Years)	aOR	CI 95%	
		Lower Limit	Upper Limit
Alemu et al. (2017)	1.04	0.43	2.47
Kassie et al. (2023)	0.96	0.64	1.43
Andegiorgish et al. (2020)	4.55	1.97	10.50
Eyeberu et al. (2021)	4.00	1.30	12.32
Seid et al. (2019)	1.54	1.06	2.25
Mohammed et al. (2022)	3.40	1.92	6.01
Thomas et al. (2022)	3.96	1.56	10.10
Ayichew et al. (2022)	3.23	1.17	8.91
Hadgu et al. (2020)	5.00	1.07	20.00
Girma et al. (2021)	3.03	0.62	14.83
Getaneh et al. (2021)	7.91	1.21	15.40

Forest plots in figure 3 were carried out on 8 primary articles to analyze the effect of village residence on newborn mortality. The results of meta-analysis research show that babies who live in villages are 4.17 times more likely to experience newborn death than babies who live in cities and this is statistically significant (aOR= 4.17; 95% CI= 2.30 to 7.58; p<0.001). The variation in data based on the I² value shows 88% so that the influence of village residence on newborn mortality uses the random effect model (REM) (Figure 3).

The funnel plot in figure 4 explains the distribution of estimates from 8 journals that have been selected to analyze the effect of rural residence on newborn mortality. The funnel plot results show that the distribution of effect estimates between studies is more skewed towards the right based on the average vertical line. Thus, the funnel plot states that there is research bias which shows overestimation bias (Figure 4).

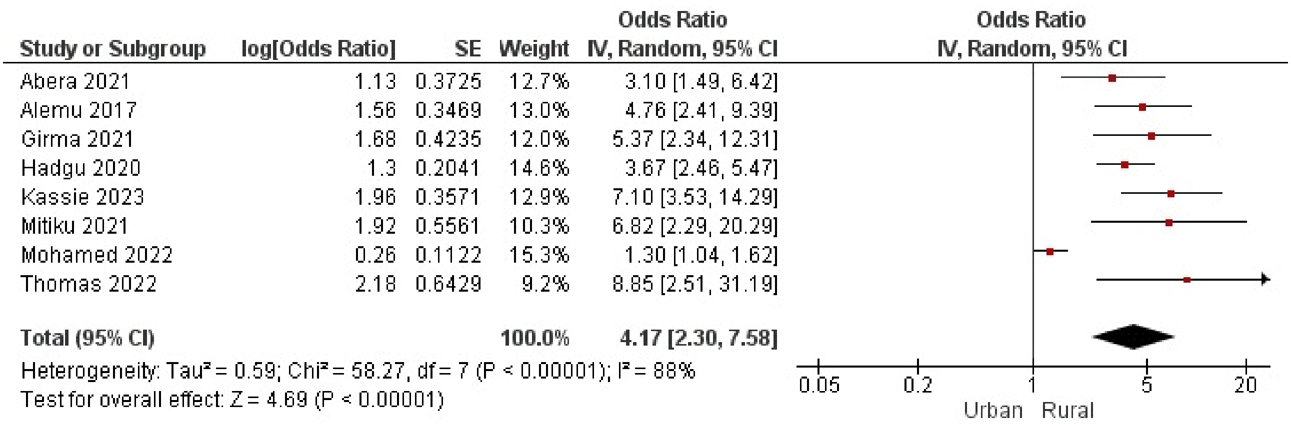

Figure 3. Forest plot of rural residence and neonatal mortality

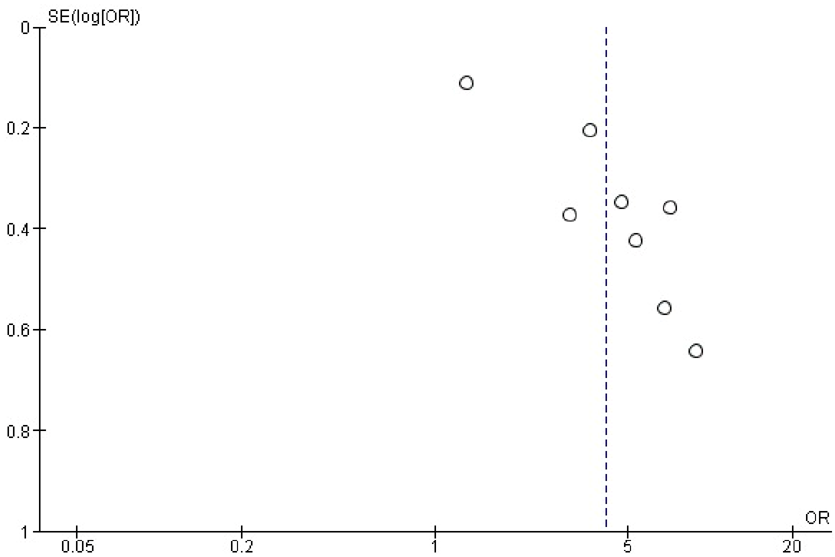

Figure 4. Funnel plot of rural residence and neonatal mortality

Forest plots in figure 5 were carried out on 12 primary articles to analyze the effect of village residence on newborn mortality. The results of meta-analysis research show that babies born prematurely are 5.17 times more likely to experience newborn death than babies born not prematurely and this is statistically significant (aOR= 5.17; 95% CI= 2.87 to 9.33; p<0.001). The variation in data based on the I² value shows 81% so that the influence of premature birth on newborn mortality uses the random effect model (REM) (Figure 5).

The funnel plot in figure 6 explains the distribution of estimates from the 12 articles that have been selected to analyze the effect of premature birth on newborn mortality. The funnel plot results show that the distribution of effect estimates between studies is more skewed towards the right based on the average vertical line. Thus, the funnel plot states that there is research bias which shows overestimate bias (Figure 6).

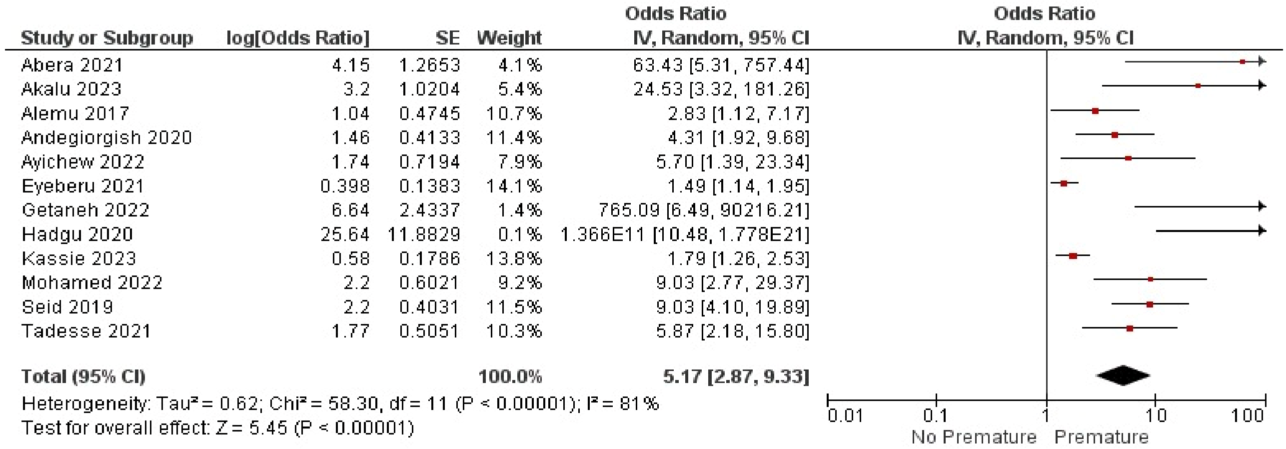

Figure 5. Forest plot of premature and neonatal mortality

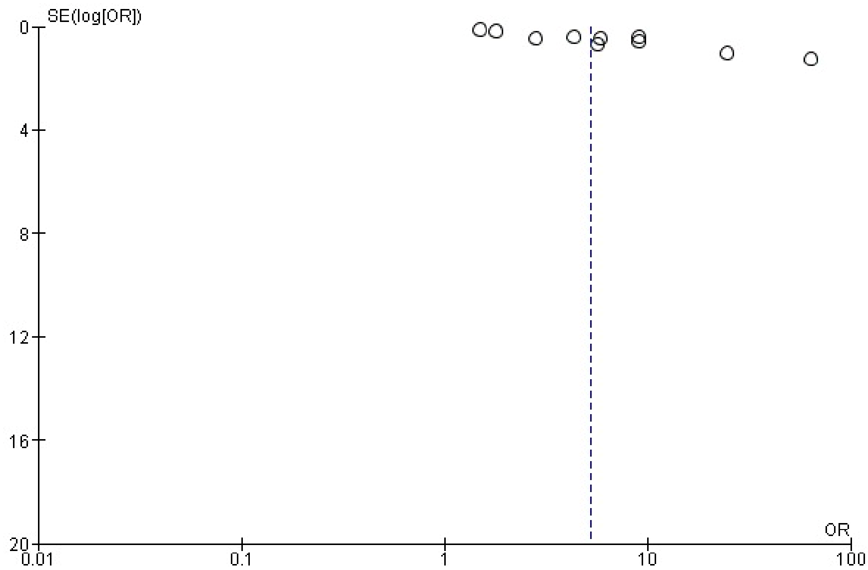

Figure 6. Funnel plot of premature and neonatal mortality

Forest plots in figure 7 were carried out on 11 primary articles to analyze the effect of light birth weight on newborn mortality. The results of meta-analysis research show that babies who have a light birth weight are 2.50 times more likely to experience newborn death than babies born with a normal birth weight and this is statistically significant (aOR=2.50; 95% CI= 1.63 to 3.85; p<0.001). The variation in data based on the I^2 value shows 68% so that the effect of light birth weight on newborn mortality using the random effect model (REM) (Figure 7).

The funnel plot in figure 8 explains the distribution of estimates from 11 journals that have been selected to analyze the effect of light birth weight on newborn mortality.

The funnel plot results show that the distribution of effect estimates between studies is more skewed towards the right based on the average vertical line. Thus, the funnel plot states that there is research bias which shows overestimation bias.

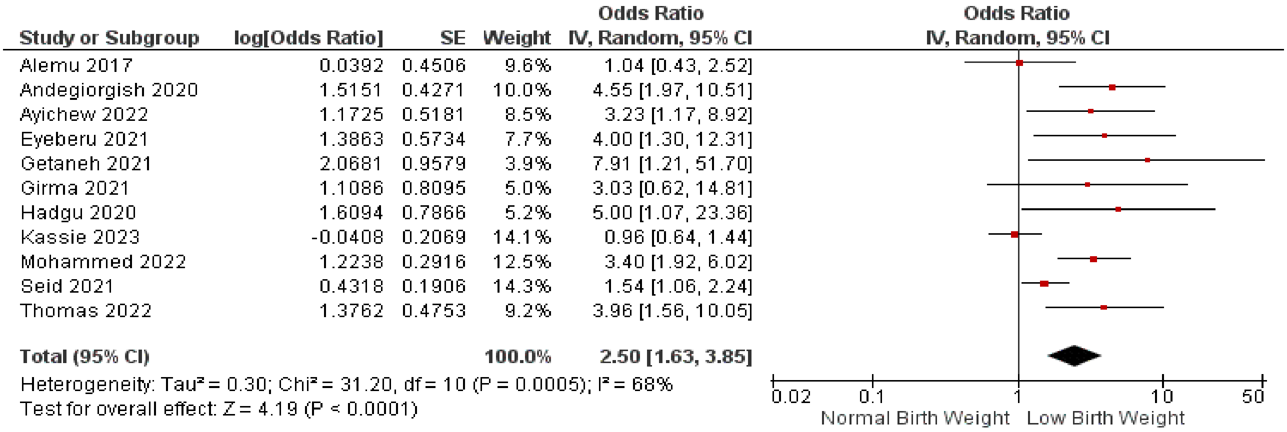

Figure 7. Forrest plot of low birth weight and neonatal mortality

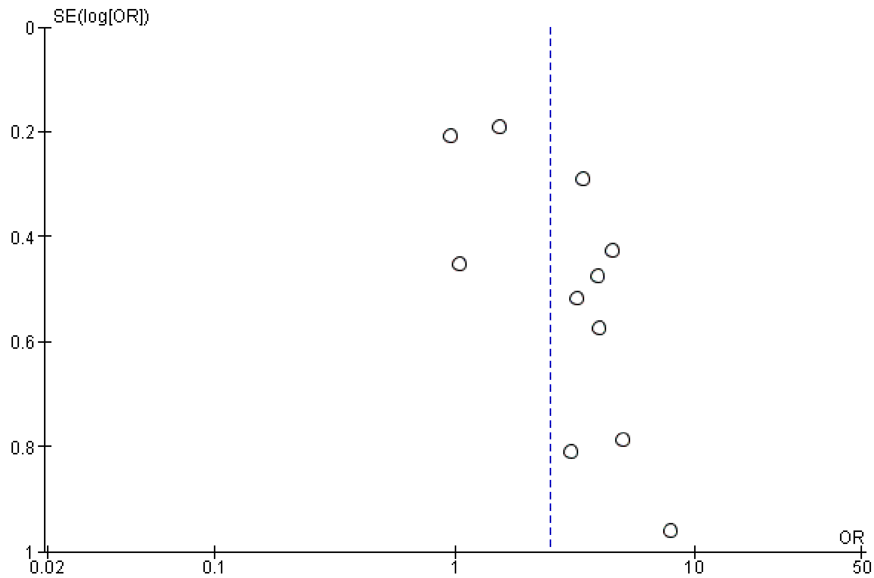

Figure 8. Funnel plot of low birth weight and neonatal mortality

DISCUSSION

1. The influence of rural residence on newborn mortality.

Babies living in villages have a 4.17 times higher risk of newborn death than those living in cities. These findings emphasize the significant role of residence factors (urban vs. rural) in maternal and infant health. Previous research, such as that conducted by Smith et al. (2019), shows that women living in urban areas have better access to health facilities, health education, and prenatal services, all of which contribute to improved maternal and infant health. On the other hand, the results of research by Johnson et al. (2020) highlighted the high rate of infant mortality in rural areas, caused by limited access to health facilities and the ability to obtain adequate medical care.

2. The influence of premature babies on newborn deaths

Babies born prematurely have a 5.17 times greater chance of experiencing newborn death compared to babies born not prematurely. These findings emphasize the importance of gestational age in the risk of infant mortality, in line with previous research. Smith et al. (2020) and Johnson et al. (2019) concluded that there is a clear relationship between gestational age and the risk of infant death. Babies born prematurely or at a very young or late gestational age have a higher risk of death. These data support the concept that the younger the gestational age, the higher the risk of infant death. Furthermore, the literature also emphasizes that babies born prematurely have a high risk of complications such as respiratory distress syndrome, sepsis, and necrotizing enterocolitis, all of which can contribute to the high mortality rate of premature babies.

3. The Effect of Low Birth Weight on Newborn Death.

Babies with low birth weight have a 2.5 times higher risk of newborn death compared to babies born with normal weight. These results are in line with the meta-analysis conducted by Smith et al. (2018), who found a significant association between low birth weight and an increased risk of infant mortality. These findings reflect the broader view of Brown et al. (2018) and Johnson et al. (2020) regarding factors related to low birth weight, such as smoking behavior during pregnancy, inadequate prenatal care, and poor nutritional conditions in the mother. These studies provide a contextual understanding of the main causes of low birth weight and how these are associated with an increased risk of newborn death.

AUTHOR CONTRIBUTION

Clelsy Sumardi Saputri, Ayun Widya Rizki, and Viola Holly Flora as the main researcher chose the theme, conducted a primary article search, processed the results and compiled interim results. Bhisma Murti and Ayu Novita provided a review of the results of the analysis, selected articles, gave directions in preparing the results of the analysis and discussion.

FUNDING AND SPONSHORSHIP

This study used personal funds.

CONFLICT OF INTEREST

There was no conflict of interest in this study.

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