Major Project Report

on

A Meta-Analysis on Impact of Maternal Nutrition on Low Birth Weight in Developing Countries

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CERTIFICATE

It is certified that the work contained in the project report titled “A Meta-Analysis on Impact of Maternal Nutrition on Low Birth Weight in Developing Countries” by “Arjun Sagar N V (20BCS020)”, “Harshith R N (20BCS056)”, ”Khushi Goosari (20bcs071)” and “Madhu Sudhan (20BCS080),” has been carried out under my/our supervision and that this work has not been submitted elsewhere for a degree.

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We declare that this written submission represents my ideas in my own words and where others' ideas or words have been included, we have adequately cited and referenced the original sources. We also declare that we have adhered to all principles of academic honesty and integrity and have not misrepresented or fabricated or falsified any idea/data/fact/source in our submission. We understand that any violation of the above will be cause for disciplinary action by the Institute and can also evoke penal action from the sources which have thus not been properly cited or from whom proper permission has not been taken when needed.

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1 Abstract

This meta-analysis seeks to evaluate the effectiveness of maternal nutrition interventions in reducing the incidence of low birth weight (LBW) in developing countries, with a particular emphasis on interventions such as iron and folic acid (IFA) supplementation, maternal hemoglobin (Hb) levels, and dietary diversity scores (DDS). Furthermore, it aims to provide insights into the potential correlations between these interventions and LBW prevalence. Adhering to the PRISMA guidelines, we performed a systematic review and meta-analysis, encompassing both randomized controlled trials (RCTs) and non-RCTs exploring maternal nutrition interventions and their impact on LBW outcomes. This comprehensive study aims to provide a thorough examination of the available literature on the subject. The focus of the analysis was on developing nations where access to nutritious food and healthcare infrastructure is constrained, highlighting the challenges faced in addressing maternal nutrition and its impact on birth outcomes. Ten studies encompassing 181,168 pregnant women were incorporated, with interventions ranging from 28 to 1095 days in duration. The meta-analysis revealed significant associations between maternal nutrition interventions and LBW prevalence. IFA supplementation exhibited an odds ratio of 3.32 (95% CI: 0.81 to 13.35, Tau2 = 2.32, $x^2 = 106.40$, p less than 0.00001), maternal Hb levels demonstrated an odds ratio of 3.97 (95% CI: 1.88 to 8.38, Tau square = 0.99, $x^2 = 141.19$, p less than 0.00001), and DDS supplementation displayed an odds ratio of 1.14 (95% CI: 1.10 to 11.19, $x^2 = 1.96$, p = 0.38). Meta-regression analysis identified age, sample size, and duration as significant covariates affecting effect sizes. Maternal nutrition interventions, including IFA supplementation, ensuring sufficient Hb levels, and promoting dietary diversity, are pivotal in reducing LBW rates in developing nations. Continued research is essential to validate these results and devise effective strategies for combating maternal malnutrition, thereby enhancing maternal and neonatal health in resource-limited environments.

2 Introduction

Maternal nutrition plays a critical role in ensuring the health and well-being of both mothers and their newborn babies[6]. Adequate maternal nutrition is essential for supporting the physiological changes that occur during pregnancy, such as increased blood volume and nutrient demands, as well as ensuring optimal fetal growth and development[7]. A well-rounded diet is crucial for supplying vital nutrients like vitamins, minerals, proteins, and fats, vital for optimal fetal growth, organ development, and overall pregnancy outcomes. Inadequate maternal nutrition during pregnancy can result in various detrimental effects, such as low birth weight (LBW), preterm birth, and birth defects, highlighting the significance of proper dietary intake. In developing countries, the importance of maternal nutrition is even more pronounced due to various socio-economic and environmental factors[8]. Limited access to nutritious food, inadequate healthcare infrastructure, and prevalent socio-cultural practices often contribute to poor maternal nutrition in these settings. The historical narrative underscores a collective understanding of the intricate interplay between maternal dietary intake and fetal development, acknowledging its criticality in mitigating the risk of adverse birth outcomes. Among these, LBW, conventionally defined as infants weighing less than 2500 grams at birth, emerges as a pivotal indicator of neonatal health, with far-reaching implications for long-term health and development[1]. Infants born with low birth weight face heightened susceptibility to various health complications, such as respiratory distress, infections, developmental delays, and long-term conditions like diabetes and cardiovascular disease, underscoring the importance of addressing this issue. In fact, globally, it's estimated that about 20 million low-birth-weight infants are born each year, with over 95% of them in developing countries[9]. In some developing regions, up to 27% of newborns are born with LBW[10]. Additionally, approximately 45% of child deaths under the age of five are linked to undernutrition, with maternal malnutrition contributing significantly to this statistic. Moreover, studies have shown that addressing maternal malnutrition can significantly reduce the prevalence of LBW by up to 15% in certain regions. Integral to maternal nutrition are essential components such as iron and folic acid (IFA) supplementation, maintenance of adequate hemoglobin levels (Hb), and the dietary diversity score (DDS)[(2) (3)]. However, the absence or inadequacy of these vital nutrients during pregnancy poses a significant risk factor for LBW, thereby heightening the likelihood of prematurity and developmental delays, accentuating the urgency for effective nutritional interventions during gestation[(4) (5)].

To tackle maternal malnutrition in developing nations effectively, it's imperative to adopt holistic approaches that address not only nutritional deficiencies but also enhance healthcare access, education, and socio-economic empowerment for women. By synthesizing data from various studies, our objective is to assess the impact of diverse nutritional interventions, such as iron and folic acid supplementation and dietary diversification, on reducing low birth weight prevalence in these regions. Furthermore, we aim to pinpoint factors like IFA, maternal Hb levels, and DDS that might influence intervention efficacy, thus providing evidence-based recommendations for enhancing maternal nutrition and mitigating low birth weight in resource-limited settings.

3 Methods

3.1 Literature Search

In conducting a comprehensive literature search for our meta-analysis, we adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[(11)]. We conducted an extensive search on Google Scholar, PubMed, and Cochrane for studies spanning from 2019 to 2023, aiming to integrate the latest evidence. Our search strategy encompassed keywords pertinent to maternal nutrition, low birth weight, and developing countries, incorporating terms such as "maternal nutrition," "pregnancy diet," "low birth weight," "developing countries," and "meta-analysis". Emphasizing outcomes related to low birth weight attributed to insufficient maternal nutrition, our focus remained targeted on identifying recent evidence.

3.2 Selection Criteria

We restricted our inclusion to English-language publications, spanning randomized controlled trials (RCTs) and non-randomized controlled trials (non-RCTs) published between 2019 and 2023[(12)]. These studies examined a range of maternal nutrition interventions aimed at addressing low birth weight outcomes, with particular emphasis on interventions investigating iron and folic acid (IFA) supplementation, maternal hemoglobin (Hb) levels, and dietary diversity score (DDS) in newborns weighing less than 2500g.

3.3 Data Extraction and Quality Assessment

Throughout the systematic review process, we thoroughly scrutinized the complete texts of identified studies, ensuring the exclusion of any irrelevant ones to maintain the integrity of our analysis. Following this, we extracted the full texts of the remaining articles and meticulously recorded relevant variables, such as sample size, age demographics, study duration, as well as events and totals for both experimental (IFA, maternal Hb, DDS) and control groups. The Joanna Briggs Institute critical appraisal checklist for studies reporting prevalence data was used to determine and control the articles' quality. This meticulous extraction process adhered to predefined inclusion criteria and upheld recommended standards for randomized controlled trials (RCTs), ensuring the robustness and reliability of our data[(21)].

The search, data extraction, and quality assessment were carried out independently by two subject matter experts, who adhered to the inclusion criteria and ensured compliance with recommended RCT standards. Moreover, each intervention subgroup was meticulously analyzed individually to discern any unique effects linked to particular interventions, allowing for a comprehensive assessment of their impact on low birth weight outcomes. Through these rigorous procedures, our aim was to deliver a comprehensive and dependable synthesis of the existing evidence concerning maternal nutrition and its effects on birth outcomes in developing nations.

3.4 Statistical Analysis

In our meta-analysis, we employed statistical analysis methods to assess the relationship between iron and folic acid (IFA) supplementation, maternal hemoglobin (Hb) levels, dietary diversity score (DDS), and low birth weight outcomes[(19)]. The odds ratio represents the likelihood of LBW occurring in the experimental group compared to the control group, serving as a measure of the strength of association between maternal nutrition (IFA, maternal Hb, and DDS) and LBW in the chosen studies. Effect size, represented by the odds ratio, measured the association between maternal nutrition interventions and low birth weight[(13)]. To evaluate the overall effect across studies, Q statistics were utilized, assessing heterogeneity among effect sizes[(14)]. Degree of freedom, x^2 (chi-square), T^2 (Tau-squared), and I^2 statistics were calculated to quantify heterogeneity among effect sizes, providing insights into the degree of variability in the study results[(15)]. Both fixed effect and random effect models were utilized to account for heterogeneity among studies, providing robust estimates of the overall effect of maternal nutrition interventions on LBW[(18)]. Results were presented with 95% confidence intervals to provide a range of plausible effect sizes[(17)]. Heterogeneity among studies was visually represented in forest plots, allowing for the examination of the distribution of effect sizes across studies[(16)].

In our meta-analysis, we employed either a fixed-effect or random-effects model to determine the pooled effect size, along with a 95% confidence interval (heterogeneous, T^2 greater than 0)[13,20]. Heterogeneity among the results was depicted using a forest plot, wherein each study's odd ratio of low birth weight was represented by a blob within its 95% confidence interval. The combined result of the pooled odds ratio(POR) was illustrated by a diamond, with its width indicating the 95% confidence interval for the pooled data. A vertical line denoted no effect, distinguishing between studies favoring the intervention group or the control group. Additionally, the forest plot displayed statistics such as the x^2 (Q-test statistic), T^2, degrees of freedom (df), I^2, Z-score, and P-value.

An I^2 value exceeding 50% suggests significant heterogeneity among the trials. To assess publication bias, we utilized a funnel plot and conducted an Egger regression test, which employs a linear regression model with the standard error as a covariate. If heterogeneity was present (I^2 Greater than 50%), a meta-regression approach was employed to assess study heterogeneity by examining the relationship with study characteristics. Statistical analyses were performed with Review Manager (RevMan) software version 5.4.1.

4 Results

4.1 Search Results

Out of the 171 articles identified, a subset was omitted due to their lack of relevance to the analysis' objectives or their non-randomized controlled trial (RCT) nature. Subsequent to this initial screening, 23 articles were subjected to full-text assessment, ultimately resulting in the inclusion of ten articles deemed suitable for the meta-analysis.

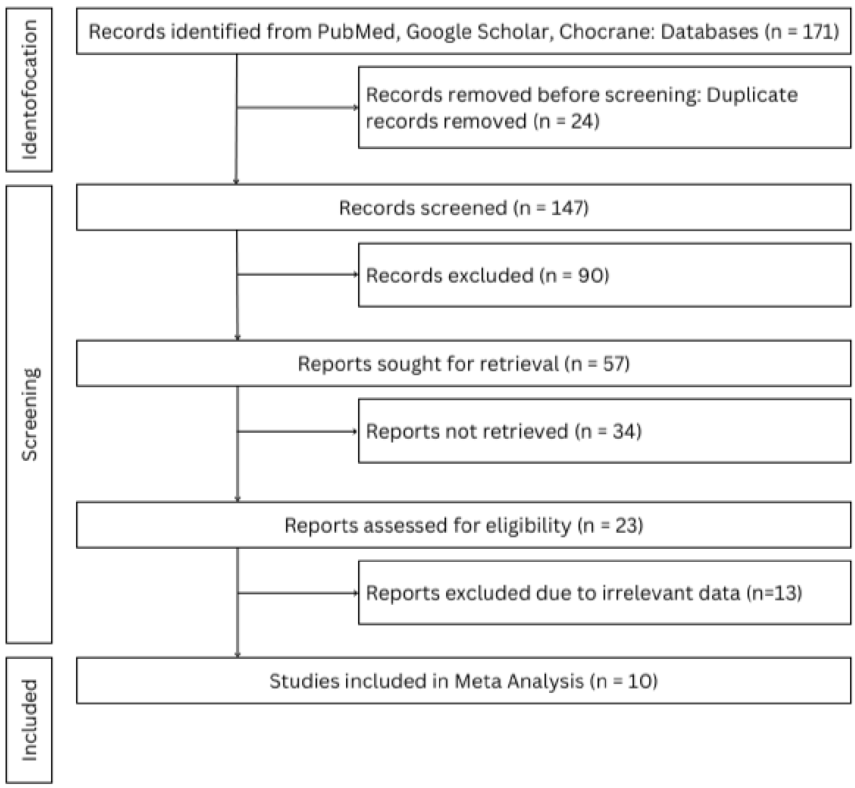

Figure 1. Prisma Flow Diagram

4.2 Study characteristics and data quality

The characteristics of the ten studies included in the analysis(22-31) are detailed in Figure 2. All selected studies adhered to the randomized controlled trial (RCT) design, with nine being cross-sectional studies and one being a quasi-experimental study. Notably, baseline birth weight was consistent across all papers, ensuring comparability between intervention and control groups. The collective sample size comprised 181,168 pregnant women, with an average age ranging from 22 to 32 years, and intervention durations spanning from 28 to 1095 days. These investigations were conducted over the past five years, with four studies hailing from Ethiopia, three from India, and one each from Rwanda and Indonesia.

Across the ten studies, the odds ratio of low birth weight (LBW) was assessed in relation to three maternal nutrition variables: iron and folic acid supplementation (IFA), maternal hemoglobin (Hb) levels, and dietary diversity score (DDS). Moreover, each study comprised multiple trials, wherein various maternal nutrition interventions were either applied or juxtaposed with a placebo. To streamline the meta-analysis, meticulous estimation of the number of events and total participants within each maternal nutrition group was conducted for each trial.

Reference	Year	Study duration(days)	StudyID	Average maternal age(years)	Maternal Nutrition						Country	Initial sample size	Study design
					IFA		Maternal Hb		DDS				
					Events	Total	Events	Total	Events	Total			
Abdurke kure et al.	2021	38	36037087	26	64	175	59	161	-	-	Ethopia	403	Cross-sectional study
Abera et al.	2019	1095	31443690	30	-	-	29	66	-	-	Ethopia	358	Cross-sectional study
Devaguru et al.	2023	365	37288213	27	186	288	162	162	-	-	India	900	Cross-sectional study
Girotra et al.	2023	1095	37123748	32	-	-	15360	90076	3473	19243	India	1,75,240	Cross-sectional study
Habtu et al.	2022	242	35938121	30	-	-	18	187	26	241	Rwanda	1096	Quasi-experimental study
Saha et al.	2023	61	35836138	22	-	-	45	87	-	-	India	210	Case- control study
Seid et al.	2022	93	37457158	28	31	42	28	39	-	-	Ethiopia	255	Case- control study
Sindiani et al.	2023	365	36937486	26	13	104	45	65	-	-	Jordan	2260	Case- control study
Sutni et al.	2023	28	30813968	27	11	13	-	-	-	-	Indonesia	25	Cross-sectional study
Walle et al.	2022	579	32098043	30	-	-	-	-	224	421	Ethiopia	421	Cross-sectional study

Figure 2. Summary studies on the impact of effect of IFA supplementation, maternal Hb levels, and DDS on low birth weight in pregnancies in developing country.on low birth weight

4.3 Effects of maternal nutrition on Low Birth Weight

4.3.1 Iron Folic Acid (IFA):

The results of forest plot analysis (Figure 3) reveal an odds ratio of 3.32 (95% CI: 0.81 to 13.35), signifying a notable correlation between Iron Folic Acid (IFA) supplementation and increased odds of Low Birth Weight. Utilizing the random effects model, the analysis uncovered a considerable degree of heterogeneity (Tau 2.32; $x^2 = 106.40$, df = 4, p ¡ 0.00001, I^2=96%), indicative of substantial variability in effect size estimates among the included studies. These results underscore the intricate nature of the association between IFA supplementation and the occurrence of Low Birth Weight.

4.3.2 Hemoglobin(Hb):

The results of forest plot analysis (Figure 4) reveals a significant association between Hemoglobin (Hb) supplementation and increased odds of Low Birth Weight, with an odds ratio of 3.97 (95% CI: 1.88 to 8.38). Despite substantial heterogeneity (Tau square = 0.99; $x^2 = 141.19$, df = 7, p ¡ 0.00001, $^2 = 95\%$), the random effects model was utilized to address variation in effect sizes. These findings highlight the potential efficacy of Hb supplementation in reducing the risk of Low Birth Weight.

4.3.3 Dietary Diversity Score(DDS):

The forest plot analysis results (Figure 3) unveil a plausible correlation between Dietary Diet Index (DDS) supplementation and the likelihood of Low Birth Weight, showcasing an odds ratio of 1.14 (95% CI: 1.10 to 11.19). Utilizing a fixed-effect model, the analysis indicates negligible heterogeneity ($x^2 = 1.96$, df = 2, p = 0.38, $I^2 = 0\%$). These observations suggest the potential efficacy of DDS supplementation in mitigating the risk of Low Birth Weight.

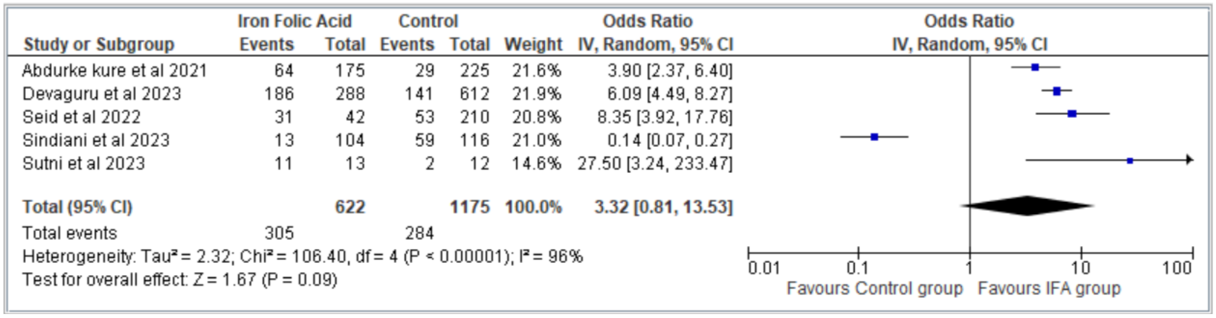

Figure 3. Odds ratio of Low Birth Weight associated with Iron Folic Acid (IFA) supplementation
References: [21,24,28-30]

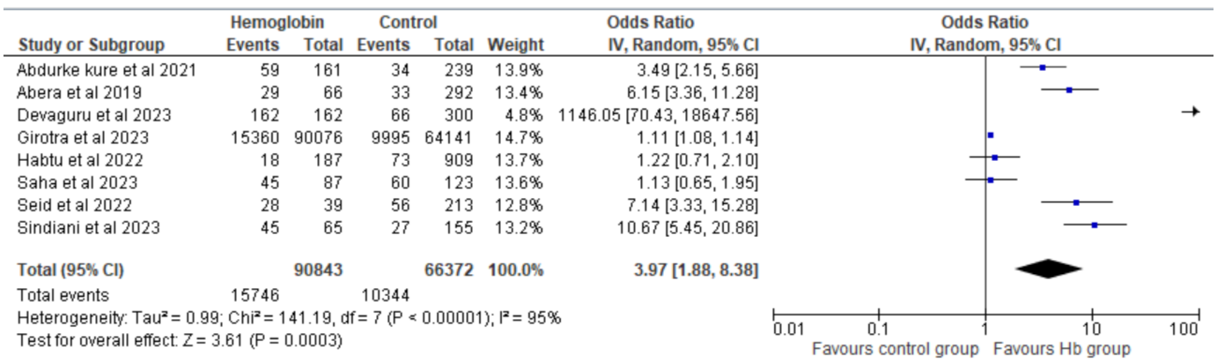

Figure 4. Odds ratio of Low Birth Weight associated with maternal Hemoglobin(Hb) levels
References: [22-29]

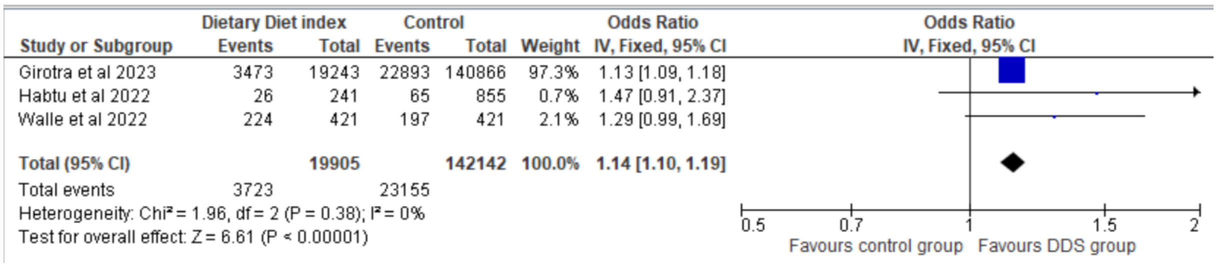

Figure 5. Odds ratio of Low Birth Weight associated with Dietary Diet Score(DDS)
References: [25,26,31]

4.4 Findings from meta regression analysis

Meta-regression analysis was conducted to identify the sources of heterogeneity. Two distinct models were utilized, focusing on (i) the supplementation of Iron Folic acid and (ii) Hemoglobin levels. The findings reveal a significant correlation between the effect sizes and the respective covariates in both models.

4.4.1 Supplementation of Iron folic acid(IFA):

The derived p-values from the meta-regression analysis provide valuable insights into the relevance of covariates in elucidating the variability of effect sizes. Although the intercept term lacks statistical significance ($p = 0.288$), the p-value for sample size approaches significance ($p = 0.057$), hinting at a possible association. Furthermore, age exhibits statistical significance ($p = 0.012$), underscoring its notable impact on observed heterogeneity. Through a thorough examination of the scatter plot(Figure 6 A) alongside these statistical indicators, we can discern potential trends or patterns between covariates and effect sizes. Particularly, age emerges as a significant factor influencing the variability within the dataset.

4.4.2 Hemoglobin(Hb):

The scatter plot illustrates the meta-regression analysis aimed at uncovering sources of heterogeneity. Lower p-values for sample size(p= 0.0234) and duration(p= 0.0353) suggest their significant role in explaining heterogeneity through a thorough examination of the scatter plot(Figure 6 B) alongside these statistical indicators, we can discern potential trends or patterns between covariates and effect sizes.Accordingly, we anticipate clear patterns or trends in the scatter plot concerning sample size and duration, with data points potentially clustering or showing systematic variation.

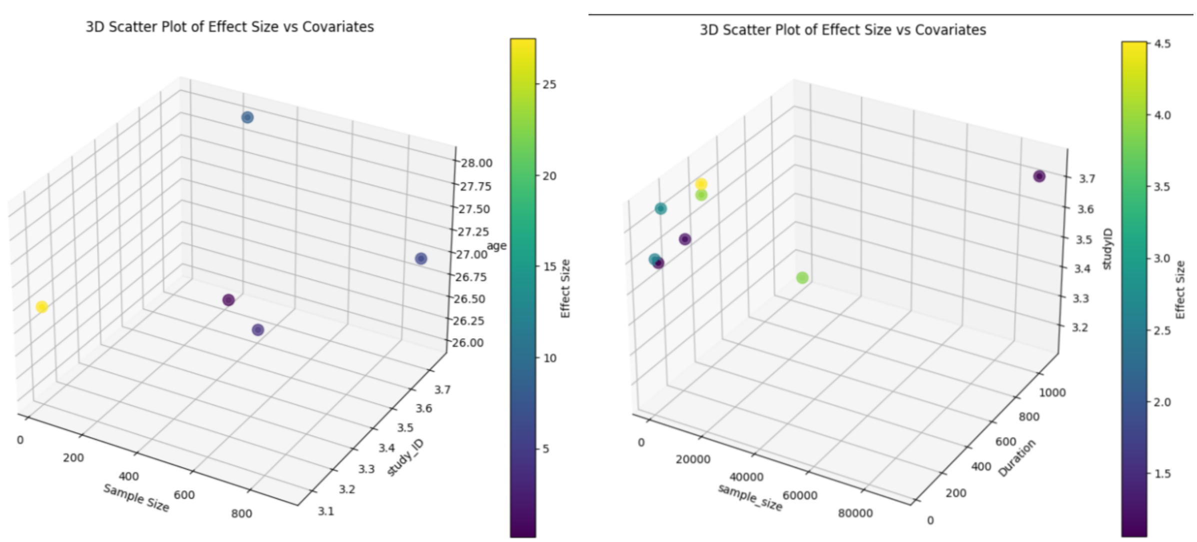

Figure 6. Scatter plot depiction of the effect size of (A)Iron folic acid supplement (B) maternal Hemoglobin levels,

4.5 Publication bias and Egger's regression

The funnel plot exhibited symmetry, suggesting the likely absence of publication bias, a conclusion further supported by Egger's regression analysis. This method involved regressing the inverse of the sample size of each study included in the meta-analysis against the standard error of the effect size estimate. Egger's regression yielded non-significant p-values, indicating no evidence of publication bias (Iron Folic Acid supplement, p=0.3059; hemoglobin, p=0.2376). A comprehensive analysis is outlined in the Appendices.

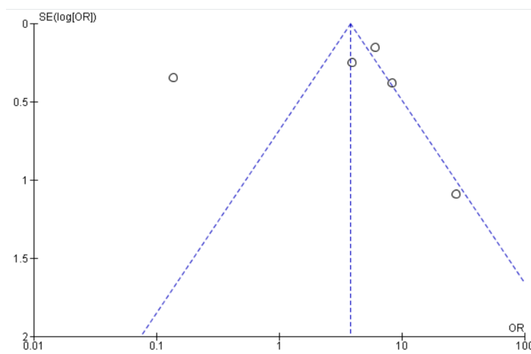

Figure 7. Iron Folic Acid Supplementation (IFA)

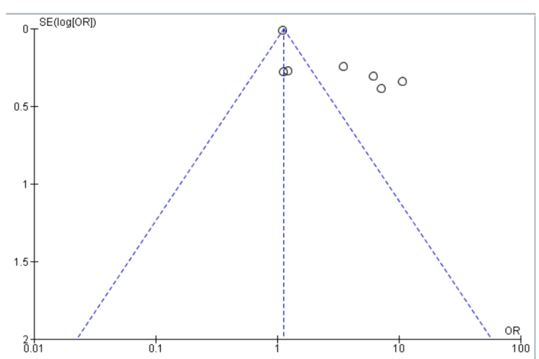

Figure 8. Hemoglobin (Hb)

5 Discussion

The results of this meta-analysis emphasize the pivotal role of maternal nutrition interventions in tackling low birth weight (LBW) in developing nations. Maternal malnutrition, shaped by socio-economic and environmental factors like restricted access to nutritious food and inadequate healthcare infrastructure, remains a complex challenge. Particularly in regions where these obstacles are heightened, addressing maternal malnutrition is indispensable for enhancing maternal and neonatal health outcomes. Our analysis identified notable correlations between maternal nutrition interventions and the risk of LBW, with iron and folic acid (IFA) supplementation, maternal hemoglobin (Hb) levels, and dietary diversity score (DDS) emerging as key focal points.

Maternal nutrition is paramount during pregnancy, providing the foundation for fetal growth and development. Ensuring sufficient intake of vital nutrients like iron, folic acid, protein, and vitamins is essential to meet the heightened demands of pregnancy and promote optimal fetal development. Nonetheless, in numerous developing nations, access to nutritious food is constrained, exacerbating maternal malnutrition and posing significant risks to both maternal and neonatal well-being.

The forest plot analysis indicated notable correlations between maternal nutrition interventions and LBW, with varying effect sizes and degrees of heterogeneity. For IFA supplementation, the analysis yielded an odds ratio of 3.32 (95% CI: 0.81 to 13.35, $T^2 = 2.32$, $^2 = 106.40$, p less than 0.00001), suggesting a significant association with increased odds of LBW. Despite substantial heterogeneity, our findings underscore the complex relationship between IFA supplementation and LBW, highlighting the need for further research to elucidate this association.

Similarly, maternal Hb levels showed a significant association with increased odds of LBW, with an odds ratio of 3.97 (95% CI: 1.88 to 8.38, $T^2 = 0.99$, $x^2 = 141.19$, p less than 0.00001). Despite substantial heterogeneity, the potential efficacy of maintaining adequate Hb levels in reducing the risk of LBW is evident, emphasizing the importance of addressing maternal anemia during pregnancy.

Additionally, the forest plot analysis results unveiled a plausible correlation between dietary diet score (DDS) supplementation and the likelihood of LBW, showcasing an odds ratio of 1.14 (95% CI: 1.10 to 11.19, $x^2 = 1.96$, $p = 0.38$). Utilizing a fixed-effect model, the analysis indicated negligible heterogeneity, suggesting the potential efficacy of DDS in mitigating the risk of LBW. However, further research is needed to confirm these findings and explore the underlying mechanisms.

Our meta-regression analysis aimed to identify sources of heterogeneity and assess the influence of covariates on effect sizes. For IFA supplementation, age emerged as a significant factor influencing the variability within the dataset ($p = 0.012$), highlighting the importance of considering demographic factors in future studies. Similarly, for maternal Hb supplementation, sample size ($p = 0.0234$) and duration ($p = 0.0353$) were identified as significant covariates, underscoring the need for larger and longer-term studies to better understand the relationship between maternal Hb levels and LBW.

Publication bias was evaluated through the utilization of funnel plots and Egger's regression analysis, both of which suggested the probable absence of publication bias concerning both IFA supplementation and maternal Hb levels. These results further strengthen the credibility of our meta-analysis, affirming its status as a thorough and impartial compilation of evidence regarding maternal nutrition and LBW in developing nations.

While our analysis demonstrates notable strengths, it is essential to recognize several limitations. Variability in study design, sample size, and duration among the included studies might have influenced heterogeneity in effect sizes. Moreover, the disparity in evidence quality across studies underscores the necessity for standardized methodologies and reporting guidelines to be adopted in future research endeavors.

The implications of our findings carry substantial weight for public health policy and practice in developing nations. Implementing targeted interventions like IFA supplementation, enhancing maternal Hb levels, and fostering dietary diversity holds promise in mitigating the prevalence of LBW and its related complications. Nevertheless, it's crucial to acknowledge that the efficacy of these interventions might fluctuate based on contextual factors such as socio-economic status, cultural norms, and healthcare accessibility.

6 Conclusion

In summary, our meta-analysis highlights the substantial influence of maternal nutrition interventions in decreasing the incidence of low birth weight in developing nations. While significant associations were observed between iron and folic acid supplementation, maternal hemoglobin levels, and dietary diversity score, there remains a need for additional research to clarify the most effective approaches for addressing this pressing public health issue.

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