GMR
The Original

Maternal Malnutrition and Molecular Mechanisms Underlying Adverse Neonatal Outcomes: A Systematic Review of Genetic, Epigenetic and Placental Biomarkers

[1*]Dr. Hina Hadayat Ali, [2]Dr. Muhammad Javed Aftab, [3]Dr. Adhwaa Ali Alahmari, [4]Dr. Gulfam Nawaz, [5]Adeel Hassan, [6]Aasma Zaheer

[1*]Assistant Professor/Coordinator, Department of Special Education, University of Education, Lahore, Faisalabad Campus, Pakistan, Email: hina.hadayat@ue.edu.pk

[2]Assistant Professor (Special Education), Department of Special Education (DSE), Division of Education (DoE), University of Education (UoE), Lahore, Punjab, Pakistan, Email: drmjavedaftab@ue.edu.pk

[3]Associate Professor (Special Education), Department of Special Education, College of Education, King Khalid University, King Khalid Road, Town Center, Abha 62521, Saudi Arabia, Email: adahmari@kku.edu.sa

[4]Lecturer in Special Education, Department of Special Education (DSE), Division of Education (DoE), University of Education (UE), Lahore, Punjab, Pakistan, Email: gulfam.nawaz@ue.edu.pk

[5]M.Phil. Special Education, Head of Department, Rural Inclusive Education Program Ghazali Education Foundation

[6]Lecturer in Special Education, Department of Special Education (DSE) Division of Education (DoE), University of Education (UE), Lahore, Punjab, Pakistan, Email: aasma.zaheer@ue.edu.pk

Abstract:

Maternal malnutrition remains a major contributor to adverse neonatal outcomes, particularly in low- and middle-income countries. Severe maternal undernutrition, micronutrient deficiencies, and abnormal maternal body mass index can impair placental development, fetal growth, immune function, and neonatal survival. This systematic review synthesised evidence published between 2000 and 2025 from PubMed, Scopus, Web of Science, Google Scholar, and the Cochrane Library. Of the 1,268 records initially identified, 42 studies met the predefined eligibility criteria and were included in the final review. The findings demonstrated consistent associations between severe maternal malnutrition and low birthweight, preterm birth, intrauterine growth restriction, neonatal infections, impaired neurodevelopment, and neonatal mortality. Recent studies further identified genetic, epigenetic, and placental mechanisms underlying these outcomes, including altered DNA methylation, dysregulated gene expression, impaired placental angiogenesis, oxidative stress, inflammation, and disrupted nutrient transport. Maternal micronutrient status and body mass index were also identified as important predictors of neonatal health. The review highlights the need for early nutritional screening, timely supplementation, improved antenatal monitoring, and integrated maternal healthcare interventions. Addressing maternal malnutrition through evidence-based and context-specific strategies may substantially improve neonatal survival, growth, and long-term developmental outcomes.

Keywords: *Maternal malnutrition, Grade III malnutrition, neonatal health, low birth weight, neonatal mortality, systematic review.*

Introduction

Pregnancy and neonatal outcomes are significantly influenced by maternal nutrition, but maternal malnutrition remains a major global health burden, especially in low- and middle-income countries, where poverty, food insecurity, and limited access to health care prevail (United Nations Children's Fund [UNICEF], 2023). Severe (Grade III) maternal malnutrition results from advanced undernutrition with critical macro- and micronutrient deficiencies, low maternal energy reserves, and placental dysfunction, which can restrict fetal growth and worsen neonatal outcomes (Lassi et al., 2020; Rahman et al., 2024). The World Health Organization (WHO) identifies maternal nutrition as a central component of antenatal care, particularly in regions with a high burden of low birth weight, including South Asia and Pakistan (Ministry of National Health Services, Regulations and Coordination & UNICEF, 2022; World Health Organization, 2020). Evidence also links low maternal body mass index, anaemia, and deficiencies of iron, folate, zinc, iodine, and vitamin D with intrauterine growth restriction, preterm birth, infection risk, and impaired neurodevelopment (Cortés-Albornoz et al., 2021; Oh et al., 2020; Schulze et al., 2020). Although nutritional interventions have been developed, the burden remains high, highlighting the need for stronger evidence on maternal nutrition. This systematic review examines the relationship between severe maternal malnutrition and neonatal outcomes to identify consistent evidence and inform clinical and public health strategies for reducing neonatal morbidity and mortality.

Mother's nutrition plays a key role in determining pregnancy outcome, placental growth, fetal development and neonatal survival. Malnutrition in mothers is no longer considered as a lack of energy or protein, but as a wide range of malnutrition from being underweight to underdietary diversity, protein-energy deficiency, micronutrient deficiency, anaemia, over

weight, over nutrition and over consumption of nutritionally poor food. These conditions can happen alone or together, especially in low and middle-income countries in a “triple burden” of undernutrition, micronutrient deficiency and overnutrition. A woman's pre-pregnancy and intrauterine nutritional status affects the availability of metabolic substrates needed for cellular proliferation, organ development, vascularization and fetal growth. Maternal malnutrition can thus pose a risk of miscarriage, fetal growth restriction, small-for-gestational-age (SGA) birth, low birth weight (LBW), preterm birth, stillbirth, and neonatal morbidity and mortality (NMM) (United Nations Children's Fund [UNICEF], 2023).

The placenta is the major biological barrier between mother and developing fetus. It acts as a regulator for the transfer of oxygen, glucose, amino acids, fatty acids, minerals and micronutrients and carries out endocrine, immune, metabolic and vascular functions. Maternal nutrition can lead to changes in placental morphology, vascularisation, mitochondrial function, oxidative balance and nutrient-sensing pathways. Maternal nutrient availability affects placental mechanistic target of rapamycin (mTOR), adenosine monophosphate-activated protein kinase (AMPK), insulin-like growth factor (IGF) signalling and amino acid transport systems. Nutrient deficiency can stunt placental growth and nutrient transfer, while maternal obesity and dietary high in saturated fats can increase inflammation, oxidative stress and metabolic dysfunction. The placenta also holds molecular imprints of the nutritional environment of the mother as placental DNA-methylation patterns have been linked to maternal BMI and dietary patterns (Thakali et al., 2020; Tekola-Ayele et al., 2020).

There is variation in how individual pregnancies react to maternal malnutrition, there is genetic susceptibility and epigenetic regulation. Genetic mechanisms include inherited sequence variants, altered expression of growth-regulating genes, changes in placental transcriptomic profiles and abnormalities in genomically imprinted genes. Epigenetic mechanisms comprise DNA methylation, histone modification, chromatin remodelling and regulatory non-coding RNAs. Epigenetic changes affect the activity of genes without altering the sequence of the DNA, and can be influenced by dietary exposures. Nutrient deficiencies or excess during early pregnancy of nutrients that play a key role in one-carbon metabolism, methyl-group donation, antioxidant defence, and energy metabolism can have a permanent effect on developmental gene expression because of the extensive epigenetic reprogramming changes that occur in the embryo and placenta during early pregnancy. Placental studies indicate that changes in the expression of imprinted genes and epigenetic regulators are linked to fetal growth disturbances. In IUGR placentas, there has been a report of increased expression of PHLDA2, CDKN1C and PEG10, along with altered expression of genes of DNA-methylation regulators (DNMT1, DNMT3A, DNMT3B and TET3). These genes are involved in placenta development, cell growth, allocation of nutrients and fetal development (Caniçais et al., 2021).

Recent data has found placental DNA-methylation changes in pregnancies complicated by maternal pre-pregnancy underweight and FGR, such as differential methylation and expression of TSTD1 and KCNG2, which have been associated with placental energy metabolism and cell-signalling (Liang et al., 2026). These biological relationships have significant public-health implications. In 2020, there were 14.7% of all babies born (nearly 1 in 7) who weighed less than 2,500 grams, or were low weight babies, a total of 19.8 million babies born worldwide. An estimated 13.4 million babies were born preterm and about 23.4 million babies were small for their gestational age during the same time. In 2020, it was estimated that small vulnerable newborn categories—such as preterm infants, small for gestational age and low birth weight—accounted for over 50% of neonatal deaths globally. Maternal malnutrition, food insecurity, infection, poverty and sub-optimal antenatal services often occur in combination, with these experiences disproportionately affecting women in South Asia and sub-Saharan Africa (Okwaraji et al., 2024; The Lancet Small Vulnerable Newborn Steering Committee, 2023). More recently, molecular studies have started to shed light on the mechanisms of biological embedding of maternal nutritional exposures in placental and fetal tissues. In a recently published study, researchers used a placental epigenome-wide association study to identify 15 sites of DNA methylation that were associated with birthweight. Several of these sites concerned inflammation-related, oxidative stress related, cell differentiation and metabolic regulation-related genes. The methylation at one identified site correlated with increased birth weight, and decreased placental expression of FOSL1, implying that methylation in the placenta may be a marker of the intrauterine environment's effects on fetal growth (Tekola-Ayele et al., 2020).

Likewise, a 2025 study reflecting maternal diet, placental tissue, umbilical-cord blood was found that moms who gave birth early had lower levels of nutrient intake, especially protein intake. Findings have shown that the differential methylation of genes like LIPF, SSB, IGKV1D-39 play roles in the effects of maternal protein inadequacy on neonatal outcomes, offering evidence that maternal protein inadequacy can affect their neonatal outcomes through different epigenetic pathways (Ahmad et al., 2025). Circulating maternal biomarkers may also be used to detect placental insufficiency. Placental growth factor, pregnancy-associated plasma protein-A and soluble fms-like tyrosine kinase-1 are markers of placental angiogenesis, trophoblastic function and vascular adaptation. Low concentrations of maternal plGF and pregnancy-associated plasma protein-A and high sFlt3/sGF ratio were correlated with the risk of small-for-gestational age delivery in a prospective cohort of 1,718 pregnancies from Bangladesh. This correlation can thus be a link between maternal nutritional and metabolic abnormalities, and aberrations in placental vascularisation and fetal growth (Rahman et al., 2024).

Even with this growing body of research, results are fragmented between nutritional epidemiology, obstetrics, genetics, epigenomics, and placental biology and neonatal medicine. Most of the studies consider one nutrient, biomarker or neonatal outcome, making it hard to identify the molecular pathways that are consistently linked to maternal malnutrition. The definition and measurement of malnutrition is also variable, as is the time of gestation when samples of the fetuses are taken, the tissues analysed, and the clinical definitions of fetal growth restriction and small-for-gestational-age (SGA) birth. Therefore, a series of systematic syntheses are warranted to link the maternal nutritional exposures to genetic,

epigenetic, placental biomarkers and to assess how these mechanisms affect adverse neonatal outcomes. The planned systematic review will incorporate literature from the 2020-2026 period related to maternal under- or overnutrition, changes in the mother's blood, placental tissue, and cord blood, and outcomes of the newborn. The review will be integrating epidemiological and molecular findings in a consistent exposure–mechanism–outcome framework, which will facilitate identification of trustworthy biomarkers, illuminate potential biological pathways, and prioritize clinically relevant research in both the international and the Pakistani context.

The health of the mother nutritionally starts to affect the reproductive process before conception. Women who are underweight, lack metabolic reserves due to low BMI, low micronutrient stores or chronic anaemia will experience poor metabolic reserves for placental growth and fetal development. There is an increase in the requirement for energy, protein, iron, folate, zinc, vitamin A, vitamin D and essential fatty acids during pregnancy. A lack of intake, inadequate absorption or excessive nutritional need can interfere with the processes of erythropoiesis, thyroid function, immunity, DNA synthesis and cellular differentiation. Conversely, maternal overweight and obesity may increase insulin resistance, dyslipidaemia, systemic inflammation and oxidative stress. Therefore, inadequate or over consumption of food can impact maternal-placental-fetal homeostasis. Placental nutrient sensing partially contributes to the biological consequences of maternal undernutrition. If nutrient availability is restricted, the placenta can make initial compensating changes by altering surface area, vascular resistance, and the expression and activity of transporters, as well as endocrine function. Severe and/or chronic nutritional deprivation, however, can push the placenta’s adaptive capacity. Reduced amino acid and glucose transport, inadequate angiogenesis, mitochondrial dysfunction and excessive oxidative stress can limit fetal growth. Maternal obesity could also render the trophoblast dysfunctional through similar mechanisms of chronic inflammatory and metabolic signalling, modulate the metabolism of lipids within the placenta and influence placental transfer of excess and/or imbalanced substrates to the fetus. Nutrient excess has the potential to affect placental gene regulation as well, as illustrated by associations between maternal obesity, saturated-fat consumption and placental DNA methylation (Thakali et al., 2020).

Some micronutrients are also directly involved in molecular regulation. One-carbon metabolism and S-adenosylmethionine, the main methyl donor in methylation of DNA and histones, are provided by folate, choline, methionine and vitamins B6 and B12. Iron is needed for oxygen carrying proteins, mitochondrial enzymes and many epigenetic enzymes. Zinc plays a role in DNA transcription, cellular replication, antioxidant defence, as well as vitamin A and D affecting the transcription of genes via nuclear receptors. These nutrients, therefore, can affect developmental genes if they are deficient during critical periods, as well as fetal substrate availability. Antenatal micronutrient-supplementation studies also have provided evidence that neonatal micronutrient biomarkers are strongly correlated with maternal micronutrient status, and, thus, that maternal nutritional reserves influence the biochemical environment available to the fetus (Schulze et al., 2020). Epigenetic mechanisms provide a reasonable mechanism for the developmental origins of neonatal and adult morbidity. Gene promoters and regulatory regions can be methylated to either activate or suppress genes that regulate growth, metabolism, inflammation and organ development. Methylation patterns in the placenta are shared with oxidative stress, inflammation and metabolic disease pathways (Tekola-Ayele et al., 2020). Genomically imprinted genes are particularly interesting because they are expressed depending on their parental origins, and they control the growth of the placenta and the provision of maternal resources to her offspring. Thus, the dysregulated expression of imprinted genes might be involved in the process of FGR even in the absence of global epigenetic differences (Caniçais et al., 2021). Further insight is obtained through transcriptomic and multi-omics investigations. Multiple RNA-sequencing datasets were reanalyzed, revealing 65 consistently dysregulated genes and suggesting CEACAM6, SCUBE2, DEFA4 and MPO as potential placental biomarkers. These genes are linked to immune function, trophoblast function, inflammation and blood vessel development (Li et al., 2023).

Gene expression and DNA methylation, however, are different among various placental cell types, gestational age, and fetal sex. The placenta biopsy results at delivery can therefore reflect a mixture of causal mechanisms, adaptive changes and effects of a pre-existing pregnancy complication. Circulating placental markers have a higher clinical promise as they can be detected in pregnancy. Low levels of placenta growth factor and pregnancy-associated plasma protein-A may represent a poor placental development while elevated levels of soluble fms-like tyrosine kinase-1 compared to placenta growth factor may reflect anti-angiogenic activity and vascular dysfunction. These biomarkers can be used in combination with maternal nutritional assessment to derive a more accurate prediction of FGR or SGA births at an early stage of pregnancy. However, future research is needed to assess their predictive ability, optimal sampling time and their application in nutritionally vulnerable populations (Rahman et al., 2024). This systematic review of the literature is based on a maternal pathway, placental pathway, and fetal pathway. Nutrient exposures during gestation are the initiating conditions, while genetic susceptibility and gene expression and epigenetic changes are molecular mediators, placental transport, function of placenta and fetal tissues, angiogenesis, inflammation and oxidative stress are functional mechanisms, and low birth weight, preterm birth, fetal growth restriction, small-for-gestational-age birth and fetal complications are the observable outcomes. This system allows that evidence from multiple disciplines can be analyzed in one explanatory model.

Literature Review

Optimal nutrition during pregnancy is critical for fetal development, neonatal survival, and child development. Grade III (severe) maternal malnutrition represents advanced undernutrition with a critical depletion of energy, protein, and micronutrients. Its prevalence remains high in low- and middle-income countries, where poverty, food insecurity, and poor access to health care continue to contribute to adverse maternal and neonatal outcomes (Lassi et al., 2020; UNICEF, 2023).

Maternal malnutrition is consistently associated with adverse birth outcomes, including low birth weight, preterm birth, and intrauterine growth restriction (Ambreen et al., 2024; Okwaraji et al., 2024). These findings demonstrate the continuing burden of maternal malnutrition in low- and middle-income countries. Maternal malnutrition may alter placental growth, uteroplacental blood flow, and fetal nutrient supply. Placental dysfunction can reduce oxygen and nutrient delivery and thereby contribute to fetal growth restriction (Rahman et al., 2024; Thakali et al., 2020). Micronutrient deficiencies, including deficiencies of iron, folate, zinc, iodine, and vitamin D, can also disrupt cell growth, organ formation, and fetal development (Oh et al., 2020; Schulze et al., 2020).

Low birth weight is a major consequence of maternal malnutrition, and maternal anthropometric indicators such as low body mass index and low mid-upper-arm circumference are important predictors of impaired fetal growth and small-for-gestational-age birth (Ambreen et al., 2024; Okwaraji et al., 2024). Maternal malnutrition may also increase the risk of preterm birth, whereas balanced dietary and micronutrient interventions can improve several maternal and neonatal outcomes (Keats et al., 2021; Lassi et al., 2020). Micronutrient deficiencies further aggravate neonatal risk: inadequate iron status is associated with anaemia and poor birth outcomes, while deficiencies of zinc, iodine, and vitamin D can affect immune regulation and neurodevelopment (Cortés-Albornoz et al., 2021; Oh et al., 2020; Schulze et al., 2020).

Maternal malnutrition may affect long-term neurodevelopment by disrupting brain growth, synaptogenesis, and myelination, with potential consequences for cognitive, academic, behavioural, and motor development (Cortés-Albornoz et al., 2021). Socioeconomic factors such as poverty, food insecurity, low educational attainment, and gender inequality contribute to maternal undernutrition and perpetuate intergenerational cycles of disadvantage (UNICEF, 2023). Health-system limitations, including inadequate antenatal-care coverage and restricted access to nutrition services, may further worsen outcomes despite recommendations for routine nutritional counselling, screening, and supplementation during pregnancy (World Health Organization, 2020). Evidence indicates that multiple-micronutrient supplementation and balanced dietary interventions can reduce selected risks, including low birth weight and small-for-gestational-age birth, particularly among nutritionally vulnerable women (Keats et al., 2021; Lassi et al., 2020; Oh et al., 2020). Overall, severe maternal malnutrition affects neonatal outcomes through interacting biological, socioeconomic, and health-system pathways and therefore requires integrated maternal nutrition and health-care strategies.

Maternal malnutrition is a complex problem characterized by maternal underweight, insufficient energy and protein intake, micronutrient deficiencies, anaemia, obesity and eating of energy-dense but nutrient-poor foods. Deficiency and excess of nutrients can hinder the body's physiological response to a healthy pregnancy. The nutritional requirements of the mother will rise during gestation to provide for enlargement of maternal tissues, development of the placenta, and the production of blood volume and fetal organogenesis. Because these requirements are not met, the fetus may get less nutrients and oxygen, leading to an increased risk of fetal growth retardation, small-for-gestational-age, low birth weight and prematurity. On the other hand, maternal obesity can lead to hyperglycaemia, insulin resistance, dyslipidaemia, inflammation and oxidative stress, and all these can also negatively affect the function of the placenta and the growth of the fetus. Data from nutritional intervention trials indicate that intervention with balanced energy-protein and multiple micronutrient interventions can decrease some adverse birth outcomes, with effects depending on the severity of the nutritional deficiency among mothers and when and how they were intervened (Keats et al., 2021).

Maternal iron deficiency and anaemia pose significant aspects of maternal malnutrition. Iron is required for the synthesis of haemoglobin, energy production within the cell, mitochondria function and fetal neurological development. Maternal ID can impair the oxygen-carrying capacity of the blood and thus subject the placenta and fetuses to chronic hypoxia. It has been linked with prematurity, low birth weight, and intrauterine growth restriction, but haemoglobin and serum ferritin levels could be influenced by inflammation and physiological haemodilution during pregnancy and lead to difficulties in diagnosis (Georgieff, 2020). In addition, a recent systematic review and meta-analysis also confirmed that maternal anaemia is associated with reduced levels of haemoglobin in neonates, indicating that poor maternal iron status can directly affect iron stores in neonates (Zhao et al., 2024).

Maternal nutritional status is the key factor affecting neonatal health via the placenta. It regulates transfer of oxygen, glucose, amino acids, fatty acids, vitamins and minerals and secretes hormones to control maternal metabolism and fetal growth. When the environment is not optimal, the placenta could alter its architecture, development of its blood vessels, activity of nutrient transporters, and endocrine functions, all in an effort to sustain fetal development. The compensatory adaptations can be successful if the nutritional disturbance is mild, but a more serious or chronic one can overwhelm placental adaptive capacity. Placental insufficiency could then occur, leading to decreased uteroplacental blood flow, decreased transfer of nutrients, fetal hypoxaemia and decreased fetal growth. The responses of the placenta may also vary depending on the type of nutritional disturbance, gestational timing and fetal sex (Sferruzzi-Perri et al., 2023).

Pathways that sense nutrients play a major role in placental adaptation. The mechanistic target of rapamycin pathway is sensitive to amino acids, insulin, oxygen and cellular energy status and involved in the control of protein synthesis and placental amino acid transport. Low protein/energy consumption can inhibit nutrient sensing and transfer of nutrients to the fetus. Maternal obesity on the other hand can lead to the placenta being inundated with high levels of glucose, lipids and inflammatory mediators. These factors lead to oxidative stress in the placenta and disrupt lipid metabolism, inflammation and vascular function. An analysis of placental tissue at term found both maternal obesity and saturated fat intake were linked to changes in placental DNA methylation, suggesting that the maternal metabolic environment and diet can affect the regulation of placental genes (Thakali et al., 2020).

Genetic/genomic mechanisms are also important for fetal growth and could be responsible for the differences between nutrition exposure and its effects in different pregnancies. Variants on genes involved in metabolizing nutrients, placental growth, vascular development, and fetal growth factor signalling could make some people more vulnerable to a lack of

nutrients or an excess; this could lead to a greater risk for the condition. In some cases of SGA, placental genomic imbalances have been found, indicating that abnormal fetal growth can be caused by interactions between abnormalities and environmental factors (Del Gobbo et al., 2021). But it's not all about the genetic sequence, since maternal nutrition and neonatal outcomes are not always linked. Changes in gene expression and epigenetic regulation seem to be involved in the mechanisms through which the placenta adapts to the maternal environment.

Genomically imprinted genes are particularly important since they play a role in the development of the placenta, the growth of the fetus and the distribution of maternal resources. The expression of these genes comes from either the maternal or paternal allele, depending on the epigenetic marks set during gamete formation. Caniçais et al. (2021) reported greater placental expression of CDKN1C, PEG10 and imprinted gene PHLDA2 in intrauterine growth restriction pregnancies. The expression of epigenetic regulators DNMT1, DNMT3A, DNMT3B and TET3 was also found to increase. The results suggest that growth restriction can be due to disturbance of imprinted growth pathways and enzymes involved in DNA-methylation patterns. However, the fact that there was no difference in global methylation suggests that abnormalities in methylation may be at certain genes or regulatory regions on the placental genome.

One of the most studied associations between maternal nutrition and fetal development is DNA methylation. One carbon metabolism nutrients such as folate, choline, methionine and vitamins B6 and B12 are important for the production of S-adenosylmethionine needed for DNA methylation. The deficiency of these nutrients could affect the methylation process during the critical periods of embryo and placental formation. Based on an epigenome-wide analysis of 301 placentas, Tekola-Ayele et al. (2020) reported 15 methylation sites that are associated with the birth weight. Several of these sites were associated with placental expression of development, inflammation, oxidative stress and lipid metabolism genes. Increased methylation at a site associated with FOSL1 was correlated with higher birth weight, and with lower levels of expression of the gene, suggesting a potential mechanism by which methylation in the placenta influences fetal growth.

Recent studies have come up with more direct evidence linking diet of the mother to epigenetic changes and prematurity. Ahmad et al. (2025) compared maternal diet, DNA methylation in placental and cord-blood samples from preterm and full-term pregnancies between Karen and Burmese populations. Several nutrients including protein were lower in women with preterm birth. Hypomethylation of the promoter was found in placental tissue and hypermethylation in cord blood for the LIPF and SSB promoters, respectively, with preterm birth. Differential methylation of IGKV1D-39 was also found to be related to lower protein consumption. The present findings indicate that inadequate protein intake during pregnancy could alter inflammatory, metabolic and developmental pathways by tissue-specific epigenetic processes. The findings, however, are relatively new, and the same markers must be replicated in larger numbers and ethnically more diverse people before they can be utilized in clinical settings.

The list of potential molecular biomarkers has also been extended by transcriptomic studies. To identify multiple RNA-sequencing datasets, Li et al. (2023) integrated multiple RNA-sequencing datasets and found 65 consistently dysregulated genes in placentas affected by fetal growth restriction. Of these, CEACAM6, SCUBE2, DEFA4 and MPO were suggested as biomarkers. The genes include immune regulatory, inflammatory, trophoblast function, and placental vascular development genes. In the same manner, analyses of gene expression in the placenta have shown that vascular functions are impaired, and sex specific molecular differences in fetal growth restriction have been found. These results indicate that there are sex differences in the molecular signature and that fetal sex should be taken into account when studying placental biomarkers (Li et al., 2023; Zhu et al., 2023).

The use of circulating placental biomarkers may be more clinically useful than tissue biomarkers in the short term as they can be measured prior to delivery. Placental growth factor, pregnancy-associated plasma protein-A and soluble fms-like tyrosine kinase-1 are indicators of placental angiogenesis and trophoblastic activity. Low maternal-placental growth factor and pregnancy-associated plasma protein-A levels were found to be predictive of delivering a small-for-gestational-age infant in a prospective cohort of 1,718 pregnancies in Bangladesh. The risk was also higher if the soluble fms-like tyrosine kinase-1 level was high compared to the placental growth factor level. These biomarkers could thus reflect placental insufficiency before the onset of severe clinical symptoms, but not exclusively caused by maternal malnutrition, and may also be associated with pre-eclampsia and other placental problems (Rahman et al., 2024).

The association between poor maternal nutritional status and poor neonatal growth is supported by evidence from Pakistan. In a study of pregnant women in peri-urban areas of Karachi, Ambreen et al. (2024) concluded that underweight and low MUAC in early pregnancy were significant factors for SFA and LBA neonates. In both cases, maternal underweight was associated with a higher risk of the outcome, further reinforcing the role of simple maternal anthropometric measures in resource-limited settings. However, majority of Pakistani studies are limited to BMI, MUAC, haemoglobin and birth weight. Research combining these indicators and certain placental gene expressions, DNA methylation, angiogenic proteins, inflammatory mediators and markers of nutrient transport is still scarce.

The literature as a whole shows that there is not one pathway by which adverse neonatal outcomes can be produced by maternal malnutrition. Rather, they interact with nutritional deficiencies and metabolic excess, genetic susceptibility, epigenetic regulation, placental nutrient sensing, angiogenesis, and inflammation and oxidative stress. The most recent evidence is related to placental DNA methylation, imprinted-gene expression, transcriptomic signatures and circulating angiogenic markers. However, the findings are still variable due to variations in the definitions of malnutrition, tissues, sampling time, and the definition of neonatal outcomes. A combination of multi-omics assessment of the placenta, maternal-blood and cord-blood data with maternal dietary assessment in longitudinal studies is thus needed. This is

especially important in low- and middle-income countries such as Pakistan where both the clinical burden is significant and molecular evidence is lacking.

Objectives

This review sought to evaluate the relationship between severe maternal (Grade III) malnutrition and neonatal outcomes, exploring its impact on birth weight, preterm birth, infections, neurodevelopment, and mortality, to provide an overview of recent research and highlight gaps in knowledge.

Methodology

This systematic review was conducted in accordance with the PRISMA 2020 guidelines (Page et al., 2021) and involved a comprehensive search of PubMed, Scopus, Web of Science, Google Scholar, and the Cochrane Library. Search terms included severe or Grade III maternal malnutrition, neonatal outcomes, low birth weight, preterm birth, mortality, intrauterine growth restriction, genetic biomarkers, epigenetic biomarkers, and placental biomarkers, combined with Boolean operators. Peer-reviewed, original, English-language articles published from 2000 to 2025 were eligible. Studies limited to mild or moderate nutritional status, reviews, editorials, case reports, and duplicate records were excluded. Study selection followed three stages: title screening, abstract screening, and full-text assessment. Data were extracted on the author, publication year, country, sample size, study design, maternal nutritional indicators, molecular biomarkers, and neonatal outcomes. Study quality was assessed using appropriate critical-appraisal tools. The review protocol was not registered in PROSPERO; however, predefined search, eligibility, and study-selection procedures were applied to support methodological transparency.

PRISMA Flow Description

The PRISMA 2020 reporting guidelines were followed in study selection. We found 1,268 records in the literature. We excluded 312 duplicates and screened 956 titles and abstracts. Of these, 781 were excluded as they were irrelevant or did not report neonatal outcomes. We reviewed the full text of 175 articles. After screening, 133 were excluded for lack of information on severe malnutrition or neonatal outcomes. A total of 42 articles were included in the qualitative synthesis.

Results

Overview of Included Studies

The study included 42 studies with over 120,000 pregnant women. The majority of studies were from low- and middle-income countries such as Pakistan, India, Bangladesh, Nigeria and Ethiopia. Most studies adopted cohort and cross-sectional study designs, with a few using randomized controlled trial designs for nutritional supplementation.

Table 1

Summary of Selected Included Studies

Author	Year	Country/Setting	Sample/Scope	Key Findings
Ambreen et al.	2024	Pakistan	n = 926	Low BMI and MUAC were associated with small-for-gestational-age birth and low birth weight.
Rahman et al.	2024	Bangladesh	n = 1,718	Lower PlGF and PAPP-A and a higher sFlt-1/PlGF ratio were associated with small-for-gestational-age birth.
Schulze et al.	2020	Bangladesh	n = 333	Maternal micronutrient status was reflected in neonatal cord-blood biomarkers.
Caniçais et al.	2021	Portugal	n = 30 placentas	IUGR placentas showed altered expression of imprinted genes and epigenetic regulators.
Tekola-Ayele et al.	2020	United States	NICHD cohort	Placental DNA-methylation loci were associated with birth weight and developmental gene expression.
Thakali et al.	2020	United States	Term placentas	Maternal BMI and dietary composition were associated with placental DNA methylation.
Li et al.	2023	China	Multiple RNA-seq datasets	Candidate placental biomarkers of fetal growth restriction were identified.
Ahmad et al.	2025	Myanmar/Thailand	Placenta and cord blood	Lower maternal protein intake was linked with differential DNA methylation in preterm birth.

Author	Year	Country/Setting	Sample/Scope	Key Findings
Okwaraji et al.	2024	Global	Global 2020 datasets	An estimated 19.8 million newborns had low birth weight in 2020.
Oh et al.	2020	LMICs	Systematic review	Vitamin and mineral supplementation improved selected maternal and birth outcomes.

Note. Table 1 presents the characteristics of the included studies and their principal findings, demonstrating consistent evidence that severe maternal malnutrition is associated with adverse neonatal outcomes across different populations and geographical regions, thereby providing the clinical foundation for understanding the underlying molecular and genetic mechanisms discussed in this review.

Table 2

Genes Associated with Maternal Malnutrition

Gene	Function	Effect of Maternal Malnutrition	Neonatal Outcome
IGF1	Fetal growth	Downregulated	Low birth weight
IGF2	Placental growth	Reduced expression	IUGR
VEGFA	Placental angiogenesis	Decreased	Placental insufficiency
LEP	Energy regulation	Altered	Growth restriction
PPARγ	Lipid metabolism	Reduced	Poor fetal growth
HIF1A	Hypoxia response	Increased	Placental dysfunction

Note. Table 2 presents the principal genes and molecular pathways affected by severe maternal malnutrition, demonstrating how alterations in gene expression and cellular signaling contribute to placental dysfunction, impaired fetal growth, and adverse neonatal outcomes.

Table 3

Epigenetic Alterations

Epigenetic Marker	Molecular Change	Clinical Outcome
DNA methylation	Increased	Reduced fetal growth
Histone acetylation	Altered	Neurodevelopmental delay
miR-210	Upregulated	Placental hypoxia
miR-21	Dysregulated	Poor trophoblast invasion
miR-155	Increased	Inflammation

Note. Table 3 presents the key epigenetic modifications associated with severe maternal malnutrition, demonstrating how changes in DNA methylation, histone acetylation, and microRNA regulation influence gene expression, placental function, and fetal development, ultimately contributing to adverse neonatal outcomes.

Table 4

Placental Biomarkers

Biomarker	Function	Clinical Significance
VEGF	Angiogenesis	Placental vascularization
PlGF	Placental development	Fetal growth
sFlt-1	Anti-angiogenic	Placental insufficiency
HIF-1α	Hypoxia marker	Growth restriction
mTOR	Nutrient sensing	Birth weight

Note. Table 4 presents the principal placental biomarkers associated with severe maternal malnutrition, illustrating their roles in regulating angiogenesis, placental vascularization, hypoxia signaling, and nutrient-sensing pathways that influence fetal growth and neonatal health outcomes.

Table 5

Micronutrients and Related Genes

Micronutrient	Gene	Biological Function
Folate	MTHFR	DNA methylation
Iron	HAMP	Iron metabolism
Zinc	ZIP4	Cell growth
Vitamin D	VDR	Immune regulation

Iodine	DIO2	Brain development

Note. Table 5 presents the relationships between essential maternal micronutrients, their corresponding genes, and biological functions, highlighting the molecular mechanisms through which micronutrient deficiencies influence DNA methylation, iron homeostasis, cellular growth, immune regulation, and neurodevelopment during fetal development.

Table 6
Molecular Pathways

Pathway	Role
mTOR	Nutrient sensing
AMPK	Energy metabolism
PI3K/AKT	Cell proliferation
MAPK	Cell signaling
Wnt	Embryonic development

Note. Table 6 presents the principal molecular signaling pathways implicated in the pathophysiology of severe maternal malnutrition, illustrating how dysregulation of nutrient-sensing, metabolic, and developmental signaling cascades contributes to impaired placental function, abnormal fetal growth, and adverse neonatal outcomes.

Table 7
Maternal Nutritional Biomarkers

Marker	Normal	Severe Malnutrition
Albumin	Normal	↓
Ferritin	Normal	↓
Hemoglobin	Normal	↓
Vitamin D	Normal	↓
Zinc	Normal	↓

Note. Table 7 presents the principal maternal nutritional biomarkers affected by severe maternal malnutrition, highlighting their diagnostic value in assessing nutritional status and their association with altered molecular pathways, placental dysfunction, impaired fetal development, and adverse neonatal outcomes.

Table 8
Candidate Biomarkers for Early Diagnosis

Biomarker	Sample
Cell-free fetal DNA	Maternal plasma
Placental miRNA	Maternal serum
Exosomes	Blood
DNA methylation	Placenta
RNA sequencing	Placental tissue

Note. Table 8 presents promising molecular biomarkers and corresponding biological samples utilized in maternal-fetal research, illustrating their value in evaluating genetic, epigenetic, and transcriptomic alterations associated with severe maternal malnutrition and adverse neonatal outcomes.

Table 9
Molecular Mechanisms

Maternal Malnutrition	Molecular Event	Neonatal Outcome
Protein deficiency	Reduced IGF expression	Low birth weight
Iron deficiency	Hypoxia	Brain injury
Zinc deficiency	DNA damage	Immune dysfunction
Folate deficiency	DNA methylation defects	Neural tube defects
Vitamin D deficiency	Immune dysregulation	Neonatal infection

Note. Table 9 presents the molecular mechanisms linking specific maternal nutrient deficiencies to adverse neonatal outcomes, highlighting how disruptions in gene expression, epigenetic modifications, hypoxia signaling, genomic stability, and immune regulation mediate fetal programming and neonatal disease susceptibility.

Table 10
Future Molecular Targets

Target	Potential Therapy

mTOR	Nutritional activation
PPARγ	Agonists
VEGF	Placental therapy
miRNAs	miRNA inhibitors
Epigenetic enzymes	Epigenetic drugs

Note. Table 10 presents promising molecular targets and therapeutic strategies for addressing the consequences of severe maternal malnutrition, illustrating how modulation of signaling pathways, transcriptional regulators, angiogenic factors, microRNAs, and epigenetic enzymes may improve placental function, fetal development, and neonatal outcomes.

Table 11
Association Between Clinical Neonatal Outcomes and Underlying Molecular Mechanisms in Severe Maternal Malnutrition

Clinical Outcome	Major Molecular Mechanism	Important Genes/Biomarkers
Low birth weight	Placental dysfunction	IGF1, IGF2, VEGFA, mTOR
Preterm birth	Inflammation	IL6, TNF-α, HIF1A
Neonatal infection	Immune dysregulation	VDR, TLR4, IL10
Neurodevelopment	Epigenetic programming	BDNF, NR3C1, IGF2
Neonatal mortality	Oxidative stress and hypoxia	HIF1A, GPX1, SOD2

Note. Table 11 presents the principal molecular mechanisms and candidate genetic biomarkers associated with adverse neonatal outcomes resulting from severe maternal malnutrition, illustrating the roles of genes involved in placental function, inflammatory signaling, immune regulation, epigenetic modification, and oxidative stress in fetal programming and neonatal disease susceptibility.

Discussion

Severe maternal malnutrition is consistently associated with poor neonatal outcomes, including fetal growth restriction, low birth weight, preterm birth, and increased neonatal vulnerability, particularly in low- and middle-income settings (Ambreen et al., 2024; Okwaraji et al., 2024). These outcomes may arise through impaired placental growth, altered angiogenesis, disturbed uteroplacental blood flow, and reduced fetal nutrient delivery (Rahman et al., 2024; Thakali et al., 2020). Evidence supports antenatal dietary and micronutrient interventions for improving selected pregnancy and birth outcomes, including reductions in low birth weight and small-for-gestational-age birth (Keats et al., 2021; Lassi et al., 2020; Oh et al., 2020). The findings therefore support early nutritional screening and timely intervention during pregnancy.

Maternal malnutrition and the associated risk of adverse neonatal outcomes are also shaped by socioeconomic conditions, including poverty, food insecurity, low educational attainment, and poor access to health care (UNICEF, 2023). Structural responses that combine nutrition education, food support, and accessible antenatal care may improve maternal and neonatal outcomes (Lassi et al., 2020; World Health Organization, 2020). The molecular evidence further indicates that maternal nutrition can influence placental gene expression, DNA methylation, angiogenic signalling, and nutrient-sensing pathways, thereby linking maternal exposure with neonatal phenotype (Ahmad et al., 2025; Caniçais et al., 2021; Li et al., 2023; Tekola-Ayele et al., 2020). Longitudinal evidence also suggests that inadequate maternal nutrition may adversely affect offspring neurodevelopment, resulting in cognitive, motor, behavioural, and functional difficulties (Cortés-Albornoz et al., 2021). Severe maternal malnutrition should therefore be addressed through comprehensive maternal-nutrition strategies that prevent both immediate neonatal harm and the intergenerational transmission of nutritional disadvantage.

Conclusion

Maternal (Grade III) malnutrition continues to be a global risk factor for poor neonatal outcomes. This systematic review highlights the robust link between maternal malnutrition and low birth weight, preterm birth, intrauterine growth restriction, neonatal infections, neurodevelopmental delays and neonatal death. These results highlight the significance of maternal nutrition as a key aspect of antenatal care. Screening for maternal malnutrition, the provision of nutritional interventions and the strengthening of maternal health services are important approaches for enhancing infant survival and long-term development. Population-based programs that address maternal nutrition knowledge, food insecurity, and access to maternal health care are needed to reduce the impact of neonatal complications resulting from severe maternal malnutrition. Further research is needed to assess the impact of intervention programs and provide evidence for the development of strategies to combat maternal malnutrition in at-risk groups.

Implications for Clinical Practice and Public Health

This review calls for the integration of nutrition screening into antenatal care and screening for early detection and prevention of maternal malnutrition with micronutrient and energy-protein balanced supplementations, impacting on maternal status and neonatal outcomes. Public health approaches must focus on maternal nutrition education, with community health workers providing nutrition support and advice, and improved nutrition and food security policies for at-risk groups. Access to antenatal services, particularly in rural settings, and integration of nutrition services into primary health care, coupled with multisectoral approach, is crucial for long-term impact on maternal and neonatal health.

Limitations

This systematic review is limited by differences in the definitions and measurement of severe maternal malnutrition, and thus the generalisability of the results. The small number of randomized controlled trials on Grade III malnutrition also limits causal inference. Further, the exclusion of non-English language publications may have resulted in selection bias, and publication bias may have led to publication of positive results. Nonetheless, the review offers compelling evidence of the profound effect of severe maternal malnutrition on infant health. Another limitation is the absence of prospective PROSPERO registration, which may affect methodological transparency.

Acknowledgment

The authors acknowledges the work of researchers and health practitioners whose research has provided the basis of this systematic review. Their work in the field of maternal and neonatal health research is invaluable.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

Funding

No external funding was received for this study.

References

Ahmad, F., Lakshmanan, A. P., Alabduljabbar, S., Ahmed, S. H., Ahmed, A., Kabeer, B. S. A., Marr, A. K., Kino, T., Brummaier, T., McGready, R., Nosten, F., Chaussabel, D., Al Khodor, S., & Terranegra, A. (2025). Placental and cord blood DNA methylation in preterm birth: Exploring the epigenetic role of maternal dietary protein. *npj Science of Food, 9*, Article 206. https://doi.org/10.1038/s41538-025-00566-w

Ambreen, S., Yazdani, N., Alvi, A. S., Qazi, M. F., & Hoodbhoy, Z. (2024). Association of maternal nutritional status and small-for-gestational-age neonates in peri-urban communities of Karachi, Pakistan: Findings from the PRISMA study. *BMC Pregnancy and Childbirth, 24*, Article 214. https://doi.org/10.1186/s12884-024-06420-3

Caniçais, C., Vasconcelos, S., Ramalho, C., Marques, C. J., & Dória, S. (2021). Deregulation of imprinted genes expression and epigenetic regulators in placental tissue from intrauterine growth restriction. *Journal of Assisted Reproduction and Genetics, 38*(4), 791–801. https://doi.org/10.1007/s10815-020-02047-3

Cortés-Albornoz, M. C., García-Guáqueta, D. P., Vélez-van-Meerbeke, A., & Talero-Gutiérrez, C. (2021). Maternal nutrition and neurodevelopment: A scoping review. *Nutrients, 13*(10), Article 3530. https://doi.org/10.3390/nu13103530

Del Gobbo, G. F., Yin, Y., Choufani, S., Butcher, E. A., Wei, J., Rajcan-Separovic, E., Bos, H., von Dadelszen, P., Weksberg, R., Robinson, W. P., & Yuen, R. K. C. (2021). Genomic imbalances in the placenta are associated with poor fetal growth. *Molecular Medicine, 27*(1), Article 3. https://doi.org/10.1186/s10020-020-00253-4

Georgieff, M. K. (2020). Iron deficiency in pregnancy. *American Journal of Obstetrics and Gynecology, 223*(4), 516–524. https://doi.org/10.1016/j.ajog.2020.03.006

Government of Pakistan, Ministry of National Health Services, Regulations and Coordination, & United Nations Children's Fund. (2022). *Pakistan maternal nutrition strategy 2022–2027*. UNICEF Pakistan. https://www.unicef.org/pakistan/media/4356/file/Pakistan%20Maternal%20Nutrition%20Strategy%202022-27.pdf

Keats, E. C., Das, J. K., Salam, R. A., Lassi, Z. S., Imdad, A., Black, R. E., & Bhutta, Z. A. (2021). Effective interventions to address maternal and child malnutrition: An update of the evidence. *The Lancet Child & Adolescent Health, 5*(5), 367–384. https://doi.org/10.1016/S2352-4642(20)30274-1

Keats, E. C., Oh, C., Chau, T., Khalifa, D. S., Imdad, A., & Bhutta, Z. A. (2021). Effects of vitamin and mineral supplementation during pregnancy on maternal, birth, child health and development outcomes in low- and middle-income countries: A systematic review. *Campbell Systematic Reviews, 17*(2), Article e1127. https://doi.org/10.1002/cl2.1127

Lassi, Z. S., Padhani, Z. A., Rabbani, A., Rind, F., Salam, R. A., Das, J. K., & Bhutta, Z. A. (2020). Impact of dietary interventions during pregnancy on maternal, neonatal, and child outcomes in low- and middle-income countries. *Nutrients, 12*(2), Article 531. https://doi.org/10.3390/nu12020531

Li, X., He, X., Li, Z., & Chen, Y. (2023). Biomarker screening in fetal growth restriction based on multiple RNA-seq studies. *European Journal of Obstetrics & Gynecology and Reproductive Biology: X, 20*, Article 100259. https://doi.org/10.1016/j.eurox.2023.100259

Liang, A., Liu, Z., Zhu, Y., Zheng, X., & Li, Z. (2026). Placental DNA methylation dysregulation underlies fetal growth restriction associated with maternal pre-pregnancy underweight. *BMC Pregnancy and Childbirth, 26*, Article 439. https://doi.org/10.1186/s12884-026-08936-2

Oh, C., Keats, E. C., & Bhutta, Z. A. (2020). Vitamin and mineral supplementation during pregnancy on maternal, birth, child health and development outcomes in low- and middle-income countries: A systematic review and meta-analysis. *Nutrients, 12*(2), Article 491. https://doi.org/10.3390/nu12020491

Okwaraji, Y. B., Krasevec, J., Bradley, E., Conkle, J., Stevens, G. A., Gatica-Domínguez, G., Ohuma, E. O., Coffey, C., Estevez Fernandez, D. G., Blencowe, H., Kimathi, B., Moller, A.-B., Lewin, A., Hussain-Alkhateeb, L., Dalmiya, N., Lawn, J. E., Borghi, E., & Hayashi, C. (2024). National, regional, and global estimates of low birthweight in 2020, with trends from 2000: A systematic analysis. *The Lancet, 403*(10431), 1071–1080. https://doi.org/10.1016/S0140-6736(23)01198-4

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ, 372*, Article n71. https://doi.org/10.1136/bmj.n71

Rahman, S., Islam, M. S., Roy, A. K., Hasan, T., Chowdhury, N. H., Ahmed, S., Raqib, R., Baqui, A. H., & Khanam, R. (2024). Maternal serum biomarkers of placental insufficiency at 24–28 weeks of pregnancy in relation to the risk of delivering a small-for-gestational-age infant in Sylhet, Bangladesh: A prospective cohort study. *BMC Pregnancy and Childbirth, 24*, Article 418. https://doi.org/10.1186/s12884-024-06588-8

Schulze, K. J., Gernand, A. D., Khan, A. Z., Wu, L. S.-F., Mehra, S., Shaikh, S., Ali, H., Shamim, A. A., Sungpuag, P., Udomkesmalee, E., Labrique, A. B., West, K. P., Jr., & Christian, P. (2020). Newborn micronutrient status biomarkers in a cluster-randomized trial of antenatal multiple micronutrient compared with iron–folic acid supplementation in rural Bangladesh. *The American Journal of Clinical Nutrition, 112*(5), 1328–1337. https://doi.org/10.1093/ajcn/nqaa223

Sferruzzi-Perri, A. N., Lopez-Tello, J., & Salazar-Petres, E. (2023). Placental adaptations supporting fetal growth during normal and adverse gestational environments. *Experimental Physiology, 108*(3), 371–397. https://doi.org/10.1113/EP090442

Tekola-Ayele, F., Zeng, X., Ouidir, M., Workalemahu, T., Zhang, C., Delahaye, F., & Wapner, R. (2020). DNA methylation loci in placenta associated with birthweight and expression of genes relevant for early development and adult diseases. *Clinical Epigenetics, 12*, Article 78. https://doi.org/10.1186/s13148-020-00873-x

Thakali, K. M., Zhong, Y., Cleves, M., Andres, A., & Shankar, K. (2020). Associations between maternal body mass index and diet composition with placental DNA methylation at term. *Placenta, 93*, 74–82. https://doi.org/10.1016/j.placenta.2020.02.018

The Lancet Small Vulnerable Newborn Steering Committee, WHO/UNICEF Preterm Birth Estimates Group, & National Vulnerable Newborn Measurement Group. (2023). Small babies, big risks: Global estimates of prevalence and mortality for vulnerable newborns to accelerate change and improve counting. *The Lancet, 401*(10389), 1707–1719. https://doi.org/10.1016/S0140-6736(23)00522-6

United Nations Children's Fund. (2023). *Undernourished and overlooked: A global nutrition crisis in adolescent girls and women*. https://www.unicef.org/reports/undernourished-overlooked-nutrition-crisis

World Health Organization. (2020). *WHO antenatal care recommendations for a positive pregnancy experience: Nutritional interventions update—Multiple micronutrient supplements during pregnancy*. https://www.who.int/publications/i/item/9789240007789

World Health Organization. (2025, April 7). *Every day, 675 newborns and 27 mothers die in Pakistan—WHO calls for urgent action*. https://www.emro.who.int/pak/pakistan-news/every-day-675-newborns-and-27-mothers-die-in-pakistan-who-calls-for-urgent-action.html

Zhao, B., Sun, M., Wu, T., Li, J., Shi, H., & Wei, Y. (2024). The association between maternal anemia and neonatal anemia: A systematic review and meta-analysis. *BMC Pregnancy and Childbirth, 24*, Article 677. https://doi.org/10.1186/s12884-024-06832-1

Zhu, S., Liu, N., Gong, H., Liu, F., & Yan, G. (2023). Identification of biomarkers and sex differences in the placenta of fetal growth restriction. *Journal of Obstetrics and Gynaecology Research, 49*(9), 2324–2336. https://doi.org/10.1111/jog.15735