



# The Impact of Multiple Micronutrient Supplementation on Hemoglobin Concentration in Pregnant and Neonatal Birth Weight

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## Abstract

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**BACKGROUND:** Anemia during pregnancy is a public health problem especially in developing countries and it is associated with maternal and perinatal adverse outcomes. Global data shows that 56% of pregnant women in low- and middle-income countries have anemia. Every year more than 20 million infants are born with low birth weight (LBW) worldwide.

**AIM:** The objective of the study is to analyze the impact of Multi Micronutrients (MMN) supplementation on hemoglobin (Hb) levels of pregnant women and infant birth weight.

**METHODS:** The databases used to obtain the literature were PubMed, ScienceDirect, MEDLINE, and PubMed Central. The keywords used were Multiple Micronutrient Supplementation, Hb, Pregnant, and Neonatal Birth Weight in studies published from 2010 to 2020. A total of 14 articles were used in this review.

**RESULTS:** Seven articles obtained about the effects of MMN on Hb levels in pregnant women. Six studies support that MMN supplementation increases Hb levels or prevents pregnant women from anemia. One study showed a significant increase in serum ferritin. One study reported ferritin levels in the MMN group, as well as the Fe-folic acid group, did not experience a significant decrease. There is only one study that shows the opposite results, which the mean maternal Hb level significantly decreased during study, being the lowest in second trimester. Ferritin and serum iron levels were decreased at trimester one and two, also the zinc and Vitamin D levels declined. Seven articles show the effect of MMN supplementation on pregnancy outcomes is better than Fe-folic acid supplementation. This can be seen in the results reported from various studies that have been carried out, which are reduce the incidence of LBW, small for gestational age, and preterm labor. Stillbirths, and neural tube defect anomaly.

**CONCLUSION:** Various empirical evidence that has been described in this paper confirms the plausibility that the provision of micronutrient supplementation in the periconceptional period is more important than only given during advanced pregnancy. MMN administration increases Hb levels in pregnant women and improves pregnancy outcomes.

## Introduction

Anemia during pregnancy is a public health problem, especially in developing countries and it is associated with maternal and perinatal adverse outcomes. The World Health Organization (WHO) has defined anemia in pregnancy as the hemoglobin (Hb) concentration of <11 g/dl. Anemia is considered of a severe public health significance if its rate of ≥40% and Global data shows that 56% of pregnant women in low- and middle-income countries have anemia [1]. The prevalence of anemia is highest among pregnant women in sub-Saharan Africa (57%), followed by pregnant women in South-East Asia (48%) and lowest prevalence (24.1%) was reported among pregnant women in South America [2].

For Indonesia, according to [3], the proportion of anemia in pregnant women is 48.9%, higher than in 2013 which was 37.1%. Additional data that we can see, the coverage of giving blood-added tablets to pregnant

women is 73.2%, but those who get tablets ≥90 items are only 24%. The proportion of anemia in pregnant women above becomes an irony amid the incessant national nutrition improvement program

Every year >20 million infants are born with low birth weight (LBW) worldwide. About 3.6 million infants die during the neonatal period. Two-thirds of these deaths occur in southern Asia and sub-Saharan Africa. MMN supplementation in pregnant women may be a promising strategy for reducing adverse pregnancy outcomes through improved maternal nutritional and immune status. The WHO currently recommends iron and folic acid supplementation to reduce the risk of iron deficiency anemia among pregnant women. Since many developing countries already have systems in place for the delivery of iron and folic acid supplements, micronutrient supplements could be provided at little additional cost [4], [5].

Based on the problems presented above this paper intends to provide an explanation of the

importance of nutritional supplementation, especially micronutrients in the periconceptional period of Hb levels in pregnant women and birth weight of infants.

## Methods

The study was conducted from October to November 2019. The databases used in the literature search were PubMed, ScienceDirect, MEDLINE, and PubMed Central. Multiple Micronutrient Supplementation, Hb, Pregnant, and Neonatal Birth Weight were used as keywords in finding appropriate literatures published from 2010 to 2020. A total of 14 articles were used in this review. The preparation, categorization, and documentation had done using Mendeley software.

## Results

The results of literature review through the Google search engine with the keywords “preconception nutrition” or “prenatal nutrition or” preconceptional supplementation of MMNs”, pregnant women, Hb levels, and LBW, obtained several research results published in various scientific journals published. The results of tracing the literature are presented in Tables 1 and 2.

### MMNs and Hb levels in pregnant women

Of the seven studies obtained about the effects of MMNs on Hb levels in pregnant women, the most research methods were randomized controlled trial (3), followed by prospective cohort study (1), Quasy experimental study (1), exploratory study (1) and Casecontrol study (1). These results are shown in Table 1.

### MMNs and LBW

Of the seven studies obtained on the effects of MMNs on LBW, the most research methods used were meta-analysis (3), systematic review (2), randomized controlled trials (1) and cohort (1). These results are shown in Table 2.

## Discussion

Refer to Planning Guidelines The first 1000 days of life Movement Program that has been compiled since 2013 and has been implemented, then nutrition interventions specific is iron folate supplementation, Zn supplementation for toddlers, substance fortification iron. If you see specific nutrition interventions in SUN framework is MMN supplementation MMN, and MMN fortification. Until now it seems that there is no signal that the government will take steps replacing added blood tablets TTD which contain 60 mg of elemental iron and 250 µg acid folate, with a MMN supplement contains various vitamins and minerals [14]. MMNs contain 15 types of Vitamins and minerals that are most

**Table 1: Effects of MMN on Hb levels and serum ferritin in pregnant women**

Study	Treatment	Hb level	Ferritin Serum
Patimah <i>et al.</i> (2013) [6]	The study was a randomized controlled trial conducted in Maros Regency. The first group (n = 35) received a MMN supplement daily, second group (n = 35) received a iron-folic acid tablet daily, respectively for 12 consecutive weeks	Mean Hb levels increased significantly after the supplementation of MMNs whereas iron folic acid supplement did not increase significantly	ferritin serum levels of the two groups were not significantly decreased after supplementation MMN and iron-folic acid
Serdula <i>et al.</i> (2019) [7]	A double-blind randomized controlled trial was conducted in China 18,775 nulliparous women with a Hb concentration >100g/L were randomly assigned to receive daily FA (400µg); IFA (FA, Fe 30mg), or MMN (FA, Fe and 13 micronutrients) from before 20 gestational weeks until delivery	Compared to FA alone, prenatal IFA and MMN provided to women with no or mild anemia did not affect anemia in women post-partum or their infants regardless of baseline maternal Hb concentration at enrollment	
Sari <i>et al.</i> (2017) [8]	A Quasi experimental study with randomized control group pre-post test design 40 pregnant women with a gestational age of 20 ± 1 week were divided into two groups, the intervention group (MMN supplementation) and the control group (Fe supplementation) for 6 weeks	The average increase in Hb levels after MMN supplementation is higher than after Fe supplementation. This difference is significant	
Wibowo and Irwinda (2015) [9]	An exploratory study in Jakarta of 100 pregnant women ≤12 weeks Subjects received milk powder formulations containing MMNs and protein supplements every month until delivery	Maternal Hb level during pregnancy cannot be maintained or enhanced by MMN and protein supplementation	Maternal ferritin and iron levels during pregnancy cannot be maintained/enhanced by MMN and protein supplementation
Hariyadi <i>et al.</i> (2015) [10]	Casecontrol with a sample of 36 respondents selected and divided into two groups; intervention and control	Blood booster tablets and vitamin C supplementation show significant results in increasing Hb levels in pregnant women who take blood-booster tablets	
Nguyen <i>et al.</i> (2016) [11]	A double blind randomized controlled trial in which 5011 Vietnamese women were provided with weekly supplements containing either only 2800 µg FA (control group), IFA (60 mg Fe and 2800 µg FA) or MMN (15 micronutrients with similar amounts of IFA)	Preconception supplementation with MMN or IFA resulted in modest increases in maternal and infant iron stores but did not impact anemia	In intention to treat analyses, prenatal ferritin was significantly higher among women receiving MMN
Kang <i>et al.</i> (2017) [12]	A prospective cohort study in rural Tibet of China. Daily supplementation with FA and MMN containing a recommended allowance of twenty-three vitamins and minerals in another county starting ≤24 weeks of gestation and continuing until delivery	Compared with the FA group, prenatal supplementation with MMN was significantly associated with reduced odds of anemia in the third trimester	

LBW: Low birth weight, MMN: Multi Micronutrients, Hb: Hemoglobin.

**Table 2: Effects of MMN on LBW and other outcomes**

Study	Treatment	LBW	other results
Kawai <i>et al.</i> (2011) [4]	To systematically review randomized controlled trials comparing the effect of supplementation with multiple micronutrients versus iron and folic acid on pregnancy outcomes in developing countries	MMN supplementation was more effective than iron and folic acid supplementation at reducing the risk of LBW and of small size for gestational age	Micronutrient supplementation had no overall effect on perinatal mortality
Smith <i>et al.</i> (2017) [13]	This two-stage meta-analysis of individual patient included data from 17 randomized controlled trials done in 14 low-income and middle-income countries, which compared MMN supplements containing iron-folic acid versus iron-folic acid alone in 112953 pregnant women	MMN supplements resulted in greater reductions in low birth weight Initiation of MMN supplements before 20 weeks gestation provided greater reductions in preterm birth	MMN supplements containing iron-folic acid provided significantly greater reductions in neonatal mortality for female neonates, small-for-gestational-age births, and 6-month mortality
Sumarmi (2017) [14]	Randomized double-blind community-based Trial in Probolinggo East Java revealed that extended MMNs intervention 2-6 months prior to pregnancy	MMNs intervention 2-6 months prior to pregnancy provided better effect on birth weight	MMNs intervention provided better effect on placental weight, maternal endocrine, and immune response
Zerfu and Ayele (2013) [15]	To systematically review the effect of supplementing various combinations and types of micronutrients on the course and outcomes of pregnancy	MMNs supplementation have beneficial effect in reducing the risk of LBW and small for Gestational Age births	significant benefit of MMN supplementation during pregnancy in reducing preeclampsia
Wang <i>et al.</i> (2013) [16]	A cohort study to determine the effect of MMN administration on pregnancy outcomes	MMNs supplementation have beneficial effect in reducing the risk of LBW and small for Gestational Age births	MMNs supplementation have beneficial effect in reducing the risk of stillbirths, and NTD anomaly
Bourassa <i>et al.</i> (2019) [17]	Two recent reviews, a Cochrane systematic review and meta-analysis and an individual participant data (IPD) meta-analysis, have assessed trials that compared the use of MMS with IFA in pregnant women and were predominantly conducted in LMIC	Recent meta-analyses demonstrate that MMS can reduce the risks of preterm birth, LBW, and small for gestational age in comparison with IFA alone	
Fall <i>et al.</i> (2009) [18]	This meta-analysis from 12 randomized controlled trials reports the effects on newborn size and duration of gestation of MMN supplementation mainly compared with iron plus folic acid during pregnancy in recent randomized, controlled trials	MMN supplementation was associated with an increase in mean birth weight, a reduction in the prevalence of LBW, and SGA birth	MMN supplementation was associated with an increase in the prevalence of LGA birth

LBW: Low birth weight, MMN: Multi Micronutrients, Hb: Hemoglobin.

important for pregnant women including Vitamin A, Vitamin E, Vitamin D, Vitamin B1, Vitamin B2, niacin, Vitamin B6, Vitamin B12, folic acid, Vitamin C, Fe, zinc, copper, selenium, and iodine [19], [20].

### **MMNs and Hb levels in pregnant women**

Table 1 shows that most studies support that MMN supplementation increases Hb levels or prevents pregnant women from anemia [6], [7], [8], [9], [10], [11], [12]. Similarly, the effect of MMN on serum ferritin, one study reported ferritin levels in the MMN group as well as the Fe-folic acid group did not experience a significant decrease [6], and one study showed a significant increase in serum ferritin [11]. There is only one study that shows the opposite results, which research using milk powder containing MMNs and proteins given to pregnant women every month from gestational age  $\leq 12$  weeks until delivery. The mean maternal Hb level significantly decreased during the study ( $p < 0.001$ ), being the lowest in the second trimester. Ferritin and serum iron levels were decreased at trimester one and two ( $p < 0.001$ ), also the zinc and vitamin D level declined [9].

### **MMNs and LBW**

Table 2 shows the effect of MMN supplementation on pregnancy outcomes is better than Fe-folic acid supplementation. This can be seen in the results reported from various studies that have been carried out, which are reduce the incidence of LBW [4], [13], [14], [15], [16], [17], [18], small for gestational age [15], [16], [17], [18], preterm labor [13], [17], [18]. Stillbirths, and neural tube defect anomaly [16].

Critical period to determine healthy pregnancy as well as the quality of the baby's being born is a

time of moments conception or so-called conception (periconceptional period). Perception concept consists of periods before conception (preconception), conception stage, implantation, placentation, and embryogenesis or stage organogenesis, as well as specific cellular events which occur during the embryogenesis stage different [14].

Related to micronutrient interventions, Unicef actually did it MMN supplementation program for pregnant women in several regions in Indonesia, among others in West Nusa Tenggara (Central Lombok District), Nusa Tenggara East (Sikka and Belu Regencies), as well as at Central Java (Klaten Regency). This program it's time to expand coverage the area, and the scope of the target not only pregnant women, but it is very important prepared for the intervention program preconception [14].

## **Conclusion**

Various empirical evidence that has been described in this paper confirms the plausibility that the provision of micronutrient supplementation in the periconceptional period is more important than only given during advanced pregnancy. MMN administration increases Hb levels in pregnant women and improves pregnancy outcomes.

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