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IS THE MULTIPLE MICRONUTRIENTS BETTER TO REDUCE ANEMIA IN PREGNANCY COMPARED TO IRON- FOLATE ACID SUPLEMENTATION? A SYSTEMATIC REVIEW

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ABSTRACT

***Background**: Prevalence of anemia continues to increase among pregnant women in Indonesia. The micronutrients that are needed to reduce the anemia is still lacking to be accessed by pregnant women. This study aims to analyze the effectiveness of multiple micronutrients (MMN) compared to the iron-folic acid to reduce the incidence of anemia among pregnant women.*
***Methods**: Systematic review was used in this study using the electronic databases Google Scholar, Science Direct, and PubMed. The articles included in this study were published in 2009-2018 and were written in English language.*
***Results:** In total, 380 papers were identified and six articles were included in this study. Study found that the MMN and iron-folic acid had the same effect in influencing the anemia status among pregnant women. However, the MMN had a potential to increase the average of body weight, to reduce the incidence of low birth weight (LBW) and preterm birth among pregnant women.*
***Conclusions:** The effectiveness of multi micronutrients in pregnant women is as good as iron-folic acid in reducing the anemia during pregnancy. Further studies need to be conducted to see the effects of MMN on pregnant women by considering other factors such as maternal nutritional status, gestational age, and duration of supplementation*
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***Keywords**: Anemia, multiple micronutrients, iron-folate acid, pregnancy*

INTRODUCTION

Anemia is a condition in which the number and size of red blood cells, or hemoglobin concentration, falls below the set limit value, consequently damaging the capacity of the blood to carry oxygen around the body. Inadequate iron absorption, increased iron requirements during pregnancy or periods of growth, and increased iron loss as a result of menstruation and worms (intestinal worms) that can cause Iron Deficiency Anemia (ABS) [1]. According to WHO, pregnant women are said to be anemia if they have a hemoglobin concentration of less than 11 g / dl (7.45 mmoL / L) and a hematocrit of less than 33% [2].

WHO states that more than 56% of developing country women have anemia [2]. It is estimated that 50% of anemia in women worldwide is caused by iron deficiency [1]. Anemia prevalence in Indonesia is 21.7% and is more prevalent in rural areas (22.8%) than in urban areas (20.6%). Women are more prone to anemia with the proportion (23.9%) than men (18.4%). The prevalence of anemia in pregnant women is 37.1% and women of childbearing age (WUS) are 22.7% [3]. WHO targets to reduce the incidence of reproductive age women (WUS) who have anemia by as much as 50% in 2025 [1].

In developing countries, anemia not only affects babies born but also contributes to the cause of maternal death [2]. Anemia causes 20% of deaths in pregnant women [4]. Retrospective and observational studies state that the greatest risk of maternal mortality with anemia is bleeding and infection [5]. In Central Java Province, deaths during pregnancy were 26.32% in 2017. The cause of maternal death in Central Java Province was 30.37% due to bleeding [6].

WHO recommends anemia preventive efforts by giving iron-folic acid supplementation in areas with anemia prevalence above 20% [7]. Efforts to reduce the prevalence of anemia in pregnant women in Indonesia are carried out through a program of giving Blood Add Tablets (iron 60 mg and 0.4 mg folic acid) of at least 90 tablets during pregnancy. This blood tablet supplement program has been going on for 20 years. The coverage of pregnant women who received tablets of blood was 73.2%, but based on the results of the Riskesdas 2013 the prevalence of pregnant women with anemia continued to increase from 33.8% in 2007 to 37.1% in 2013 and 48.9% in 2018 [8][9].

In low-income countries, pregnant women cannot meet the needs of micronutrients due to poor diet. This allows a lack of micronutrients during pregnancy. Interventions for giving micronutrients are very important given to pregnant women [10]. Many researchers now question whether supplementation of multiple micronutrients (MMN) is more beneficial in improving maternal and infant nutrition compared to the administration of single iron-folic acid [11]. The aim of this study was to analyze the effectiveness of multi micronutrient supplementation compared to iron and / or iron-folic acid in reducing anemia in pregnant women. Researchers hope the results of this study can be used as a reference in providing intervention as an effort to reduce anemia in pregnant women.

METHODS

Literature Search Strategy

Literature searches were carried out on electronic journal sites namely Google Scholar, Science Direct, and PubMed published in the range of 2009 to 2018 in February until April 2019. The author searched for articles that were in line with the effectiveness of iron-folic acid and multi-micronurien supplements for anemia in pregnant women and analyze the effects caused on maternal anemia status and the condition of the baby at birth (outcome). Journals included in the research data are only journals that use English and Indonesian. use English

Inclusion Criteria

Article that is reviewed must be an original study that is reviewed and written in English, experimental study comparing the effects of MMN supplementation with iron / folic acid in pregnant women with iron-deficiency anemia, study evaluating MMN supplementation to maternal iron status and / or infant's condition at birth (outcome) and there is no limit on gestational age and duration of supplementationArticle that is reviewed must be an original study that is reviewed and written in English, experimental study comparing the effects of MMN supplementation with iron / folic acid in pregnant women with iron-deficiency anemia, study evaluating MMN supplementation to maternal iron status and / or infant's condition at birth (outcome) and there is no limit on gestational age and duration of supplementation.

Exclusion Criteria

Exclusion criteria in this study are study in animals, non-intervention study, and study of pregnant women with comorbidities (malaria, HIV and other infectious diseases).

Research Quality Evaluation Method

Assessment of the quality of articles in this study used the old school score. The old school score is a scale commonly used to determine the quality of clinical trial methodology. The old school score has an assessment range of 0.5 to 5. The results of the old school score are categorized as excellent (score

5), good (score 4), fair (score 3), poor (score 2), and very poor (score 1). Articles that meet the inclusion and exclusion criteria in this study were calculated by the old school score. The criteria for the old school score can be seen in Table 1**.**

Data analysis

The researcher conducted a literature evaluation that was relevant to multi micronutrient supplementation in pregnant women with anemia and its effects on maternal anemia status and the condition of the baby at birth. We conducted a systematic review that had the inclusion / exclusion criteria and with comparable exposure and outcome. Presentation of research results in narrative form. The effects of the intervention group and control groups were reported in this analysis, including significant and insignificant findings.

Table 1. Jadad Score for Randomized Controlled Trial

Question/response	Score
Was the study described as randomized	
Yes	1
No	0
Was the method of randomization appropriate	
Yes	1
No	0
Was the study described as blinded	
Yes (single blinded)	0,5
Yes (double blinded)	1
No	0
Was the method of blinding appropriate	
Yes	1
No	0
Was there a description of withdrawals and drop out	
Yes	1
No	0

RESULTS

Trial flow

The amount of literature obtained in the initial search was 380 articles published between 2009 and 2018 related to multi micronutrient supplementation therapy in pregnant women with anemia. The researcher screened the title and abstract until it was filtered into 150 articles. The article was then selected based on eligibility according to the inclusion and exclusion criteria to become 16 articles. The articles reviewed were 6 articles that discussed anemia status in the mother and 3 articles including measuring the status of the outcome (**Figure 1**.).

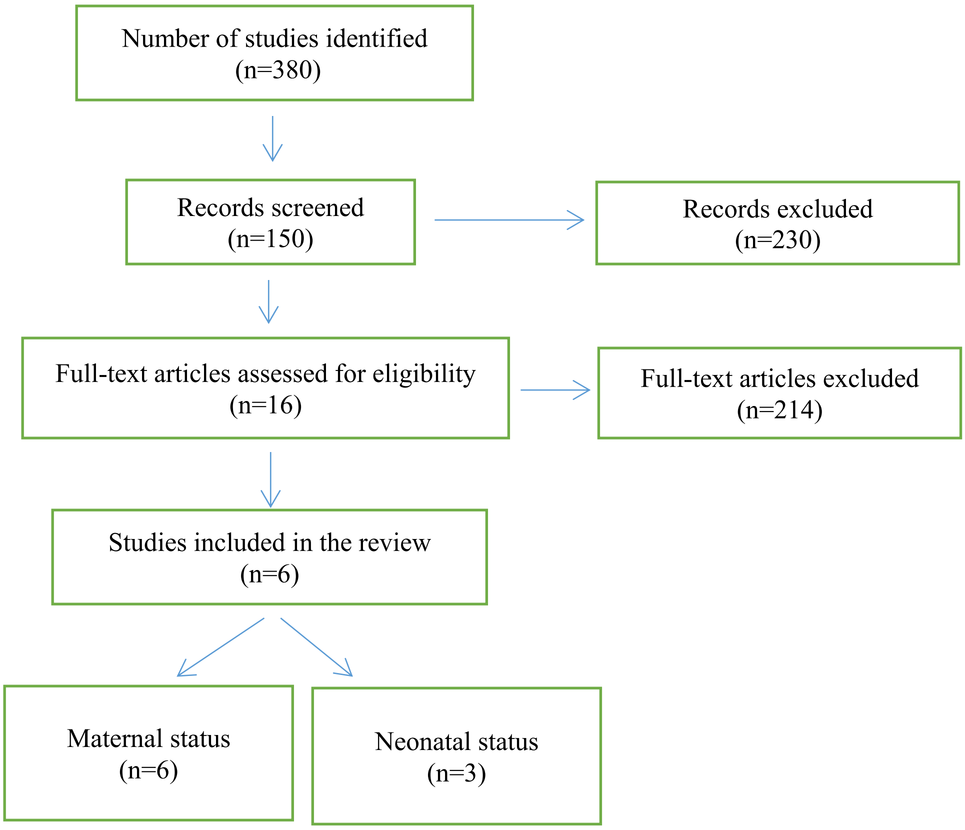

Figure 1. Flow diagram showing identification of studies

The articles reviewed in this study were then assessed by the jadad score. The results of the article evaluation based on the jadad score can be seen in **Table 2.**

Table 2. Jadad Score for the Methodological evaluation of randomized controlled trials

Author and year	described as randomized	Appropriate method of randomized	Description of blinding	Appropriate method of blinding	Description of withdrawal and drop out	∑Jadad score
Lars Ake et al, 2012	Yes	Yes	Yes (single blind)	Yes	Yes	4,5
Choundury et al, 2012	Yes	Yes	No	No	Yes	3
Mei et al, 2014	Yes	Yes	Yes	Yes	No	4
Yijun Kang et al, 2017	No	No	No	No	Yes	1
Aalia et al, 2012	No	No	No	No	Yes	1
Sunawang et al, 2009	Yes	Yes	Yes (single blind)	Yes	Yes	4,5

Characteristics of Study

The total articles that meet the criteria are 6 articles. The researcher analyzed the effect of micronutrients and iron / iron-folic acid supplementation on iron status in pregnant women and the condition of the baby. The subjects in the article were mostly carried out on pregnant women living in developing countries. Two studies were conducted in Bangladesh, two studies were conducted in China, one study was conducted in Pakistan, and one study was conducted in Indonesia. Analysis of articles included in the review can be seen in **Table 3**. and **Table 4.**

Tabel 3. PICOT Analysis

No	Little	Population and Sample	Intervention	Comparison	Outcome	Time
	Title: *Effect of prenatal micronutrient and early food supplementation on maternal hemoglobin, Birth weight, and infant mortality among children in Bangladesh* Author: Lars Ake P, Shams Arifeen, Eva - Charlotte, Kathleen MR, Edward AF, Md Yunus, MINImat Study Team. Journal: Journal of the American Medical Association. JAMA, May 16, 2012. Vol. 307, No.19: 2050-2059.	Population: Pregnant women Samples: 4436 pregnant women in Matlab, Bangladesh. Method: MINIMIZED Randomized Trial, Single Blind Trialassigned	Samples were randomlyinto 6 groups: initial supplementation intervention in GA 9 weeks and supplementation in the GA 20 weeks in the form of supplying 30 mg iron and 0.4 mg folic acid, 60 mg iron and 0.4 mg folic acid, or 15 micronutrients, 30 mg iron, 0.4 mg folic acid with a daily dose	Comparing Hb levels, infants weight and infant mortality to 6 groups at GA 30 weeks	There were no significant differences between the intervention groups in the GA 9 weeks and 20 weeks. The mean maternal Hb level and BBL mean in the intervention and control groups did not differ significantly. Infant mortality rates were lower in the intervention group (16.8 per 1000 live births vs 44.1 per 1000 live births).	November 2001-June 2009
	Title: *Relative efficacy of micronutrient powder versus iron-folic acid*	Population: Pregnant women in	Giving micronutrient powder (60 mg iron, 0.4 mg folic acid, 30 mg vitamin C, and 5 mg zinc) in the intervention group and supplementation of 60 mg	Comparing weight, height, Hb levels in the GA 24, 28 and 32 weeks.	The mean Hb levels, weight, and height in the intervention and control groups did not differ significantly.	October 2005-March 2006

controlling women in the second trimester of pregnancy Author: Nuzhat Choudhury, Ashley Aimone, Ziauddin Hyder, Stanley H. Zlotkon Journal: Food and Nutrition Bulletin, Vol. 33, No.2, 2012.	Kaliganj, Bangladesh. Samples: 478 pregnant women with 14-22 weeks gestation Method: Cluster Randomized noninferiority trial	iron-0.4 mg folic acid in the control group. Intervention is given until 32 weeks' gestation at a dose of 1 tablet per day.			
Title: *Iron-Containing Micronutrient Supplementation of Chinese Women with No or Mild Anemia during Pregnancy Improved Iron Status but Did Not Affect Perinatal Amenia* Author: Zuguo Mei, Marry KS, Jian-meng Liu, Rafael CF-Alya, Linlin Wang, Rongwei Ye, Laurence MD Grummer-Strawn Journal: The Journal of Nurition: Nutrition	Population: Pregnant women in Beijing, China Samples: 834 pregnant women with HB> 100 g / L before 20 weeks' gestation Method: Randomized, double blind Trial	Supplementation of 0.4 mg of folic acid (group control); 0.4 mg folic acid, 30 mg iron; and 0.4 mg folic acid, 30 mg iron and 13 micronutrients (intervention group) with daily doses.	Comparing iron deficiency status based on SF and sTfR in the intervention and control groups. Measurements are made in GA 28-32 weeks.	Iron deficiency based on SF and sTfR was more common in the control group, compared to the intervention group.	March 2008-February 2009

	Epidemiology. Published online: April 2014. 144: 943-948,2014.					
.	Title: Multi-micronutrient supplementation for maternal anemia and high birth altitude areas: prospective cohort study in rural Tibet of China Author: Yijun Kang, Shaonong Dang, Lingxia Zeng, Duolao Wang, Qiang Li, Jianpeng Wang, Luobo Ouzhu, Hong Yan Journal: British Journal of Nutrition. 2017. 118. 431-440.	Population: Pregnant women living in villages, Tibet, China Samples: 1149 pregnant women UK ≤ 24 weeks. Methods: Prospective cohort study	supplemented 0.4 mg of folic acid as a control group and supplemented 22 multi micronutrients as an intervention group. Dosage 1 tablet per day, after meals, at the same time every day.	Comparing Hb and GA levels at delivery in the intervention and control groups. Comparing birth size, preterm birth, and neonatal mortality in the intervention and control groups	There was a significant increase in HB levels in the intervention group compared to the control group in the Trimester 3 measurement. In the intervention group the gestational age was longer. There were no significant differences in the measurements of infants weight /length, there was a significant decrease in preterm births, in the intervention group there were fewer neonatal deaths but had no effect on infant mortality rate.	2007-2012
.	Title: *effect of iron with minerals and multivitamin supplementation on transferrin saturation index in iron*	Population: Anemic primigravida pregnant women in midwifery outpatient services in	The control group received a supplementation tablet of 60 mg ferro sulfate at a dose of three tablets per day, the intervention group received 60 mg iron supplementation, vitamins and minerals with a dose of one tablet per day.	Comparing Transferrin Saturation Index in the intervention and control groups.	TIBC levels or transferrin saturation increased significantly in the intervention group.	2012

deficiency anemia during pregnancy Author: Aalia Dilawar, Ghazala Qureshi, Usman Khurram, Ramsha Khan, Samina Malik Journal: Pak J Physiol 2012; 8 (1)	Lahore Hospital, Pakistan Samples : 200 people				
Title: *Preventing low birthweight through maternal multiple micronutrient supplementation: A cluster-randomized, controlled trial in Indramayu, West Java* Author: Sunawang, Budi Utomo, Adi Hidayat, Kusharisupeni, and Subarkah Journal: Food and Nutrition Bulletin, vol. 30, no. 4. 2009	Population: Pregnant women Samples: 843 pregnant women in Indramayu, Indonesia 432 people intervention group 411 control group Method: Cluster randomized community trial, Single Blind Trial	Intervention was given from gestational age 12-20 weeks then continued until 30 days postpartum. The intervention group was given multiple micronutirents based on recommendations from UNICEF / UNU / WHO. The control group was given 60 mg of iron and 0.25 mg of folic acid. Supplementation is given at a dose of 1 tablet per day.	Comparing birth size (lenght, weight, head circumference) and gestational age at delivery, micronutrient status or maternal anemia status (Hb, serum ferritin, zinc status, serum retinol), iodine concentration in urine in the intervention group and the control group.	In the intervention group the incidence of low birth weight was lower than the control group. miscarriages, stillbirths, or newborn deaths in the intervention group were lower than the control group. Serum retinol increased significantly in the intervention group. There were no significant differences in zinc status in the intervention and control groups. The iodine concentration increased in both groups. The level of maternal anemia in both groups was the same.	May 2001-September 2003

GA, gestational age; HB, hemoglobin; SF, serum ferritin; STfR; serum transferrin receptor

Table 2. Source of data on indicators of maternal and neonatal status

			Maternal status							Neonatal status		
Study	Control	Multiple micronutrients	Hemoglobin	Weight/ Height	Ferritin	Serum transferrin receptor	Zink	retinol	iodine	Gestational age /preterm	Birth size	Neonatal/Infant mortality rate
Bangladesh [12]	Iron 30 mg Folic acid 0.4 mg	Iron 30 mg Folic acid 0.4 mg 15 micronutrient[a]	v								v	v
Bangladesh [13]	Iron 60 mg Folic acid 0.4 mg	Iron 60 mg Folic acid 0.4 mg 30 mg of vitamin C 5 mg of zinc	v	v								
China [14]	Folic acid 0.4 mg	Folic acid 0.4 mg Iron 30 mg 13 micronutrient UNIMMAP[b]			v	v						
China [15]	Folic acid 0.4 mg	Folic acid 1 mg 22 micronutrients[c]	v							v	v	v
Pakistan [16]	Iron 60 mg	Iron 60 mg multivitamin and mineral			v	v						
Indonesia [17]	Iron 60 mg Folic acid 0.25 mg	Iron 30 mg 15 multiple micronutrient UNICEF/UNU/WHO	v		v		v	v	v	v	v	v

a. 30 mg of iron (fumarate); 400 ug of folic acid, 800 ug of RE vitamin A (retinyl acetate); 200 IU of vitamin D (D3); 10 mg of vitamin E (tocopherol acetate); 70 mg of vitamin C; 1.4 mg of vitamin B_1 (thiamine mononitrate); 1.4 mg of vitamin B_2 (riboflavin); 18 mg of niacin; 1.9 mg of vitamin B_6 (pyridoxine hydrochloride); 2.6 ug of vitamin B_{12} (cyanocobalamin); 15 mg of zinc (sulphate); 2 mg of copper (sulphate); 65 ug of selenium (sodium selenite); and 150 ug of iodine (potassium iodine).
b. The United Nations International Multiple Micronutrient Preparation (UNIMMAP) supplement contains 15 mg of zinc; 2 mg of copper; 65 ug of selenium; 150 ug of iodine; 800 ug of RE of vitamin A; 1.4 mg of vitamin B1; 1.4 mg of vitamin B2; 18 mg of niacin; 1.9 mg of vitamin B6; 2.6 mg of vitamin B12; 70 mg of vitamin C; 200 IU of vitamin D; 10 mg of vitamin E.
c. 450 ug Vitamin A; 900 ug beta carotene; 6,25 ug of Vitamin D; 30 mg of Vitamin E; 3 mg of Vitamin B_1; 3,4 mg of Vitamin B_2; 10 mg of Vitamin of B_6; 12 ug of Vitamin B_{12}; 100 mg of Vitamin C; 30 mcg of biotin; 1 mg of folic acid, 20 mg of nicotinamide; 10 mg of asam panthotenic acid; 150 ug of iodin; 25 ug of Mo; 250 ug of Ca; 25 mg of Zn; 60 mg of Fe; 20 mg of Cu; 250 ug of Cr; 5 mg of Mn; 50 mg of Mg; 250 ug of Se.

According to research conducted in Bangladesh with the title "Effect of prenatal micronutrient and early food supplementation on maternal hemoglobin, Birth Weight, and Infant mortality among children in Bangladesh", with a total sample of 4436 pregnant women. This study included inclusion criteria, namely the population living in villages in Bangladesh who received health services from the International Center for Diarrheal Disease Research, Bangladesh (ICDDR, B), pregnant women with less than 14 weeks' gestation who were examined using USG, did not have severe illness, and willing to be a sample in the study. The purpose of this study was to see whether prenatal multi micronutrient supplementation (MMS) and food supplementation would increase maternal hemoglobin, infant birth weight and reduce infant mortality rate. The sample group in this study was divided into 2 large groups, namely in the first group the administration of supplementation was carried out at 9 weeks gestation while the second group was given supplementation at 20 weeks' gestation. In each group 3 types of supplementation were given, namely 30 mg iron + 0.4 folic acid, 60 mg iron + 0.4 folic acid, and 15 micronutrients + 30 mg iron + 0.4 mg folic acid with daily doses combined with food supplement (608 kcal, 6 days a week). The intervention is given until 30 weeks' gestation. The researchers compared maternal hemoglobin levels, infant weight at birth and infant mortality in 6 groups. Measurements are taken at 30 weeks' gestation. The results of the study based on maternal hemoglobin levels were no difference in mean hemoglobin levels in the group given micronutrients [12].

According to research conducted entitled "*Relative efficacy of micronutrient powder versus iron-folic acid controlling women anemia in the second trimester of pregnancy*" with a sample of 478 pregnant women in the Kalijan region, Bangladesh. The sampling method uses a cluster randomized noninferiority trial. The purpose of this research is to compare the effectiveness of powder micronutrient administration in the intervention and iron-folic acid supplementation group in the control group. The researchers compared the hemoglobin level, height, and maternal weight at 32 weeks' gestation. This study has inclusion criteria, namely pregnant women with 14-22 weeks gestational age. Interventions in micronutrient powder (60 mg iron, 0.4 mg folic acid, 30 mg vitamin C, and 5 mg zinc) were given in the intervention group, while in the control group supplemented with 60 mg iron + 0.4 mg folic acid. The intervention was given since the first time the data was collected until 32 weeks' gestation at a dose of 1 tablet per day. The data collected was in the form of demographic data, height, body weight and maternal hemoglobin level at 24, 28 and 32 weeks' gestation. The hemoglobin level measuring instrument used is a hemoglobin photometer (HemoCue). The results of the study mention micronutrient powder as effective as iron-folic acid supplementation in controlling moderate to severe anemia in pregnant women [13].

According to a study entitled "*Iron Containing Micronutrient Supplementation of Chinese Women with No or Mild Anemia during Pregnancy Improved Iron Perinatal Amenia*" with a sample of 834 pregnant women with Randomized, Double Blind Trial. The aim of this study was to describe iron status as seen from the indicator [serum ferritin (SF), serum transferrin receptor (sTfR), and body iron (BI)] before and after micronutrient supplementation during pregnancy. This research has inclusion criteria, which are under 20 weeks with maternal hemoglobin level> 100 g / L. Samples were randomly grouped into 3 groups, the first group (control) was given 0.4 mg folic acid, the second group was given 30 mg iron + 0.4 mg folic acid, and the third group was given 30 mg iron + 0.4 folic acid + 13 micronurient with a daily dose. The researcher measured using deficiency indicators such as ferritin serum, sTfR, and BI which were carried out during the pre-intervention period and at 28-32 weeks' gestation. The results of the study state that based on the three iron indicators in the IFA and MM group, the prevalence of ID was significantly lower at 28-32 weeks gestational age compared to the FA group [14].

Next research entitled "*Multi-micronutrient supplementation for maternal anemia and adverse birth outcomes in a high-altitude area: a prospective Tibetan study in rural Tibet of China*" and involved 1149 pregnant women with <24 weeks gestation. The population lives in 2 villages in the highlands in China (Qushui and Dazi in Lhasa). This study aims to investigate the effectiveness of daily antenatal supplementation with several micronutrients (MMN) compared to folic acid (FA) against anemia in pregnant women and their baby's health. The sample in this study was divided into two groups that were supplemented with 22 micronutrients compared with 0.4 mg of folic acid. Supplementation is given at a dose of one tablet per day, tablets are consumed after meals, and repeated every day. The researchers then measured the mother's hemoglobin level and concluded that there was a significant increase in hemoglobin with MMN supplements compared with FA supplements in the third trimester [15].

Another study titled "*Effect of Iron With Mineral and Multivitamin Supplementation On Transfer Saturation Index In Iron Deficiency Anemia During Pregnancy*" involving 200 samples of primigravida pregnant women with Hb levels <11.0 gm / dl with gestational age between 14 and 18 weeks who examined themselves at the Midwifery Outpatient Service at Lahore Hospital. The purpose of this study was to find out whether supplementation Oral iron (three times a day) will affect Transferrin Saturation Index as effectively as supplementation with combination therapy (iron with multi vitamins and minerals) in pregnant women with iron deficiency anemia. The first group consisted of 100 women who received supplementary tablets containing 60 mg of iron and vitamins and minerals with a dose of one tablet per day. In the second group consisted of 100 women who received 60 mg of ferro sulfate at a dose of three tablets per day. Serum iron levels and total iron binding capacity (TIBC) are estimated by the standard kit method. The level of hematological parameters was compared before and after therapy at weeks 14 to 18 and weeks 36, respectively. TIBC levels increased significantly (p <0.001) after combination therapy. The researchers concluded that iron supplementation with multivitamins and minerals had a role in increasing TIBC in pregnant women with iron-deficiency anemia [16].

The study entitled "*Preventing low birthweight through maternal multiple micronutrient supplementation: A cluster-randomized, controlled trial in Indramayu, West Java*", 843 pregnant women in Indramayu, Indonesia. The purpose of this study was to compare the birth size and anemia status of pregnant women in the intervention group and the control group. In the intervention group multiple micronutrients were supplemented based on UNICEF / UNU / WHO recommendations, while the control group was supplemented with 60 mg ferosus sulfate and 0.25 mg folic acid. The supplementation dose is given one tablet per day for 5 days a week. Provision of supplementation is carried out during pregnancy and continues until 30 days postpartum. The use of multivitamin supplements among pregnant women is as effective as iron-folate acid in improving anemia status [17].

DISCUSSION

All articles that were sampled in this study were the results of experimental research. The population used was the youngest pregnant women, 9 weeks [12] up to 22 weeks [13]. The intervention is carried out maximally at 32 weeks' gestation [13] [14]. The total sample used in this study has a range of 200-4436 people. The samples are grouped randomly. This is important so that research results can be generalized and to reduce bias in research. Mikonutrien plays a big and important role in pregnancy generally given as a supplement [10]. Multi micronutrient administration in the sample consists of iron, folic acid, vitamins A, D, E, C, Vitamins B1, B2, B6, B12, niacin, zinc, iron sulfate, selenium, iodine, biotin, nicotiamide, Panthotenic Acid, Calcium , Magnesium, Manganese.

The inclusion and exclusion criteria used vary greatly according to the objectives of each study. Researchers have considered the sample criteria not to influence the results of the study. The majority of the studies provided only multi micronutrients or combined with iron and / or folic acid in the intervention group, while in the control group iron and / or folic acid were given. The dependent variable in this literature study varied, namely maternal anemia status which was seen based on hemoglobin level, serum ferritin, sTfR, serum iron level, and Total Iron Binding Capacity (TIBC), body iron, body weight and maternal height, and baby's condition, namely weight the body of the baby at birth and the incidence of infant mortality.

Multiple Micronutrients and Maternal Status

Based on the results of the research obtained, measurements carried out in the third trimester are known to only one study mentioning micronurient administration in pregnant women can reduce the prevalence of anemia (AOR: 0.63; 95% CI, 0.45-0.88; P = 0.007) and increase hemoglobin levels (mean difference : 5.18; 95% CI, 2.98-7.37 g / l; P = 0.001). Micronurient deficiencies such as vitamins and minerals indirectly play a role in carbon metabolism and synthetic DNA. Therefore, giving micronutrients to respondents can increase hemoglobin levels and reduce the prevalence of anemia. In addition, respondents have a monotonous diet so that the possibility of micronurient deficiencies is more likely [15]. One study showed that there was an increase in transferrin saturation in the group given iron 60 mg ferrous sulfate with a dose of three tablets a day (P <0.001) [16].

Other studies suggest that the administration of micronutrients did not show a significant difference compared to supplementation of iron and / or iron-folic acid. This is in line with the results of the study [5] [18] giving multiple micronutrient supplements did not show significant benefits in pregnant women with anemia when compared with iron-folate supplements. There was no difference in the hematologic state of the mother given multiple micronutrients compared with mothers who were given iron alone or a combination of iron with folic acid in the third trimester (RR = 1.03 [95% CI, 0.94-1.12]). Micronutrient administration has the same effect as iron-folic acid supplementation in anemic pregnant women [19].

Multiple Micronutrients and Neonatal Status

Multiple micronutrients administration in pregnant women does not have a significant effect on iron deficiency in pregnant women, but can improve the outcome produced by reducing the risk of preterm birth (AOR: 0.31 [95% CI, 0.15-0.61; P = 0.001) and reducing incidence low weight babies (AOR: 0.58; 95% CI, 0.36-0.91; P = 0.019) [15]. The results of this study are in line with other studies that mention multi micronutrient administration significantly reduces the incidence of severe low birth weight and increases the mean weight of babies [18] [20] [21]. The reduction in the risk of birth weight and preterm birth is thought to be caused by the administration of micronutrients containing vitamin A, zinc, and folic acid which play a role in fetal growth, prevention of infection, and reducing nutritional loss due to diarrhea [22].

CONCLUSION

From the study that has been conducted, it can be concluded that multi micronutrient supplementation is as good as iron-folic acid in increasing hemoglobin concentration in pregnant women with anemia and multi micronutrient supplementation has the potential to reduce preterm birth and the incidence of low birth weight babies in pregnant women with anemia.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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