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Effect of Giving MMS (Multiple Micronutrient Supplement) Tablets on Changes in Anemia Status in Pregnant Women: A Quasi-Experimental Study

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ABSTRACT

Anemia in pregnancy is a health problem which impacts the mother and fetus, includes the risk of bleeding, premature birth, and low birth weight. Data from the Indonesian Health Survey (SKI) in 2023 showed that the prevalence of anemia in Indonesia in pregnant women was 27.7%. This study aims to evaluate the effectiveness of administering MMS tablets in increasing hemoglobin levels in pregnant women. The research method used a randomized controlled study design such as *an experiment* with pre-test dan post-test with control group design. The total population of pregnant women at Telaga Biru Health Center was 204 pregnant women and total sample was 34 respondents. Respondents were pregnant women in their third trimester with a diagnosis of mild to moderate anemia, who were given MMS tablets for 30 days. Hemoglobin level data were measured before and after the intervention. The results showed Before the intervention, as many as 10 respondents (58.8%) were included in the anemia category, and only 7 respondents (41.2%) were not anemic. After the intervention, the number of pregnant women who were still anemia decreased drastically to only 2 people (11.8%), while those who were not anemic increased to 15 people (88.2%) and significant increase in hemoglobin levels after the administration of MMS with *p-value*($0.01 \leq 0.05$), indicating that MMS tablets are effective as nutritional therapy to treat anemia in pregnancy. This study confirms that giving MMS supplements can be an alternative strategy in anemia control programs in pregnant women, especially in areas with high anemia incidence.

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INTRODUCTION (CHAPTER)

Anemia in pregnant women is one of the public health problems that is still widely found, especially in developing countries (1–3). The World Health Organization (WHO) states that around 40% of pregnant women in the world experience anemia, with a higher incidence in Southeast Asia, including Indonesia (1,4,5). According to the World Health Organization (WHO), in 2023, around 35.5% of pregnant women worldwide will experience anemia. A meta-analysis covering more than 1.2 million pregnant women reported a prevalence of anemia of 36.8%, with the highest rate occurring in the third trimester of pregnancy. The highest prevalence of anemia was found in Africa (around 61.3%) and Southeast Asia (around 52.5%), indicating that anemia in pregnancy is a serious public health problem in developing countries (1).

Anemia in pregnancy can have negative impacts on both the mother and the fetus, such as fatigue, impaired fetal development, premature birth, and increased risk of maternal and infant death (6,7). The main cause of anemia in pregnant women is iron deficiency, but it is not uncommon for it to be accompanied by deficiencies in other micronutrients such as folic acid, vitamin A, vitamin B12, and zinc (7). So far, the intervention commonly used is the administration of iron (Fe) tablets, but its success is often hampered by low compliance with consumption and a lack of micronutrient components that support red blood cell formation (7,8).

The incidence of anemia in pregnant women in the first trimester of pregnancy is 20%, the second trimester is 70%, and the third trimester is 70%. This is because in the first trimester of pregnancy, the iron needed is small because menstruation occurs and fetal growth is still slow (9–11). Entering the second to third trimester, the blood volume in a woman's body will increase by 35%, this is equivalent to 450 mg of iron to produce red blood cells (12–14). Red blood cells must carry more oxygen for the fetus. Meanwhile, during childbirth, an additional 300-350 mg of iron is needed due to blood loss. Until giving birth, pregnant women need around 40 mg of iron per day or twice the requirement for non-pregnant women (14)

The hemoglobin level of pregnant women is related to the length of the baby that will be born, the higher the HB level, the longer the size of the baby that will be (15,16). Iron is very much needed during pregnancy, lack of iron can affect pregnancy such as abortion, premature birth, fetal growth retardation in the womb and easy amniotic infection). Iron deficiency causes a decrease in hemoglobin levels so that anemia occurs (17,18).

Data from the Indonesian Health Survey (SKI) in 2023 showed that the prevalence of anemia in Indonesia in pregnant women was 27.7%. When compared with the 2018 Riskesdas data, it showed a decrease of 21.2%, from 48.9% to 27.7% (19). In Gorontalo Province in 2021, the incidence of anemia in pregnant women was around 39.6%, where Boalemo was the regency with the highest incidence of anemia in pregnant women which was 16.9%, the second highest was North Gorontalo Regency at 12.1%, the third highest was Gorontalo Regency at 4.1%, the fourth was Gorontalo City at 3.4%, and Bone Bolango Regency was the fifth highest at 1.9% and finally Pohuwato Regency at 1.2%.

One of the government's efforts to overcome anemia in women of childbearing age and pregnant women is through a program that provide Fe tablets. Each Fe tablet contains 200 mg of ferrous

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sulfate and 0.25 mg of folic acid or equivalent to 60 mg of iron (20,21). Fe tablets have long been used as the main intervention in treating anemia in pregnant women, but their effectiveness is often limited because they only address iron and folic acid deficiencies, while anemia in pregnancy is generally multifactorial (21,22). As a more comprehensive solution, Multiple Micronutrient Supplement (MMS) offers advantages with a content of 15 essential micronutrients that support hemoglobin formation, energy metabolism, and overall pregnancy health (23)). Based on scientific evidence and WHO recommendations, MMS administration has been proven to be more effective in increasing hemoglobin levels, reducing the risk of anemia, and improving pregnancy outcomes compared to single Fe tablets, so it is worthy of consideration as the main alternative in pregnancy supplementation programs, especially in areas with a high prevalence of anemia and malnutrition (23,24).

As an alternative and innovative effort, Multiple Micronutrient Supplement (MMS) supplementation began to be recommended by WHO in 2020 as a potential intervention to replace single Fe tablets in pregnant women. MMS contains iron, folic acid, and 13 other important micronutrients that play a role in the formation of hemoglobin and body metabolism (25,26). Several studies have shown that MMS administration is more effective in increasing hemoglobin levels, reducing the incidence of anemia, and improving the overall nutritional status in pregnant women.

In addition, adequate intake of essential vitamins and minerals (micronutrients) is essential during pregnancy for maternal health and fetal development. Inadequate nutrient intake before and during pregnancy, coupled with increased metabolic needs during pregnancy, can result in individuals suffering from one more micronutrient deficiencies, especially in low- and middle-income countries (27,28). Micronutrients are essential for pregnant women for healthy development, disease prevention, and well-being. Although only needed in small amounts, micronutrients are not produced by the body, so they must be obtained from food or supplements. The MMS tablet formula contains 15 micronutrients to support a healthy pregnancy (Tuncalp et al., 2022). MMS tablets are not just supplements, but strategic nutritional interventions that are important for protecting maternal and fetal health during pregnancy. With a more complete composition and broader effects than regular Fe tablets, MMS deserves to be part of the standard of antenatal care, especially in areas with a high prevalence of anemia and malnutrition (29).
However, the application of MMS in antenatal care is still limited and uneven in various regions, so further research is needed to see its effects directly on anemia status. Therefore, this study was conducted to determine the effect of MMS administration on changes in anemia status in pregnant women using a quasi-experimental design (quasi-experimental).The results of this study are expected to be the basis for consideration in developing nutritional supplementation policies during pregnancy.

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METHOD

Type of Research

This is a quantitative research using Quasi Experimental design called Equivalent Pretest-Postest With Control Group Design. This research was conducted on January 03rd of 2024 to February 03rd of 2024 at the Telaga Biru Health Center.

Population and Sample

The sampling technique used was purposive sampling, which is determining the sample to be taken based on inclusion and exclusion criteria. Inclusion criteria are 1) pregnant women in the third trimester, 2) pregnant women who experience mild and moderate anemia, 3) pregnant women who only consume Fe tablets (without consuming any vitamins), 4) pregnant women who are willing to be respondents, and 5) pregnant women who are registered in the Telaga Biru Health Center work area. Meanwhile, exclusion criteria are 1) pregnant women with anemia who experience complications and complications in pregnancy, 2) pregnant women who are not compliant in consuming MMS tablets according to recommendations (intervention group) and those who are not compliant in consuming Fe tablets according to recommendations (control group). The total population of pregnant women at Telaga Biru Health Center was 204 pregnant women, with the number of pregnant women in the third trimester add up to 53 pregnant women. After that, a sampling technique was carried out according to the inclusion and exclusion criteria, hence the 36 respondents were obtained consisting of 19 subjects in intervention grous and 17 in control group. However, there were 2 respondents in the intervention group who drop out, so that the total respondents analyzed were 17 pregnant women in the intervention group and 17 pregnant women in the control group.

Data Collection

The HB measurement tool used was a digital hemoglobin device to measure hemoglobin levels in pregnant women before and after the intervention.There is also MMS tablets given to the intervention group as many as 30 tablets for 30 days consumed 1 tablet/day. In administering MMS tablets, researchers will be assisted by health cadres to fill out the compliance control sheet for consuming MMS tablets. In addition to the two instruments above, the instruments used are the MMS consumption control sheet and the Hb level examination result sheet for pregnant women. This is done to ensure that the intervention given is appropriate and controlled. In addition, researchers made a whatsapp group as a medium of communication between researchers and respondents.

Intervention

MMS from UNIMMAP, KIRK (Humanitarian). MMS tablets amount is 180 tablets each containing the following composition iron, folic acid, vitamin A, vitamin B1, B2, B6, B12, vitamin C, vitamin D, vitamin E, niacin, zinc, copper, selenium, and iodine. MMS tablets were given to the intervention group with a dose of 1 tablet per day and consumed by pregnant women with anemia for 30 days, then the hemoglobin levels of pregnant women with anemia were measured using a digital hemoglobin device.

Procedure

First, the researcher gave informed consent to the pregnant women with anemia as an agreement to administer MMS tablets to the intervention group after being given education regarding the

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administration of MMS tablets. Furthermore, the pregnant women with anemia were given 30 MMS tablets, with a dosage of 1 tablet/day while the control group was given Fe tablets with a dosage of 1 tablet/day.

Data Analysis and Processing

This study uses Wilcoxon and Man-Whitney statistical tests with a confidence interval of 95% for $\alpha = 0.05$. Testing the difference between two paired or repeated measurements in the same group, namely the hemoglobin level before (pre-test) and after (post-test) administration of MMS tablets in the intervention group.

RESULTS

Respondent Characteristics

Table 1. Distribution of respondents based on respondent characteristics in the Telaga Biru Health Center Work Area (n=17)

Characteristic	Groups			
	Intervention (n=17)	Frequency (%)	Control (n=17)	Frequency (%)
Age				
<20	1	5.8	0	0
20-35	14	82.4	15	88.2
>35	2	11.8	2	11.8
Education				
High	3	17.65	3	17.65
Low	14	82.35	14	82.35
Occupation				
House Wife	13	76.5	12	70.6
Private Sector	4	23.5	3	17.6
Government Officer	0	0	2	11.8
Parity				
Primipara	8	47.1	7	41.2
Multipara	6	35.3	5	29.4
Grandemultipara	3	17.6	5	29.4
LILA				
≤23.5	3	17.6	3	17.6

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>23.5	14	82.4	14	82.4
IMT				
Very Thin	1	5.9	1	5.9
Thin	0	0	2	11.8
Normal	7	41.2	6	35.3
Overweight	4	5.88	3	17.6
Obese	5	29.41	5	29.4

Based on the respondent characteristics table, it can be seen that both groups, both intervention and control, have relatively homogeneous or comparable characteristics, thus supporting the validity of the intervention comparison. The majority of respondents in both groups were aged 20–35 years, had low education, and were unemployed. Most were primipara and multipara, with fairly good nutritional status based on LILA and BMI. The characteristics between the intervention and control groups were relatively comparable, so that the intervention could be assessed more objectively.

Univariate Analysis

Table. 2 Distribution of respondents based on pretest and posttest hemoglobin levels in the intervention group for pregnant women

Hb (gr/dL)	***Pretest***		**Hb (gr/dL)**	***Posttest***	
	N	%		N	%
Anemia	10	58,8	Anemia	2	11,8
No Anemia	7	41,2	No Anemia	15	88,2
Total	17	100	Total	17	100

The data in Table 2 shows that there was a significant increase in the hemoglobin status of pregnant women after the administration of MMS tablets, seen from the number of pregnant women who experienced improvement in anemia status. Before the intervention, as many as 10 respondents (58.8%) were included in the anemia category, and only 7 respondents (41.2%) were not anemic. After the intervention, the number of pregnant women who were still anemic decreased drastically to only 2 people (11.8%), while those who were not anemic increased to 15 people (88.2%).

Table. 3 Distribution of respondents based on pretest and posttest hemoglobin levels in the control group of pregnant women

Hemoglobin (gr/dL)	***Pretest***		**Hemoglobin (gr/dL)**	***Posttest***	
	N	%		N	%
Anemia	4	23,5	Normal	7	41,2

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No Anemia	13	76,5	No Normal	10	58,8
Total	17	100	Total	17	100

The data in Table 3 shows that in the control group, changes in anemia status in pregnant women did not show significant improvement. Before the intervention, there were 4 pregnant women (23.5%) who had anemia, and 13 mothers (76.5%) who were not anemic. However, after the intervention, the number of mothers with abnormal Hb levels actually increased to 10 people (58.8%), while those in the normal category were only 7 people (41.2%).

Bivariate Analysis

Table 4. Pretest and posttest hemoglobin levels in the intervention group of pregnant women

	Hemoglobin Percentage			
	(Mean±SD)	**Mean Difference**	**(Minimum-maximum)**	***p-value***
Pretest	10,612±1,2149	1,682	8,9-12,1	0,001
Postest	12,294±0,9148		10,6-13,8	

The results showed a statistically significant increase in hemoglobin (Hb) levels in pregnant women with anemia after receiving intervention in the form of MMS tablets. Before the intervention, the average Hb level was at 10.612 ± 1.2149 g/dL, while after the intervention it increased to 12.294 ± 0.9148 g/dL, with a mean difference of 1.682 g/dL. The range of Hb levels also showed improvement, from 8.9–12.1 g/dL before the intervention to 10.6–13.8 g/dL afterward. These results are supported by statistical tests showing a p value = 0.001, which means the increase is very statistically significant ($p \leq 0.05$).

Table 5. Pretest and posttest hemoglobin levels in the control group of pregnant women.

	Hemoglobin Perecentage			
	(Mean±SD)	**Mean Defference**	**(Minimum-maximum)**	***p-value***
Pretest	11,553±0,8875	-0,277	9,8-13,1	0,214
Posttest	11,276±0,8757		9,4-12,8	

The results showed that there was a significant difference in hemoglobin (Hb) levels before and after the intervention between the group receiving MMS tablets and the control group. In the intervention group, Hb levels increased from 10.612 ± 1.2149 g/dL to 12.294 ± 0.9148 g/dL, with a mean difference of 1.682 g/dL and a p value = 0.001, indicating a statistically significant increase ($p \leq 0.05$). Meanwhile, in the control group, Hb levels actually decreased slightly from 11.553 ± 0.8875 g/dL to 11.276 ± 0.8757 g/dL, with a mean difference of -0.277 g/dL and a p value = 0.214, indicating that the difference was not statistically significant

Table 6. Differences in Hemoglobin Levels in pregnant women after being given MMS Tablets in the intervention group and leaflets in the control group.

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Posttest	(Mean±SD)	(Minimum-maximum)	*p-value*
Intervention and Control Groups	11,785±1,0219	9,9-13,8	0,004

In the intervention group that received MMS tablets, Hb levels increased significantly from 10.612 ± 1.2149 g/dL to 12.294 ± 0.9148 g/dL, with a mean difference of 1.682 g/dL and a p value = 0.001. In contrast, in the control group that only received education through leaflets, Hb levels decreased from 11.553 ± 0.8875 g/dL to 11.276 ± 0.8757 g/dL, with a mean difference of -0.277 g/dL and a p value = 0.214, which was not statistically significant.

Discussion

The results showed that giving Multiple Micronutrient Supplement (MMS) tablets significantly increased the hemoglobin levels of pregnant women with anemia. Before the intervention, as many as 10 respondents (58.8%) were included in the anemia category, and only 7 respondents (41.2%) were not anemic. After the intervention, the number of pregnant women who were still anemic decreased drastically to only 2 people (11.8%), while those who were not anemic increased to 15 people (88.2%). In the intervention group, hemoglobin levels increased from mean ± SD 10.612 ± 1.2149 to 12.294 ± 0.9148, with mean difference of 1,682 and p-value of 0.001, which indicates a statistically significant increase. In addition, the analysis of anemia status categories also showed significant changes. Before the intervention, 58.8% of pregnant women were anemia, but after the intervention, this number decreased drastically to 11.8%, and 88.2% of women were categorized as not anemic. This shows that MMS is not only effective in increasing Hb levels numerically, but also has a clinical impact in changing the anemia status of pregnant women (25,30,31). In contrast, in the control group that was only given education through leaflets, hemoglobin levels actually decreased from 11.553 ± 0.8875 to 11.276 ± 0.8757, with mean difference -0.277 and p-value 0.214, which is not statistically significant. Even in terms of category, the number of mothers with abnormal Hb levels increased from 23.5% to 58.8%. The significant difference between the two groups is supported by the results of the difference post-test, where the p-value of 0.004 shows that the hemoglobin levels of pregnant women after being given MMS were significantly higher than the control group.

This study is in line with research showing that Hb levels in the Fe and MMS tablet groups increased significantly ($p<0.001)<\alpha(0.05$) after being given MMS intervention for 90 days. The lowest percentage was in the Fe group. The results of the study showed that giving MMS tablets for 90 days can increase Hb levels in pregnant women ((29,31). Pregnant women who consumed multiple micronutrient supplements including iron and folic acid during pregnancy had a lower risk of delivering a low birth weight, preterm birth, or a small for gestational age baby (24,29,32).

MMS is a multi-micronutrient supplement formulation containing 30 mg of iron and FE tablets containing 60 mg of iron (Ida Ayu Eka Padmiari & Pande Putu Sri Sugiani, 2022). The iron content in MMS is set at 30 mg to be similar to all other nutrients, and to avoid the risk of side effects due to the presence of other micronutrients (eg vitamin A, vitamin C, and riboflavin) is expected to

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increase the absorption or utilization of iron compared to iron in FE tablets alone (29,31). MMS replaces Fe tablets for pregnant women so that pregnant women should not consume MMS and Fe tablets simultaneously or on the same day (31,33). This can cause higher iron which can cause side effects such as constipation, vomiting, nausea and diarrhea (34,35). Consuming MMS during pregnancy can meet increased nutritional needs. Adequate intake of essential vitamins and minerals (micronutrients) is essential during pregnancy for maternal health and fetal development (35). Insufficient nutritional intake before and during pregnancy, coupled with increased metabolic needs during pregnancy, can result in individuals suffering from one or more micronutrient deficiencies resulting in unmet nutritional needs, one of which causes anemia (36,37)

MMS had a greater impact in reducing the risk of low birth weight (RR 0.81; 95%CI 0.74–0.89) and small birth weight for gestational age according to Oken standards (0.92, 0.87–0.97). MMS(Multiple Miconutrient Supplement) reduce the risk of preterm and premature births to a greater extent in pregnant women weighing less than 18.5 kg/m2 compared to pregnant women who are not underweight (38–40). The researcher's assumption is that MMS tablets can be used as an alternative to increase hemoglobin levels in pregnant women without side effects. Compared to Fe tablets with side effects, pregnant women prefer MMS tablets, in addition, during consuming MMS tablets 1 tab/night for 30 days, one of the positive effects provides a comfortable and deep sleep at night, better appetite and a fresher body (25,41). The decrease in Hemoglobin which is a protein in red blood cells in pregnant women can be influenced by several factors including blood cell division, increased oxygen requirements in the body of pregnant women which function to carry oxygen to the nervous system, lungs, and throughout the body (13,42). The content of MMS with 15 multivitamin tablets, can maximize iron absorption and meet nutritional needs during pregnancy in order to prevent maternal mortality (MMR) and infant mortality (IMR) (13,43).

MMS tablets contain iron, folic acid, vitamin A, vitamin B1, B2, B6, B12, vitamin C, vitamin D, vitamin E, niacin, zinc, copper, selenium, and iodine (44,45). Compared to regular Fe tablets (iron + folic acid, MMS has a broader benefits because it supports the hematopoiesis process, increases iron absorption, and improves the mother's nutritional status in general. Providing MMS during pregnancy is an evidence-based nutritional intervention that is superior to single Fe-folate supplements, because it is able to overcome anemia multi-factorially and improve the quality of pregnancy and delivery outcomes (46). This strategy is very important to implement in the antenatal care system, especially in areas with a high prevalence of anemia and micronutrient deficiencies. Considering the complexity of nutritional needs of pregnant women, MMS is considered more appropriate as a nutritional intervention because it is able to address various micronutrient deficiencies that occur simultaneously, especially in pregnant women with low nutritional status or limited socioeconomic conditions ((31,47). A meta-analysis study found that pregnant women who consumed MMS had a lower risk of anemia compared to those who only received iron and folic acid supplements. Similarly, a study by (29) showed that giving MMS during pregnancy increased hemoglobin levels and significantly reduced the prevalence of anemia, without increasing side effects.

Limitations

The limitations of this study are that the number of samples used is still relatively small and the intervention period is only one month.

Conclusion

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Administration of Multiple Micronutrient Supplement (MMS) tablets significantly increased hemoglobin levels in pregnant women with anemia. It was proven that there was an increase in the average hemoglobin level from 10.612 ± 1.2149 g/dL to 12.294 ± 0.9148 g/dL after the intervention, with a p value ≤ 0.05 indicating a significant difference. In contrast, the control group that was only given Fe tablets did not show a significant increase. This proves that MMS is more effective than non-nutritional interventions in improving anemia status in pregnant women

Author Contributions

All authors contributed actively throughout the entire research and publication process. DNOK and LS were responsible for drafting and finalizing the manuscript, while FM contributed to data analysis and conducted fieldwork at the Public Health Center. All authors approved the final version of the manuscript and were fully involved in the development of this research article

Conflict of interest

All authors declare no conflict of interest in this research.

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