International Journal Publishing
INFLUENCE: International Journal of Science Review
Volume 5, No. 2, 2023
https://influence-journal.com/index.php/influence/index

# Efficacy of Macro and Micronutrient Interventions in Adolescent Nutritional Status: A Systematic Review

**Sulfianti[1], Lina Fitriani[2], Hasnidar[3], Mustar[4], Damai Yanti[5]**
*[1,3,4]Universitas Sipatokkong Mambo, Indonesia*
*[2]Universitas Mega Buana, Indonesia*
*[5]STIkes Budi Luhur Cimahi, Indonesia*
*Email: sulfianti0712@gmail.com*

Academic Editor: Nguyen Ngoc Anh


**Abstract.** The authors conducted a systematic review of adolescents receiving a macronutrient (iron, zinc) intervention compared to a multi-micronutrient intervention to investigate their efficacy on nutritional status. Systematic searches were conducted in four database sources—Science Direct, ProQuest, EBSCO, and Google Scholar. A PICO worksheet was used to define keywords, including 1) Patient/Problem: Preconception for adolescent OR girl student, 2) Intervention: Iron and zinc OR Fe and Zn OR macronutrients, 3) Comparison: Multi-micronutrient, and 4) Outcome: Nutritional status. Inclusion criteria included female adolescents aged 9–24 years and English and Indonesian articles published from 2013 to 2020. The risk of bias was assessed by minimizing four potential sources of bias: sample selection, research design, control of confounding variables, and data collection techniques. Result: 10 relevant studies discussing iron, zinc, and multi-micronutrient supplements for adolescents were identified. Iron and zinc interventions are efficacious in preventing anemia, enhancing hemoglobin concentration, improving body mass index, and reducing the risk of low birth weight and preeclampsia for women in the preconception phase. The multi-micronutrient intervention has similar efficacy, but it can better affect the maternal immune response and the production of the human placental lactogen hormone, which ultimately increases placental weight and birth weight while lowering the risk of abortion and prematurity. Conclusion: Iron, zinc, and multi-micronutrient interventions play a pivotal role in improving the nutritional status of adolescents in preparing the preconception phase because they provide positive benefits and can prevent nutritional deficiencies before pregnancy, during pregnancy, and after delivery.

***Keywords:*** *Iron, Zinc, Multi-micronutrient, Adolescent Nutritional Status.*

## A. INTRODUCTION

Nutrition is one of the critical factors in the growth and development process of adolescents. Nutrition is required to achieve adolescents' full developmental potential. In Southeast Asia, one in four women experiences anemia due to nutritional deficiencies, which increases the risk of maternal and paternal death (Nguyen et al., 2016; Bexter et al., 2018). Adequate nutrition can affect the next generation's reproduction. Therefore, the need for adequate nutrition during puberty, particularly for female adolescents, is essential. This is because the nutritional status of women in the preconception phase may affect the growth and development of the fetus.

The nutritional status of women during the preconception period affects the prospective mother's pregnancy readiness because it can affect their pregnancy later. Women who are malnourished during the preconception phase have a 7-fold risk of their child experiencing stunting, 11 times more likely to be underweight, and 12 times more vulnerable to wasting compared to women with an adequate nutritional status (Prabandari et al., 2018; Swain et al., 2021).

The provision of nutrients such as iron and zinc is one of the interventions to prevent anemia in female adolescents during the preconception phase. The World Health Organization

recommends women of reproductive age consume iron supplements intermittently (WHO, 2011; Tofail et al., 2008)). Zinc consumption may increase the concentration of zinc in the blood, which plays a role in the implantation process. Zinc also helps the remodeling process of arterial blood vessels and forms decidual tissue integrity during pregnancy (Sumarni, 2017; Dhaded et al., 2020).

In addition, a multi-micronutrient (MMN) intervention has been known to reduce the risk of pregnancy complications. Micronutrient deficiency in adolescents is significantly associated with the risk of reproductive disorders, such as structural defects in the fetus, infertility, and long-term diseases (Muqni, 2013; Guodet et al., 2018). Adolescents who experience nutritional deficiency can experience anemia and hemoglobin deficiency to the point of disrupting pregnancy outcomes, such as a low birth weight, preterm birth, intrauterine growth restriction, prematurity, preeclampsia, disability, and an increased risk of fetal death (Nguyen, 2016; Ramakrishnan, 2020).

The importance of iron, zinc and multi-micronutrient interventions in the nutritional status of female adolescents is the background of this study. This study aims to investigate the efficacy of macronutrient interventions, especially iron and zinc, compared to multi-micronutrient interventions in the nutritional status of female adolescents.

## B. METHOD

This study used a systematic review method with a comprehensive narrative analysis approach in describing iron, zinc, and another multi-micronutrient intervention on the nutritional status of female adolescents. This study follows the Preferred Reporting Items for Systematic Review and Meta-Analyses with (PRISMA) checklist (Page, 2021; von Slmuth et al., 2021).

This article discusses the effectiveness of macro and micronutrients interventions in adolescent nutritional status. Some minerals such as iron and zinc as well as several other micronutrients are effective in preventing anemia, plays an important role in increasing the concentration of hemoglobin in the blood, improving the body's mass index and reducing the risk of LBW and the risk of preeclampsia in women who are in the preconception phase. Nutritional interventions during preconceptions great for preventing malnutrition. The provision of macro and micronutrient supplements can also be given during the premarital program and through family planning services.

### 1. Selection Criteria

The inclusion criteria in literature search included a) cross-sectional study, randomized control trial (RCT), descriptive study, descriptive survey, systematic review, meta-analysis, and other studies relevant to the research objectives; b) female adolescents aged 19-24 years; c) articles published between 2013 and 2020; d) articles published in English or Indonesian; e) articles in full text.

### 2. Search Strategy

Four databases, including ScienceDirect (Elsevier), ProQuest, EBSCO, and Google Scholar were used to search the articles/ studies. Using the search mode set to boolean/ phrase with because this mode allows searching for the exact phrase according to the desired destination. The search keywords used the PICO Worksheet, including a) Patient/Problem Patient: Pre-Conception for adolescent OR girl student; b) Intervention: Iron and zinc OR Fe and Zn OR Macronutrient; c) Comparison: Multi-micronutrient; d) Outcome: Nutritional Status.

### 3. Data Extraction

Data of the included studies were extracted into a template containing the following elements: a) research database; b) author; c) research objectives; d) research methods; e) research results; and f) conclusion.

### 4. Risk of Bias Assessment

The risk of bias was assessed by minimizing four potential sources of bias: sample selection, research design, control of confounding variables, and data collection techniques. The bias risk assessment aimed to maintain the quality of the research.

## C. RESULT AND DISCUSSION

A total of 250 articles were identified from databases, and 35 articles were eligible for inclusion in this review (Figure 1). Hospitalized adolescents (15 papers) and adolescents with chronic diseases (10 papers) were excluded. Hence, only ten articles were included in the review.

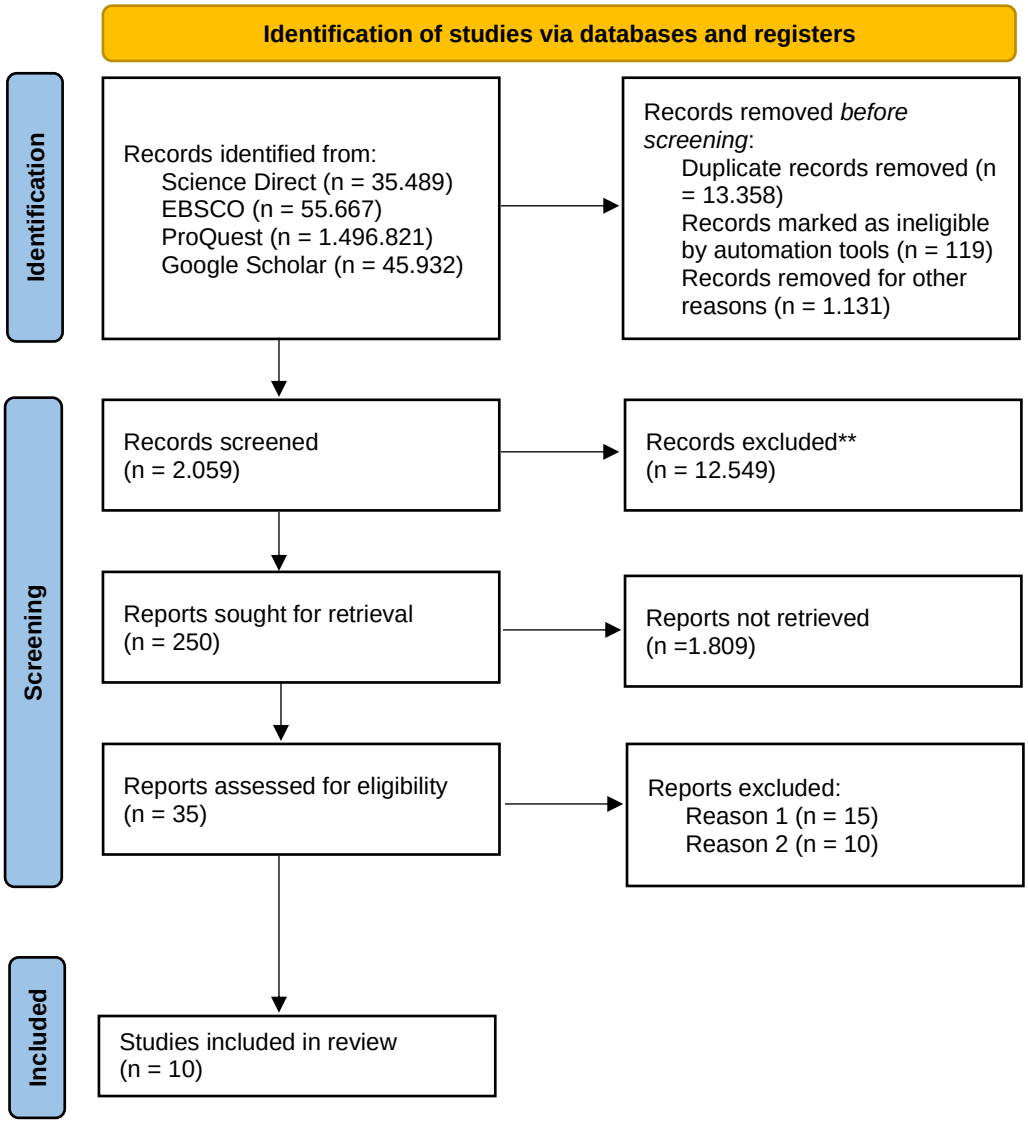


**Figure 1. Flowchart of the systematic search in the databases using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework (2020)**

## 1. Characteristics of the Study

This review included ten articles published from 2013 to 2020. The types of the included studies were: systematic review and/or meta-analysis (Salam et al., 2016; Salam et al., 2020; Stephenson et al., 2018); narrative review, letters, and opinions (Sumarni, 2017; Bhutta et al., 2017; Sumarni, 2017); randomized control trial (Nguyen et al., 2016; Bexter et al., 2018); and nested-retrospective cohort (Wijayanti et al., 2016). Most of the studies targeted the pre-conceptional adolescent population, and one study targeted the pregnant adolescent population. All studies synthesized MMNs, and six studies discussed macronutrients. The characteristics of the included studies are presented in Table 1.

**Table 1. Characteristics of the Study**

| Author | Type of study | Participant/paper | Setting | Specific intervention | |
|---|---|---|---|---|---|
| | | | | Macro-nutrient | Micro-nutrient |
| Salam et al. (2020) | Systematic review dan meta-analysis | 15 research paper | - | √ | √ |
| Stephenson et al. (2018) | Meta-analysis | 14.844 data from ALSWH & 509 data from UK NDNS RP | ALSWH & UK NDNS RP | √ | √ |
| Salam et al. (2016) | Systematic review dan meta-analysis | 31 research paper | - | - | √ |
| Baxter et al. (2018) | Cluster-randomized trial & MaPPS Trial | 78,000 female adolescents aged 15–24 years | Matiari district in Sindh province, Pakistan | √ | √ |
| Dijkhuizen et al. (2019) | Narrative review | - | Southeast Asia | - | √ |
| Bhutta et al. (2017) | Letters, Opinions | - | LMICs | - | √ |
| Nguyen et al. (2016) | Randomized control trial | 5011 Vietnamese women | Rural Vietnam | √ | √ |
| Wijayanti & Sumarni (2016) | Observational analytics with a nested-retrospective cohort approach | 60 adolescents | Probolinggo regency, East Java Province, Indonesia | √ | √ |
| Muqni (Muqni, 2013) | Letters, Opinions | - | Indonesia | √ | √ |
| Sumarmi & Sumarmi (2017) | Letters, Opinions | - | Indonesia | - | √ |

Abbreviation: MaPPS (The Matiari emPowerment and Preconception Supplementation); ALSWH (The Australian Longitudinal Study on Women's Health); UK NDNS RP (National diet and Nutrition Survey Rolling Program); LMICs (Low- and middle-income countries)

## 2. Risk of Bias

The included studies were assessed for risk of bias. Review Manager software was used to assess the systematic reviews and meta-analysis studies (Curtis et al., 2016; Dreger et al., 2012)) and the Cochrane risk-of-bias assessment tool was used for the randomized control trials *Carrion et al., 2019; Cho et al., 2019).

## 3. Efficacy of Macro and Micronutrient Interventions

All included studies concluded the efficacy of macro and micronutrient interventions for adolescents during preconception and pregnancy (Table 2).

**Table 2. Efficacy of Macro and Micronutrient Interventions**

| Author | Efficacy of Macro and Micronutrient Interventions |
|---|---|
| Salam et al. (2020) | Iron and zinc interventions increased serum levels of iron and zinc in the blood to prevent anemia. Multi-micronutrition, such as vitamin D and calcium, prevented adolescents from experiencing micronutrient deficiencies in the preconception phase to prevent stunting during pregnancy later. |
| Stephenson et al. (2018) | It is important for prospective mothers and female adolescents to have adequate micronutrients during the preconception phase to meet the needs of the prospective fetus to avoid diseases that may occur during pregnancy and delivery. |
| Salam et al. (2016) | Iron and zinc interventions could prevent anemia in female adolescents in the preconception phase. This study aimed to prepare the women's health in the preconception phase, reduce the risk of low birth weight, improve fetal birth weight, prevent premature birth, and improve body mass index. |
| Baxter et al. (2018) | Multi-micronutrient interventions for female adolescents during the preconception period could improve fetal nutrition in pregnancy and provide long-term positive effects on growth and neurodevelopment in the fetus. |
| Dijkhuizen et al. (2019) | Iron and zinc interventions could improve a woman's nutritional status in the preconception phase and prevent anemia, the risk of low birth weight, and preeclampsia. Furthermore, multi-micronutrient interventions could significantly fulfill the micronutrient needs of women in the preconception phase to prevent nutritional deficiencies of the mother during pregnancy and later to the fetus. |
| Bhutta et al. (2017) | Iron and zinc interventions played an essential role in preparing the physiology of female adolescents for the conception phase. Nutritional intervention could prevent anemia and hemoglobin deficiency in the blood, which could be harmful to both the mother and the fetus. |
| Nguyen et al. (2016) | Iron interventions could significantly prevent anemia and improve hemoglobin concentration for women in the preconception phase. Multi-micronutrient interventions could also significantly fulfill the micronutrient needs of women in the preconception phase to prevent complications during pregnancy and postpartum, both for the mother and the fetus. |
| Wijayanti & Sumarni (2016) | Multi-micronutrient supplementation during pregnancy did not have an effect until the children were 16–39 months old if nutritional intake was inadequate. Low birth weight was present in the group of children of mothers who received iron-folate during pregnancy. However, there was no difference in Z-scores on the growth parameters (height/age, weight/age, and BMI/age) of children aged 16–39 months from mothers who received MMN supplements. Therefore, children should consume sufficient and various foods to fulfill their nutritional needs for optimal growth. |
| Muqni (2013) | The nutritional status of adolescents who received MMN and iron-folate was better than those who did not receive additional supplements at all. It is vital for women in the preconception phase to consume supplements, both iron-folate and MMN, to maintain good nutritional status, especially in meeting their micronutrient needs to optimize their physiological condition to prevent health disorders due to malnutrition, such as anemia, low birth weight, and postpartum bleeding. |
| Sumarmi & Sumarmi (2017) | An MMN intervention is essential to maintain the nutritional status of women in the preconception phase because insufficient nutrients during preconception is highly related to pregnancy complications, such as congenital abnormalities, prematurity, fetal growth disorders, and preeclampsia. |

Four of ten studies included in this review examined the efficacy of iron and zinc interventions on adolescent nutritional status. The remaining studies evaluated the effectiveness of MMN supplements, iron, calcium, folic acid, and vitamins A, vitamin D, and vitamin C. Iron supplements and micronutrient (folic acid) can be beneficial to enhance the hemoglobin concentration of female adolescents to prevent anemia. Multi-micronutrient including vitamin D can increase serum concentration 25(OH)D. Calcium and vitamin D can increase bone mineral density. Zinc can improve the iron concentration to improve nutritional status. This study reviewed the various benefits of macro and micronutrient interventions in

adolescents. However, the side effects of consuming excess iron and other micronutrients were not examined in the articles included in this study.

Micronutrient adequacy during the preconception period affects the mothers' ability to provide optimal nutrition. Micronutrient deficiency can be one of the factors contributing to low birth weight and developmental disorders in children. Therefore, nutritional intervention, such as specific nutrition management and sensitive nutrition during preconception in female adolescents, is pivotal to preventing malnutrition.

Evidence shows that the supplementation of macro and micronutrients during the preconception phase and pregnancy is crucial. Several studies suggested the advantages of multi-micronutrient supplementation in improving maternal and fetal health. Macro and micronutrient interventions for 2–6 months before pregnancy are beneficial to overcome the problem of low-quality pregnancy outcomes. The provision of macro and micronutrient supplements can be made through premarital programs and family planning services.

## D. CONCLUSION

The provision of iron, zinc, and other multi-micronutrients is efficacious in improving the health and nutritional status of female adolescents during the preconception period, that is, 2–6 months before pregnancy, and can prevent pregnancy complications and fetal development disorders. This study can be used as a current reference that summarizes the nutritional status of adolescents can be improved by maintaining specific macro- and micronutrient intakes.

## ACKNOWLEDGMENT

The author would like to thank Universitas Hasanuddin for facilitating access to the literature search database and the Denarya Education Center for contributing to the literature synthesis.

## AUTHOR CONTRIBUTIONS

The authors confirm contribution to the paper as follows: study conception and PICO Worksheet: LN & VH; search strategy and data extraction: LN & SN; sintesa grid: VH & SN; analysis and interpretation of results LN. All authors reviewed the results, draft manuscript preparation and approved the final version of the manuscript.

## TRANSPARENCY DECLARATION

The author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

## REFERENCES

1. Baxter, J. A. B., Wasan, Y., Soofi, S. B., Suhag, Z., & Bhutta, Z. A. (2018). Effect of life skills building education and micronutrient supplements provided from preconception versus the standard of care on low birth weight births among adolescent and young Pakistani women (15–24 years): a prospective, population-based cluster-randomized trial. *Reproductive health*, *15*(1), 1-13.
2. Baxter, J. A. B., Wasan, Y., Soofi, S. B., Suhag, Z., & Bhutta, Z. A. (2018). Feasibility and effect of life skills building education and multiple micronutrient supplements versus the standard of care on anemia among non-pregnant adolescent and young Pakistani women (15–24 years): a prospective, population-based cluster-randomized trial. *Reproductive Health*, *15*(1), 1-9.
3. Bhutta, Z. A., Lassi, Z. S., Bergeron, G., Koletzko, B., Salam, R., Diaz, A., ... & Hanson, M. (2017). Delivering an action agenda for nutrition interventions addressing adolescent

girls and young women: priorities for implementation and research. *Annals of the New York Academy of Sciences*, *1393*(1), 61-71.
4. Dhaded, S. M., Hambidge, K. M., Ali, S. A., Somannavar, M., Saleem, S., Pasha, O., ... & Krebs, N. F. (2020). Preconception nutrition intervention improved birth length and reduced stunting and wasting in newborns in South Asia: The Women First Randomized Controlled Trial. *Plos one*, *15*(1), e0218960.
5. Dijkhuizen, M. A., Greffeille, V., Roos, N., Berger, J., & Wieringa, F. T. (2019). Interventions to improve micronutrient status of women of reproductive age in Southeast Asia: a narrative review on what works, what might work, and what doesn't work. *Maternal and Child Health Journal*, *23*, 18-28.
6. Goudet, S., Murira, Z., Torlesse, H., Hatchard, J., & Busch-Hallen, J. (2018). Effectiveness of programme approaches to improve the coverage of maternal nutrition interventions in South Asia. *Maternal & child nutrition*, *14*, e12699.
7. Guideline, W. H. O. (2011). Intermittent iron and folic acid supplementation in menstruating women. *Geneva: World Health Organization*.
8. Muqni, A. D. (2013). Faktor Risiko Reproduksi Yang Berhubungan Dengan Mikronutrien Dengan Kerusakan Gen Selama Periode Periconcepsional. *Media Gizi Masy Indones*, *3*(1).
9. Nguyen, P. H., Young, M., Gonzalez-Casanova, I., Pham, H. Q., Nguyen, H., Truong, T. V., ... & Ramakrishnan, U. (2016). Impact of preconception micronutrient supplementation on anemia and iron status during pregnancy and postpartum: a randomized controlled trial in rural Vietnam. *PloS one*, *11*(12), e0167416.
10. Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., ... & Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *International journal of surgery*, *88*, 105906.
11. Prabandari, Y., Hanim, D., AR, R. C., & Indarto, D. (2016). Hubungan kurang energi kronik dan anemia pada ibu hamil dengan status gizi bayi usia 6-12 bulan di kabupaten boyolali (correlation chronic energy deficiency and anemia during pregnancy with nutritional status of infant 6–12 months in Boyolali regency). *Nutrition and Food Research*, *39*(1), 1-8.
12. Ramakrishnan, U. (2020). Nutrition education during the preconception period. In *Nutrition Education: Strategies for Improving Nutrition and Healthy Eating in Individuals and Communities* (Vol. 92, pp. 19-30). Karger Publishers.
13. Salam, R. A., Das, J. K., Irfan, O., Ahmed, W., Sheikh, S. S., & Bhutta, Z. A. (2020). Effects of preventive nutrition interventions among adolescents on health and nutritional status in low-and middle-income countries: A systematic review. *Campbell Systematic Reviews*, *16*(2), e1085.
14. Salam, R. A., Hooda, M., Das, J. K., Arshad, A., Lassi, Z. S., Middleton, P., & Bhutta, Z. A. (2016). Interventions to improve adolescent nutrition: a systematic review and meta-analysis. *Journal of Adolescent Health*, *59*(4), S29-S39.
15. Stephenson, J., Heslehurst, N., Hall, J., Schoenaker, D. A., Hutchinson, J., Cade, J. E., ... & Mishra, G. D. (2018). Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. *The Lancet*, *391*(10132), 1830-1841.
16. Sumarmi, S., & Sumarmi, S. (2017). Tinjauan Kritis intervensi multi mikronutrien pada 1000 hari pertama kehidupan. *Nutrition and Food Research*, *40*(1), 17-28.
17. Swain, D., Begum, J., & Parida, S. P. (2021). Effect of preconception care intervention on maternal nutritional status and birth outcome in a low-resource setting: Proposal for a nonrandomized controlled trial. *JMIR Research Protocols*, *10*(8), e28148.
18. Tofail, F., Persson, L. Å., El Arifeen, S., Hamadani, J. D., Mehrin, F., Ridout, D., ... & Grantham-McGregor, S. M. (2008). Effects of prenatal food and micronutrient

supplementation on infant development: a randomized trial from the Maternal and Infant Nutrition Interventions, Matlab (MINIMat) study. *The American journal of clinical nutrition*, *87*(3), 704-711.

19. von Salmuth, V., Brennan, E., Kerac, M., McGrath, M., Frison, S., & Lelijveld, N. (2021). Maternal-focused interventions to improve infant growth and nutritional status in low-middle income countries: A systematic review of reviews. *PloS one*, *16*(8), e0256188.
20. Wijayanti, R., & Sumarmi, S. (2016). Pertumbuhan anak dari ibu yang mendapat suplemen multi-mikronutrien dan anak dari ibu yang mendapat suplemen besi folat selama hamil. *The Indonesian Journal of Public Health*, *11*(1), 1-13.