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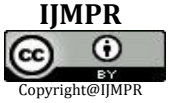

Correlation of Dha (Docosahexanoic Acid Supplementation to Underweight Pregnant Women Regarding the Inflammatory Mediator Il-6 (Interleukin-6)

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ABSTRACT

Background: Based on the Basic Health Research in 2018, the prevalence of pregnant women at risk of nutritional deficiencies in Indonesia is 17.3%. According to the Ministry of Health in 2020, out of 4,656,382 pregnant women from all provinces in Indonesia, 451,350 pregnant women were identified as at risk of nutritional deficiencies. Therefore, the percentage of pregnant women experiencing underweight in 2020 was 9.7%. Underweight conditions in pregnant women can lead to disturbances in fetal growth and development, a reduction in nutrient supply to the fetus posing a risk of low birth weight, and additionally blood flow to the fetus decrease leading tp reduced oxygenation which can cause tissue damage and trigger inflammatory reactions. Docosahexanoic Acid is an omega-3 fatty acid whose demand is high during pregnancy, essential not only for the development and growth od the fetus but also crucial for the mother. The administration of DHA supplementation is expected to improve the underweight condition and reduce the impacts resulting from this condition, especially the levels od inflammation in pregnant women.

Method: This study focuses on investigating the mediator correlation of inflammation, specifically IL-6 as a proinflammatory cytokine, with DHA supplementation for 2 months in underweight pregnant women. The research was conducted using a one group pre and post-test experimental design, involving 21 underweight pregnant women samples from Made Community Health Center in Surabaya. Result: Body weight (P = 0.000); Height (P = 0.929); BMI (P = 0.000); MUAC (P = 0.003); Systolic BP (P = 0.108); Diastolic BP (P = 0.631); Fundal height (P = 0.001); IL-6 (P = 0.008).

Conclusion: In this study, a correlation was found between DHA supplementation and the body weight, BMI, MUAC, Fundal height, and IL-6 in underweight pregnant women.

Key Words: *Correlation; DHA; Underwight; IL-6*

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INTRODUCTION

Pregnancy results in changes in the body's structure, such as the enlargement of the uterus due to the growth of the conception, the resting of the ovaries as there is no formation and maturation of new follicles, enlargement and stretching of the breasts, skin hyperpigmentation, especially in the areola area, an increase in oxygen needs by around 20%, an increase in the mother's blood volume, frequent urination caused by the pressure of enlarging uterus on the urinary bladder and vesical urinaria, as well as the appearance of the linea alba and striae livide on the mother's abdomen

Based on the Basic Health Research in 2018, the prevalence of pregnant women at risk of nutritional deficiencies in Indonesia is 17.3% [1]. According to the Ministry of Health in 2020, out of 4,656,382 pregnant women from all provinces in Indonesia, 451,350 pregnant women were identified as at risk of nutritional deficiencies. Therefore, the percentage of pregnant women experiencing underweight in 2020 was 9.7% [2].

Chronic energy deficiency (CED) in pregnant women is a condition of prolonged or chronic insufficient food intake. Pregnant women with CED experience a lack of nutrients such as calories and protein. CED in pregnant women can be identified by assessing the value of MUAC (Mid-Upper Arm Circumference) with a value of < 23, 5 cm. pregnant women with CED show a decrease in vitamin D levels and decrease in ferritin. After analyzing in ferritin in pregnant women with CED [3].

Cytokines function as regulators that mediate communication between cells, serving as messengers that caryy signal and transmit them to target cells, thereby causing changes in the course of metabolism. Interleukin-6 (IL-6) is a pleiotropic cytokine primarily produced by monocytes, lymphocytes, fibroblast, and endothelial cells. In the netural immune system response, macrophages produce IL-6 in response to PAMPs binding to recognition receptors. An

increase in its concentration correlates with tissue damage and inflammation, making it an indicator to assess the level of inflammation [4].

Docosahexaenoic acid (DHA) is an essential fatty acid derived from long chain unsaturated fatty acids, commonly referred to as omega-3 fatty acids. The body cannot synthesize DHA, so it must be obtained from food. DHA has effective anti-inflammatory effects and can reduced inflammatory by decreasing the production of inflammatory cytokines.

In normal pregnancy, there is an incrase in the mother's blood volume by approximately 30-50%, aimed at meeting the metabolic needs during fetal growth and development. In a normal pregnancy, the placenta releases remnants of trophoblast, involving processes of apoptosis and necrotic trophoblast in response to axidative stress. These debris are normaly expelled and considered foreign material that can trigger and inflammatory process within reasonable limits. Nutritional defeciencies can result in a reduction in blood flow volume to the placenta and uterus, subsequently reducing the transfer of nutrients and oxygen to the fetus, leading to oxidative stresss and tissue damage. As a consequence, the production of proinflammatory cytokines such as IL-6 tends to increase [5].

In this study, we will investigate the mediator correlation on inflammatory cytokine IL-6 with the supplemention of DHA to underweight pregnant women. We anticipate that this research will help us understand the role of DHA in improving inflammation aspects of underweight pregnancies.

METHODS

The research we conducted is of the experimental type with a cohort study using a quantitative method by examing a specific sample using specific instruments. Its objective is to determine the influence ot the given treantment and to prove or test the hypotheses that have formulates. We employed a one-group pretest-posttest design in this study, involving examinitaions before and after supplementations od the treatment. The aim od this research is to study the correlation of behavioral interventions in the form od DHA supplementation to underweight pregnant women with IL-6 levels as an inflammatory mediator within a specified time frame and in a designated district.

RESULTS

Based on the research conducted the period of June 1 to August 31, 2023, involving 21 underweight pregnant women through pre- and post-tests, the analysis of the basic characteristicits of our research sample is accordance with the following tabel.

The characteristics of the sample obtained in the study include 21 pregnant women with an age rage of 16 to 36 years and a mean age of (27.24 ± 4.48), gestational age raging from 6 to 38 weeks with a mean of (18.43 ± 9.05), weight raging from 38 to 47 kg with a mean of (42.47 ± 3.26), height raging from 144 to 161 cm with a mean of (152.3 ± 5.4), BMI raging from 17.33 to 18.80 kg/m^2 with a mean of (18.26 ± 0.31), MUAC ranging from 21.5 to 28 cm with a mean of (24.38 ± 1.619), systolic blood pressure raging from 90 to 128 mmHg with a mean of (103.76 ± 9.49), and diastolic blood pressure ranging from 59 to 80 mmHg with a mean of (66.05 ± 6.71).

Based on Table 2, differences in initial and final weight values can be observed where the final weight is higher than the initial weight, indicating a statistically significant difference. Thus, the supplementation of DHA can increase weight. For initial and final height, it can be said that there is no influence of DHA supplementation on height. In terms of initial and final BMI, the final values are higher that the initial ones, indicating a statistically significant difference, suggesting an influence od DHA supplementation. Intitial and final MUAC values show statistically significant difference, indicating an impact of DHA supplementation on MUAC. Systolic and diastolic blood pressure

DISCUSSION

DHA, or *Docosahexanoic Acid*, is a type of essential fatty acid that cannot be physiologically synthesized by the body; therefore, DHA must be obtained through dietary intake. Source of DHA include green vegetables, grains, nuts, tuna, mackerel, salmon, eggs, shrimp, meat and fish oil. The benefits of DHA involve maternal health and the development of the fetus or infant, especially during pregnancy, lactation, and infant growth. In pregnant women, DHA can improve nutritional status, prevent preeclampsia, premature birth, placental apoptosis, and the risk of low birth weight [6]. According to research by Liss Dyah and Erma Nurhayati, it is known that DHA consumption by mothers has a positive impact on fetal weight and length, where DHA can influence the nutritional status of pregnant women. The better the nutritional status, the greater the likelihood of givinf birth to a healthy baby [7]. Evaluation of the nutritional status of pregnant women can be done through anthropometric measurements, such as BMI and MUAC [8].

Based on the research conducted, significant changes were observed between pre and post-DHA supplementation regarding maternal weight (P=0,021). In a study by Salmon Siahaan [9] on nutrient supplementation for underweight pregnant women, significant weight changes were also found after dHA supplementation (P <0,001) [9]. Another study by AASP. Chandradewi [10] on the influence of supplementary food on maternal weight gain found significant changes

(P < 0.05) in maternal weight after the provision od additional food. The nutritional status of pregnant women is greatly influenced by theidietry intake; in dietry needs are not met, supplementation like DHA can be beneficial. Maternal nutritional deficiencies can significantly impact fetal growth and development, leading to low birth weight, congenital disabilities, stillbirth, and more [10]. The research by Salmon Charles and Rahajoe Imam Santosa (2021) supports our findings, where significant changes (P<0,001) in maternal weight were observed after micronutrient treatment, indicating an increase in weight after the intervention. Similar results were obtained in a study by Fitri Juliasari and Elsa Fitriana Ana [11] on the impact of providing additional food on the weight of underweight pregnant women, showing weight gain (P<0.05) in pregnant women after providing food additional. This suggests a relationship between providing food additional and weight gain [11, 12].

The body mass index or BMI is a measurement used to determine nutritional status, and the nutritional adequacy of pregnant women significantly influences the nutritional status of the developing fetus, supporting its growth and development. If the nutritional status of pregnant women is inadequate, it can lead to disruptions in the child's brain development, intelligence, shoocl performance, low birth weight and other persistent. These adverse effects can be prevented by monitoring and maintaining the nutritional status of pregnant women [13]. Improving the nutritional status of pregnant women can be achieved through the consumption of balanced nutrition, accompanied by additional food intake such as DHA supplementation, especially for underweight pregnant women. Based on our research and the data presented, a significant change (P= 0,036) was observed, indicating an increase in the BMI of underweight pregnant women after two months of DHA supplementation.

The Upper Arm Circumgerence is another methos that can be used to mesure the nutritional status of pregnant women. Measurement easly done using a MUAC tape, which is wrapped around the upper arm of the mother. This measurement can serve as a screening tool for the potential presence of poor nutrition in pregnant women. If the LILA values is <23.5 cm, it indicated malnutrition, while a values >23.5 cm suggest adequate nutrition. In a study conducted by Wahyuni (2019), it was concluded that if the MUAC values of pregnant women is >23.5cm, the likehood of giving birth to a baby with LBW is low rendah (Wahyuni, 2019). Based on our research and the data, there were significant changes between the values before and after DHA supplementation regarding the MUAC of pregnant women (P = 0.003). thus DHA supplementation to pregnant women has an impact on LILA values. The findings of this study are support by research conducted by Salmon charls, Rahajoe Imam Santosa, and others (2021), regarding micronutrient supplementation for underweight pregnant women, where significant changes (<0.001) was observed in MUAS values before and after. In contarcct, a study by Salom Siahaan and Hendera Henderi [3] on micronutrient supplementation for underweight pregnant women found no changes (P=0.754) in MUAC before and after [12].

Pregnant women with poor or inadequate nutritional status are at risk of experiencing various complications during pregnancy, including an increase in blood pressure or hyperthension. If a pregnant woman has hypertentsion along with underweight conditions, it can lead to health problems affecting both the fetus and herself. Based od study conducted by Alyssa Atikah and Shella Salsabila [14] on the impact of undernutrition on pregnant women, it was concluded that nutritional status affects blood pressure [14]. Additionaly, the blood pressure of pregnant women is also influenced by their dietary intake. Several nutrients obtained from food can be affect blood pressure, such as sodium, potassium, and vitamin D. the balance of sodium and potassium levels in the mother's body is useful in reducing the risk of hypertension during pregnancy; high sodium and low potassium levels can trigger hypertension. Low levels of vitamin D in the body can also increase the risk of hypertension in pregnant women. This is supported by a study conducted by Anugrah Novianti et al [15] on the influence of nutrients on the blood pressure of pregnant women, finding a significant effect of sodium intake (P=0.001), no significant effect pf potassium intake (P=0.056), and a significant effect of vitamin D intake (P=0.028) on the increase in blood pressure in pregnant women [15]. In contrast, a study by Abdelrahman et al. [16] on the influence of omega-3 supplementation during pregnancy states of significant relationship (P=0.008) between omega-3 supplementation and the occurrence of preeclampsia resulting from increased blood pressure during pregnancy [16]. Therefore, the results of Anugrah Novianti et al. can support the findings of our research based on table 2. The results show no significant effect og DHA supplementation on systolic BP (P=0.208) and diastolic BP (P>0.05). This is because the DHA supplement provided is not among the nutrients mentioned that can increase blood pressure during pregnancy.

Estimating the Fundal Height in pregnant woment can be used as one of the methods to determine gestational age and the weight of the ferus being carried. If there is an error in estimating gestational age, it can affect the diagnosis and the subsequent plan od action to be given to the mother. The simple measurement of fundal height can be done using a measuring tape, measured from the top of the mother's pubic symphysis. The measurement can be determining the size of the fetus in the womb, and if the babby's size does not correspond to the gestational age, it may indicate disturbances in pregnancy and fetal growth, such as condition of low birth weight. This condition can be cause by poor maternal nutritional status, hindering the development and growth of the fetus [17]. Based on the research conducted and the data presentes in table 2., significant changes (P=0.001) were observed between before and after DHA supplementation regarding TFU. The results of this study are supported by research conducted by Anis Setyowati et al. [18] on the provision of supplementary food to underweight pregnant women for 3 months, where the fundal height before was 19.51 cm and after it increased to 33.57 cm, showing an increase of 14.06 cm.in the study by Salmon Siahaan and

Hendera Henderi [3] on the influence of DHA supplementation on underweight and normal oregnant women, a significant difference in TFU values (P<0.00001) wa found before treatment between normal and underweight pregnant women. It was concluded that fundal height values in underweight pregnant women were smaller. After supplementation, there was no significant difference (P=0.101) in fundal height values between normal and underweight. Thus, it can be concluded that there is a change in TFU due to DHA supplementation [12, 18].

IL-6 belongs to the group of proinflammatory sytokines, functioning to stimulate the body's immune response during the ongoing infection process. An increase in its levels is associated with tissue damage and inflammation. The normal serum level og IL-6 is < 4 pg/ml. Underweight conditions in pregnant women leat to a decreased volume of blood directed to the placenta and uterus, resulting in reduced nutrient supply to the placenta and suboptimal nutrition for the fetus from the mother. Additionally, the transfer of oxygen from placenta to the fetus is also reduced. There conditions cause tissue amaged and an increase in the production is result of poor mivronutrient regulation in the mother [4, 19. 5 & 20]. Based on our research, a significant change (P=0.008) was found in the supplementation of DHA on IL-6 levels in underweight pregnant women. It can be concluded that DHA supplementation has an effect in reducing IL-6 levels, indicating a decrease in inflammation. This research is supported by a study by Muhamad Ilham Aldika et al. on micronutrient (omega-3) deficiency in pregnancy, stating that insufficient omega-3 levels can trigger exssesive inflammation and oxidation, hindering fetal development. It is also mentioned that DHA, containing omge-3 fatty acids, can reduces placental oxidative stress, preventing tissue damage. DHA can decrease that production of inflammatory cytokines by altering the expression of inflammatory genes through its effect on transcription factor activation and COX inhibition. Moreover, DHA supplementation can enhance immunity to prevent infections in pregnant women [21].

CONCLUSION

Based on the research on The Correlation of DHA (Docosahexanoic Acid) Supplementation to Underweight Pregnant Women Regarding the InflammatoryMediator IL-6 (Interleukin-6) at the Made Surabaya Community Health Center, it can be concluded that the correlation of IL-6 levels in underweight pregnant women before and after the treatment results in a significant change. There it noticeable decrease in IL-6 levels before and after DHA supplementation. Therefore, providing DHA supplementation to underweight pregnant women can be benefical in their pregnancy to avoid the negative impact associated with being underweight.

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DECLARATIONS

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Conflict of interest: there are no conflicts that could influence the results or interpretation of this research.

Ethical approval: This research has obtained a research clearance letter from the National Unity and Politics Body with approval number 070/7145/209/2023. All procedurs involving research subjects were carried out in accordance with the guidelines stated in the ethical clearance from the Research Ethics Commission of the Faculty of Medicine, University, with approval number 122/UC-SoM/Skel/VI/2023. All participants provided written consent before participating in this research.

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Table 1: Characteristics of research sample

No	Category	Mean ± SD
1	Age	27.24 ± 4.48
2	Gestational age	18.43 ± 9.05
3	Weight	42.47 ± 3.26
4	Height	152.3 ± 5.4
5	BMI	18.26 ± 0.31
6	Systolic	103.76 ± 9.49
7	Diastolic	66.05 ± 6.71

Tabel 2: Research results of several factors in underweight pregnant women

No.	Description	Before	After	p-value
1	Weight	42.47 ± 3.26	52.5 ± 6.35	P 0.000
2	Height	152.3 ± 5.40	152.1 ± 5.05	P 0.929
3	BMI	18.26 ± 0.31	22.64 ± 2.28	P 0.000
4	MUAC	24.38 ± 1.619	25.39 ± 2.28	P 0.003
5	Systolic BP	103.7 ± 9.49	107.33 ± 13.71	P 0.108
6	Dyastolic BP	66.05 ± 6.71	67.33 ± 11.37	P 0.631
7	Fundal height	15.57 ± 7.11	17.95 ± 6.61	P 0.001
8	IL-6	10.21 ± 18.70	7.50 ± 11.51	P 0.008