International Journal of Medical and Pharmaceutical Research
Website: https://ijmpr.in/ | Print ISSN: 2958-3675 | Online ISSN: 2958-3683
NLM ID: 9918523075206676
Volume: 4 Issue:6 (Nov-Dec 2023); Page No: 201-207

Original Article

IJMPR

The Effect of Docosahexaenoic Acid (DHA) on Changes in Insulin in Underweight Pregnant Woman

Philip Fernando[1], Salmon Charles P.T. Siahaan[2*], Natalia Yuwono[2]

[1]Medical Student, Faculty of Ciputra University, Citraland CBD Boulevard, Surabaya, Indonesia
[2]Medical Faculty of Ciputra University, Citraland CBD Boulevard, Surabaya, Indonesia

ABSTRACT

Background: According to the Ministry of Health in 2020, the percentage of underweight pregnant women in Indonesia is 9.7%. Underweight is a condition of low body weight for age which is related to height. The condition of being underweight during pregnancy must be addressed immediately because influence fetal development. Insulin is an important factor in pregnant women for fetal development, such as the brain and eyes. Underweight conditions can cause pregnant women to experience insulin resistance since the beginning of pregnancy. This study identified the effect of DHA on changes in insulin in underweight pregnant women at the Made Surabaya Community Health Center.
Methods: This research includes pre-experimental research with one group pre-test post-test using 21 samples of underweight pregnant women who were examined physical, obstetrics, ultrasonography, and venous blood collection procedures were carried out for examination before and after DHA supplementation. Testing was carried out using the paired t-test and Wilcoxon test.
Results: The research results show that there was a significant difference between before and after DHA supplementation was given to underweight pregnant women. The difference is body weight (p=0.001), body mass index (p=0,002), upper arm circumference (p=0.000), body height (p<0.001), and insulin (p<0.001).
Conclusions: The research results showed that there was a significant effect of giving DHA on body weight, body mass index, upper arm circumference, height, and insulin.

Key Words: *DHA, insulin, pregnant women, underweight*

***Corresponding Author**
Salmon Charles P.T. Siahaan
Medical Faculty of Ciputra University, Citraland CBD Boulevard, Surabaya, Indonesia

INTRODUCTION

The coverage of healthcare services pregnant women for the fourth visit (K4) tends to fluctuate. In the year 2021 nationally healthcare services pregnant women K4 has reached the target National Medium-Term Development Plan 2021 amounting to 88,8% from target 85%. Overview the highest province located in the Special Capital Region of Jakarta in Indonesia amounting to 114,5%, followed by West Java amounting to 98,8% and Banten amounting to 95,7%. The data also shows there are two provinces that reach less than 50%, which is Papua and West Papua. Healthcare services pregnant women for the sixth visit (K6) the year 2021 in Indonesia amounting to 63% with the highest province which is North Sumatra Province amounting to 84,6%, followed by Banten amounting to 84,2%, and Bangka Belitung Islands amounting to 82,8%[1].

World Health Organization (WHO) in the year 2019 stated that underweight defined as low birth weight according to age or there are other terms such as wasting which is low birth weight related to towards height[2]. Burnie et al. in the year 2022 stated underweight during pregnancy is Body Mass Index <18,5 kg/m^2 from the beginning of pregnancy[3]. Basic Health Research (RISKESDAS) in the year 2018 stated that prevalence pregnant women who are at risk underweight in Indonesia is amounting to 17,3%.

Ministry of Health in the year 2020 stated that from 4.656.382 pregnant women from all provinces which is in Indonesia, as much as 451.350 pregnant women with conditions underweight. So that it is obtained percentage underweight pregnant women in the year amounting to 9,7%.

One of the factors related to condition underweight in pregnant women is insulin. Insulin itself is a peptide hormone that secreted by Beta cell from Langerhans islands of the pancreas and function to maintain normal blood glucose level. Insulin works by facilitate cellular glucose uptake, regulates carbohydrate metabolism, lipids, and proteins, also encourage division and cell growth through its mitogenic effects. Insulin resistance happens when normal or high insulin levels produce responds biologically weak, classically this pertains to sensitivity disorder to glucose mediated by insulin disposal[4].

Insulin resistance in normal pregnancy is a common occurrence. This is an adaptive response diverting glucose and lipids to the fetus that is developing and thinking due to combined effects from human placental lactogen, progesterone, estradiol, and cortisol, which acts as a counter-regulatory hormone to insulin. Normal pregnant women there is a lot of insulin resistance in the third trimester, meanwhile in underweight pregnant women insulin resistance occurs from the beginning of pregnancy[5]. The important thing that needs to be cautious about if insulin resistance happens since the beginning of pregnancy is the development of vital organs in the fetus such as the brain and eyes.

DHA is a saturated fatty acid that significant importance during the development of the brain and eyes and its function in the fetus. DHA concentrated mainly in the grey matter of the brain and in the outer segment of the retina. DHA involved in transmitting nerve signals in the brain and involved in visual quality in the eyes. DHA accumulates in the brain and eyes at the end of pregnancy and in the beginning of the baby period. Low DHA content causes cognitive development and visual function becomes impaired. Therefore, DHA is very important for pregnant women and breastfeeding women as well as babies for supports the development and function of the brain and eyes[6].

DHA can also induce and activate Peroxisome Proliferator Activated Receptor (PPAR) and increases number of PPAR target genes. This is at least responsible for the ability of DHA to reduce fasting plasma triglyceride concentrations and to improve insulin sensitivity. Through this effect, DHA acts to reduce the risk of insulin resistance, metabolic syndrome, hyperlipidemia, and cardiovascular disease[6].

We chose the title of this research because concrete data regarding the influence of DHA has not been obtained yet towards underweight pregnant women and no related research has been conducted on this matter. Therefore, we will research the correlation insulin with the administration of DHA to underweight pregnant women. From this research, we hope to gain insights into the role of DHA in providing improvements in underweight pregnancy in terms of insulin metabolism.

METHODS

This research employs an experimental research type with a cohort study design. We use one group pretest – posttest in this research, which involves conducting examinations before and after the treatment is administered. This research aims to study the effect of behaviour in the form of DHA supplementation to underweight pregnant women on insulin levels within a predetermined timeframe as the focus of the research and at the specified community health centre. This research aims to examine the effect of DHA supplementation (omega 3) and its impact on insulin levels, using a prospective approach to clearly observe the effects of DHA administration (omega 3) with insulin levels in underweight pregnant women in the Made Surabaya Community Health Centre.

The research respondents are pregnant women registered at the Made Surabaya Community Health Centre and underweight pregnant women, identified by a mid-upper arm circumference <23,5 cm or a body mass index <18,5 kg/m^2. In this research, the sampling is done with using the technique non-probability sampling with quota and purposive sampling. The sample consists of 21 underweight pregnant women who will be categorized into the experimental group and will get treatment, which involves receiving DHA supplementation and undergoing insulin examinations before and after the treatment, and with this technique, the influence of DHA supplementation on insulin in underweight pregnant women will be observed.

In this research, the collected data will be analysed using univariate and bivariate analysis. Univariate analysis used to describe the characteristics of each variable under researched without connecting it to other variables. Bivariate analysis used to analyse the relationship between two variables, that is the dependent variable and the independent variable. Variables that will be tested with bivariate analysis is the relationship between DHA supplementation and insulin levels to underweight pregnant women.

Statistical analysis is conducted using simple regression analysis because there is only one independent variable. Regression analysis examines the relationship between the independent variable and the dependent variable. The calculation analysis in regression testing involves several statistical calculations such as significance testing (t-test, F-test), anova, and hypothesis testing. In this research, the independent variable is the administration of DHA supplementation, while the dependent variable is the change in insulin levels.

RESULTS

In Table 1, the characteristics of subjects based on age during pregnancy and gestational age were obtained. Two pregnant women were found to be outside the productive age range, while 95 percent of pregnant women fall within the productive age range. At gestational age, there are differences in each trimester. Pregnant women before receiving treatment were mostly found in the first trimester, while after the treatment obtained pregnant women are evenly distributed across trimesters.

Table 1. Subject characteristics

Characteristics	Before		After	
	N	%	N	%
Age during pregnancy	**21**	**100**	**21**	**100**
Young (<20 Years old)	1	4.75	1	4.75
Productive (20-35 Years old)	19	90.5	19	90.5
Elderly (>35 Years old)	1	4.75	1	4.75
Gestational age	**21**	**100**	**21**	**100**
Trimester one (0-17 Weeks)	10	47.6	7	33.3
Trimester two (17-28 Weeks)	6	28.6	7	33.3
Trimester three (28-40 Weeks)	5	23.8	7	33.3

The normality test is useful to determine the test that will be used by the researcher. In this case, the normality test is mandatory to determine whether the obtained data is normally distributed or not. When data is normally distributed, parametric methods are used for data testing. However, if data is not normally distributed, nonparametric methods are used for data testing[7]. The researcher in conducting the research used the Shapiro-Wilk test because the sample size in this study is less than 50 samples. In this case, the data is categorized as normally distributed if the significance value is greater than 0.05 (>0.05)[8].

The normality test results revealed some characteristics that follow a normal distribution and some that do not follow a normal distribution. The age of the mother, gestational age, initial body weight, initial and final body height, initial and final systolic blood pressure, and initial insulin are included in the normally distributed data. While the final body weight, initial and final BMI, initial and final UAC, initial and final diastolic blood pressure, and final insulin are included in the non-normally distributed data.

Wilcoxon Signed Ranks Test is a nonparametric test used to assess the significance in paired data that have ordinal or interval scale and are not normally distributed[9].

According to the normality test in Table 2, it is indicated that the variables of final body weight, final insulin, as well as BMI, UAC, and diastolic blood pressure from before to after DHA supplementation do not meet the normality assumption. Therefore, the data test used for the final body weight, final insulin, as well as BMI, UAC, and diastolic blood pressure before and after DHA supplementation is the Wilcoxon Signed Ranks Test.

Table 2. Normality test

Characteristics	N	P
Age of pregnancy	21	.718
Gestation age	21	.322
Initial body weight	21	.270
Final body weight	21	.015
Initial body height	21	.765
Final body weight	21	.758
Initial body mass index	21	.000
Final body mass index	21	.000
Initial upper arm circumference	21	.000
Final upper arm circumference	21	.000
Initial systolic blood pressure	21	.154
Final systolic blood pressure	21	.124
Initial diastolic blood pressure	21	.005
Final diastolic blood pressure	21	.019
Initial insulin	21	.087
Final insulin	21	.011

At a significance level of 5%, if the p-value is <0.05, then there is a significant difference in the final body weight, final insulin, as well as BMI, UAC, and diastolic blood pressure before and after DHA supplementation.

Table 3 shows the results of the Wilcoxon Signed Ranks Test with initial and final body weight, obtaining a p-value of .001. This probability value falls below <0.05, where H1 can be accepted, indicating a significant difference between body weight before and after 30 days of DHA supplementation.

Table 3. Wilcoxon Signed Ranks Test for initial and final body weight after supplementation

Variable	N	*Mean*	Deviation Standard	p-value
Initial body weight	21	44.45	4.775	.001
Final body weight	21	45.62	5.094	

Table 4 shows the results of the Wilcoxon Signed Ranks Test with initial and final BMI, obtaining a p-value of .002. This probability value falls below <0.05, where H1 can be accepted, indicating a significant difference between BMI before and after 30 days of DHA supplementation.

Table 4. Wilcoxon Signed Ranks Test for initial and final body mass index after supplementation

Variable	N	*Mean*	Deviation Standard	p-value
Initial body mass index	21	18.666	2.2989	.002
Final body mass index	21	18.933	2.4428	

Table 5 shows the results of the Wilcoxon Signed Ranks Test with initial upper arm circumference, obtaining a p-value of .000, where this probability value falls below <0.05. Thus, H1 can be accepted, indicating a significant difference between upper arm circumference before and after the treatment.

Table 5. Wilcoxon Signed Ranks Test for initial and final upper arm circumference after supplementation

Variable	N	*Mean*	Deviation Standard	p-value
Initial upper arm circumference	21	22.962	1.2432	.000
Final upper arm circumference	21	23.176	1.1747	

Table 6 shows the results of the Wilcoxon Signed Ranks Test with initial and final systolic blood pressure, obtaining a p-value of .111, where this probability value is greater than 0.05. Thus, H1 cannot be accepted, meaning there is no significant difference between systolic blood pressure before and after the treatment.

Table 6. Wilcoxon Signed Ranks Test for initial and final systolic blood pressure after supplementation

Variable	N	*Mean*	Deviation Standard	p-value
Initial systolic blood pressure	21	102.90	7.867	.111
Final systolic blood pressure	21	106.14	12.195	

Table 7 shows the results of the Wilcoxon Signed Ranks Test with initial and final diastolic blood pressure, obtaining a p-value of .776, where this probability value is greater than 0.05. Thus, H1 is rejected, meaning there is no significant difference between diastolic blood pressure before and after the treatment.

Table 7. Wilcoxon Signed Ranks Test for initial and final diastolic blood pressure after supplementation

Variable	N	*Mean*	Deviation Standard	p-value
Initial diastolic blood pressure	21	66.10	67.10	.776
Final diastolic blood pressure	21	6.811	11.036	

Table 8 shows the results of the Wilcoxon Signed Ranks Test with initial and final insulin, obtaining a p-value <0.001, where this probability value is less than 0.05. This falls under the significance level, where H1 can be accepted, indicating a significant difference between insulin before and after 30 days of DHA supplementation.

Table 8. Wilcoxon Signed Ranks Test for initial and final insulin after supplementation

Variable	N	*Mean*	Deviation Standard	p-value
Initial insulin	21	31.3857	18.35822	p<0.001
Final insulin	21	13.6705	9.94016	

The paired t-test is one of the hypothesis testing methods with paired or dependent data, where the respondents in this study belong to one group, but two different treatments are applied[10]. This test is conducted when a variable meets the criteria of normality testing beforehand.

The results of the normality test in the previous statement indicate that the height variable meets the normality criterion. So, the data analysis technique for height will involve using the paired t-test. If the significance level is set at 5% ($p < 0.05$), then there is a significant difference in height before and after DHA supplementation.

Table 9 shows the results of the paired t-test for initial and final height, obtaining a p-value < 0.001, where this probability value is less than 0.05. This meets the significance level, where H1 can be accepted, indicating a significant difference between height before and after 30 days of DHA supplementation.

Table 9. T Test for initial and final body height after supplementation

Variable	N	*Mean*	Deviation Standard	p-value
Initial body height	21	154.452	5.4724	p<0.001
Final body height	21	155.357	5.5478	

DISCUSSION

This research involved data collection from a single group comprising 21 samples of underweight pregnant women at the Made Health Centre by being given 2 treatments. The first intervention involved blood collection before DHA supplementation, while the second intervention included DHA supplementation for 30 days.Underweight is a condition of low body weight according to age, and underweight can occur during pregnancy[2]. Often, individuals experiencing underweight also have a high risk of nutritional deficiencies[2].One of the nutritional needs in the body is insulin, which serves as the main regulator of amino acid transport in the placenta, where amino acids are crucial for fetal development and organ formation[4]. To meet the micronutrient needs in the body, supplementation is required, and one beneficial supplementation during pregnancy is DHA. So, in this research the data was collected to observe changes in insulin levels in underweight pregnant women before and after DHA supplementation.

Based on Table 4, the research findings indicate an impact on the BMI of pregnant women, with an increase in BMI after receiving DHA compared to before DHA supplementation.Fatty acids (omega-3, EPA, DHA, omega-6, AA) are used to overcome BMI abnormalities that commonly occur in individuals aged 14 and older, especially in adults experiencing obesity and pregnant women[11].The research conducted to compare EPA and DHA dose groups in terms of age, BMI, systolic or diastolic blood pressure found that there was no significant difference ($p = 0.68$ or $p > 0.05$) between EPA and DHA[12]. Similarly in relation to other research conducted on the obesity group before and after receiving EPA and DHA, it was found that there was no significant effect ($p = 0.91$ or $p > 0.05$) before and after EPA and DHA supplementation[3]. Meanwhile the research on obese adolescents aged 16-18 years found a relationship ($p = 0.001$ or $p < 0.05$) between the ratio of omega-6 or omega-3 intake and BMI[7].

Based on Tables 6 and 7, it was found that in this research, there was no influence on both systolic and diastolic blood pressure, neither before nor after consuming DHA. However, in another research regarding the administration of DHA or olive oil at 3 g/day for 12 weeks, a decrease in resting systolic and diastolic blood pressure was observed compared to EPA treatment in healthy young men and women (p systolic = 0.008 and p diastolic = 0.002), which is not consistent with the findings of this study[13]. Furthermore, according to Zhang's research, DHA and EPA, which are omega-3 fatty acids, can lead to a decrease in blood pressure, with a p-value of 0.0001 for the systolic pressure model and a p-value of 0.0073 for the diastolic pressure model. This means that Zhang's research is also inconsistent with the findings of this research[14]. On the other hand, in this research on blood pressure before and after in the omega-3 PUFA group and placebo group (p systolic = 0.082 and p diastolic = 0.235), it was found that there was no significant difference, aligning with the findings of this research[15].

Based on Table 3, the research findings indicate a significant difference between body weight before and after DHA supplementation, with an increase in body weight in pregnant women after consuming DHA supplements.The results of this research align with research conducted on young rats fed a healthy diet, where fish oil and DHA supplementation led to a change ($p = 0.036$ or $p < 0.05$), specifically an increase in body weight[16]. Furthermore, in another research, the findings are consistent with this research, showing a significant difference ($p < 0.001$) in body weight before and after DHA supplementation[17]. However, according to the research by Barbosa-Cortes, the results different from this research, as the research found that DHA and EPA supplementation at 100 mg/kg bw/day for the first three months could reduce non-fat body mass loss ($p = 0.044$ or $p < 0.05$)[18].

Based on Table 5, the research results indicate an impact on UAC pregnant women before and after DHA consumption. According to the research conducted in 2019 in Surabaya, a significant difference on UAC was found between normal pregnant women and underweight pregnant women before receiving DHA, with values of 27.4 + 2.22 vs. 20.6 + 1.298 ($p < 0.005$), aligning with the findings of this research[19]. Furthermore, another research also states that there is a significant difference on UAC size before and after the intervention, with values of 22.26 + 0.28 vs. 22.88 + 0.28 ($p < 0.0001$)[17]. As for the research conducted by Bulu, it also states a significant on UAC with a $p = 0.048$ or $p < 0.05$) which aligns with the findings of this research[5].

The research results indicate that there is a relationship between DHA and changes in insulin levels in underweight pregnant women, as shown in Table 8.This is not in line with the research by England, where DHA and EPA did not cause a significant effect on insulin sensitivity ($p = 0.68$ or $p > 0.05$)[20]. In other research that have found DHA and EPA can increase insulin resistance depending on the gender of the consumers[21]. Based on this research, there is a relationship between DHA and changes in insulin levels. The research conducted by Wei strengthens the association between DHA and insulin changes. Different concentrations of DHA or EPA can increase body weight and fat in insulin-resistant conditions by inhibiting adipogenesis, increasing insulin resistance, and suppressing food intake[22].

ACKNOWLEDGEMENTS

We want to express pur deepest gratitude to everyone who played a role in the successful completion of this research. We are particulary grateful to the team at Ciputra University Faculty of Medicine, whose expertise and steadfast support greatly enhanced the quality of this study. Special thanks are due to Dr. Salmon Charles P.T. Siahaan, dr., Sp.OG., Natalia Yuwono, dr., M.Ked.Trop., and the laboratory team for their invaluable guidance and constructive feedback throughout the research process. Our appreciation also goes to the Made Health Centre for generously providing resources all the facilitated the execution of this study. Lastly, I would like to acknowledge and thanks to all the participants and individuals who devoted their time and effort to contribute to this study. The successful completion of this work is the result of the collective efforts and support of many, and for this, we are truly thankful.

DECLARATIONS

Funding: This research was conducted using personal funds.

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 070/7038/209/2023. All procedures 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 060/EC/KEPK-FKUC/VII/2023. All participants provided written consent before participating in this research.

REFERENCES

1. Rasuna, J.H.R. and Blok, S. (2022). Kementerian Kesehatan Republik Indonesia DirektoratJenderal Kesehatan Masyarakat.
2. World Health Organization. (2019). Malnutrition. World Health Organization. Available at: https://www.who.int/health-topics/malnutrition#tab=tab_1 (Accessed: 2023).
3. Borja-Magno, A.I. et al. (2023). Supplementation with EPA and DHA omega-3 fatty acids improves peripheral immune cell mitochondrial dysfunction and inflammation in subjects with obesity. The Journal of Nutritional Biochemistry, 120(109415), p. 109415. doi:10.1016/j.jnutbio.2023.109415.
4. Nasution, Y.F., Lipoeto, N.I. and Yulizawati, Y. (2019). Hubungankadar insulin-like growth factor 1 serum maternal denganberat badan dan panjang badan bayibarulahir pada ibuhamil KEK.MajalahKedokteranAndalas, 42(3S), p. 19. Available at: https://doi.org/10.25077/mka.v42.i3s.p19-29.2019
5. Kasuga, Y. et al. (2022). Impaired early phase insulin secretion associated with gestational diabetes mellitus in underweight women. Journal of Maternal-Fetal and Neonatal Medicine, 35(12), pp. 2411–2413. Available at: https://doi.org/10.1080/14767058.2020.1779692.
6. Calder, P.C. (2016). Docosahexaenoic acid. Annals of Nutrition and Metabolism, 69(1), pp. 8–21. Available at: https://doi.org/10.1159/000448262.
7. Mahesty, I.R., Sulchan, M. and Kartini, A. (2022). Rasioasupan omega-6/omega3 dan IMT (Indeks Massa Tubuh) pada remajaobesitasusia 16-18 tahun. Sport and Nutrition Journal, 4(2). doi:https://doi.org/10.15294/spnj.v4i2.60903.
8. Raharjo, S. (2021). Cara uji normalitasshapiro-wilk dengan SPSS lengkap. SPSS Indonesia. Available at: https://www.spssindonesia.com/2015/05/cara-ujinormalitas-shapiro-wilk-dengan.html (Accessed: 2023).
9. Raharjo, S. (2017). Panduan lengkapcaramelakukan uji wilcoxondengan SPSS. SPSS Indonesia. Available at: https://www.spssindonesia.com/2017/04/carauji-wilcoxon-spss.html (Accessed: 2023).
10. Nuryadi et al. (2017). Dasar – dasar 67tatistic penelitian. Yogyakarta, Indonesia: Sibuku Media
11. Diana, F. M., Ramadani, M. R., & Fitria, N. (2022). The Effects of Fatty Acid in Population Related to Body Mass Index. Jurnal Kesehatan Masyarakat Andalas, 16(1), 45-50.
12. Sparkes, C., Sinclair, A. J., Gibson, R. A., Else, P. L., & Meyer, B. J. (2020). High variability in erythrocyte, plasma and whole blood EPA and DHA levels in response to supplementation. Nutrients, 12(4), 1017.
13. Lee, J.B. et al. (2019). Docosahexaenoic acid reduces resting blood pressure but increases muscle sympathetic outflow compared with eicosapentaenoic acid in healthy men and women. American Journal of Physiology-Heart and Circulatory Physiology, 316(4). doi:10.1152/ajpheart.00677.2018.
14. Zhang, X., Ritonja, J. A., Zhou, N., Chen, B. E., & Li, X. (2022). Omega-3 polyunsaturated fatty acids intake and blood pressure: a dose-response meta-analysis of randomized controlled trials. Journal of the American Heart Association, 11(11), e025071.

15. Pipingas, A. et al. (2023). Post-prandial cognitive and blood pressure effects of a dha-rich omega-3 powder in middle-aged males: A pilot study. Nutrients, 15(9), p. 2198. doi:10.3390/nu15092198.
16. Veronica, F. et al. (2020). Effects of DHA-enriched fish oil supplements on dopamine receptor gene expression in the cerebral cortex and hippocampus related to the male rats weight gain. Journal of Global Pharma Technology, 12(6).
17. Siahaan, S. C. (2023). Korelasi suplementasi nutrisi terhadap ibu hamil kurang energi kronis untuk pencegahan kejadian stunting. Jurnal Kedokteran Syiah Kuala, 23(1).
18. Barbosa-Cortés, L. et al. (2023). Pilot study on the effect of supplementation with long-chain ω-3 polyunsaturated fatty acids on body composition in children with acute lymphoblastic leukemia: randomized clinical trial. Clinical Nutrition, 42(9), 1759-1769.
19. Siahaan, S.C., Henderi, H. and Sudibyo. (2021). Intervensiibuhamildengankurangenergikalori pada trimester ketigamelaluisuplementasimikronutrien di Surabaya tahun 2019.MajalahKedokteranAndalas, 44(1). doi:https://doi.org/10.25077/mka.v44.i1.p17-27.2021.
20. England, J.A. et al. (2019). Effect of prenatal EPA and DHA on maternal and cord blood insulin sensitivity: A secondary analysis of the mothers, omega 3, and mental health study. BMC Pregnancy and Childbirth, 19(1). Available at: https://doi.org/10.1186/s12884-019-2599-6.
21. Abbott, K. A., Burrows, T. L., Acharya, S., Thota, R. N., & Garg, M. L. (2020). DHA-enriched fish oil reduces insulin resistance in overweight and obese adults. *Prostaglandins Leukotrienes and Essential Fatty Acids*, *159*. https://doi.org/10.1016/j.plefa.2020.102154
22. Wei, W. et al. (2021). Anti-obesity effects of DHA and EPA in high fat-induced insulin resistant mice. Food & Function, 12(4), 1614-1625.