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Effect of Fish Oil on Anxiety in Pregnant Women with Gestational Diabetes

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ABSTRACT

East Java has the fourth-highest number of pregnant women with gestational diabetes mellitus among all provinces in Indonesia. While there were 65 pregnant women at the Kediri District Hospital, there were as many as 57 pregnant women with gestational diabetes mellitus at the Aura Syifa Hospital during the study. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in ω-3 are unsaturated fatty acids recognized as essential for child development and recommended for pregnant and breastfeeding mothers. This study aims to see the effect of fish oil supplementation on anxiety levels in pregnant women with GDM. The fish oil product used is "Healthy Care Fish Oil 1000 mg Omega-3," which was registered by the BPOM on February 8, 2021. It has also been certified as halal by MUI. This research used a quasi-experimental design and a pre-test-post-test control group design with a sample of 60 people obtained from a purposive sampling technique. Data were collected using a questionnaire that tested validity and Reliability, with a Cronbach's alpha ranging from 0.446 to 0.837 (r table = 0.444). The study's findings showed that the respondents who obtained fish oil had better results than the control group, with a difference of 4,700 ± 7,415 in anxiety levels. Statistical tests showed ρ value = 0.002 < α = 0.05, so there was a notable distinction between the two groups. The results of the data analysis show that the use of fish oil for anxiety in pregnant women is effective in reducing the level of anxiety in the control group in the Kediri District area.

Introduction

Pregnancy is always associated with psychological changes that affect macronutrient and micronutrient deficiencies (Supadmi et al., 2020). Based on WHO data, there are three common causes of death worldwide, including cardiovascular disease, respiratory disease, and maternal and neonatal complications (WHO, 2023). As stated by the International Diabetes Federation (IDF), one in seven pregnancies in the Western Pacific region, which includes Indonesia, is affected by gestational hyperglycemia (IDF, 2021). Meanwhile, in Indonesia, the percentage of women with gestational diabetes who are pregnant is 1-14% of all pregnancies, but there are data on the frequency of pregnancy-related diabetes and undetected gestational diabetes mellitus (GDM) as high as 10-25% (Kurniawan, 2017). East Java ranks in the AT group of all provinces in Indonesia (Riskesdas, 2018).

Various factors underlying the development of gestational diabetes mellitus (GDM) include metabolic changes, increased caloric intake, obesity, maternal gestational age, socioeconomic status, history of gestational diabetes, diabetes in the family, membership of high-risk ethnic groups, polycystic ovarian syndrome, persistent glucosuria, history of macrosomic delivery and history of fetal death

(Alfadhli, 2015; Chen et al., 2015). Epidemiological studies have shown that maternal GDM or glycemia risk is influenced by, for example, fetal sex, multiple gestation, paternal age, and paternal ethnicity (Jääskeläinen & Klemetti, 2022).

The long-term effects of GDM can include obesity, cardiovascular disease, poor glucose metabolism, and obesity in the mother and child (McIntyre et al., 2019). In terms of fetal growth, hyperglycemia in pregnancy has been found to cause unfavorable offspring growth and development, prematurity, inhibitory effects on fetal period growth, and easily inflamed neonatal induction (Huang et al., 2021). Gestational diabetes mellitus patients are also highly susceptible to anxiety disorders, and anxiety itself can worsen the condition of GDM (Fitri Jeharut et al., 2021). Studies show that there is a reciprocal relationship between the incidence of anxiety and GDM. Anxiety and chronic hypothalamic-pituitary-adrenal hyperactivity brought on by depression can lead to elevated cortisol release and insulin resistance, which increases the danger of developing GDM in pregnant women.

To date, international guidelines have recommended early antenatal screening for high-risk women (Sweeting et al., 2022; Yanti, 2019), non-pharmacological therapy with dietary management and advice on ideal weight (Kawasaki et al., 2023), as well as adequate rest and antenatal monitoring or screening (Munawarah et al., 2020). In addition, fish oil supplements containing ω-3, DHA, and EPA can be given to patients with gestational diabetes (Ostadrahimi et al., 2016).

Recent research suggests that fish oil is crucial for pregnant women and their developing fetuses. The eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in ω-3 are unsaturated fatty acids recognized as crucial for infant development and have been recommended for pregnant and breastfeeding women (Devarshi et al., 2019). Studies have found that the PUFA content of fish oil can act as a metabolic enhancer for pregnant women, help improve blood flow from the placenta to the fetus, and reduce the risk of growth and neurodevelopmental abnormalities in the offspring of mothers with GDM (Elshani et al., 2021). This study aims to determine whether fish oil reduces anxiety levels in pregnant women with gestational diabetes and to identify their anxiety levels before and after receiving fish oil therapy.

Method

The design of this study is quasi-experimental, utilizing a pre-test and posttest control group design. The sample consisted of respondents with gestational diabetes from Kediri Regency Hospital and Aura Syifa Hospital, totaling 60 respondents, divided into 30 in the intervention group and 30 in the control group. A questionnaire was used to collect personal data from the respondents. Data was collected using the PRAQ-R2 anxiety questionnaire, which was tested for validity by Wardani with an external validity test r value of 0.446-0.837 (r table = 0.444) (Wardani et al., 2018). The Reliability was verified using the Cronbach alpha statistical test with satisfactory to outstanding values for the total PRAQ-R2 subscales (α =.77 to .90) and the overall scale (Cronbach's α =.85) (Mudra et al., 2019). The statistical test used was the paired t-test.

Data collection was carried out in two stages: preparation and implementation. The preparation stage involved obtaining research permission and agreeing with the coordinating midwife to collect data

on the number of women of childbearing age who were obese. The implementation stage involved obtaining ethics committee approval, selecting respondents according to criteria, explaining the aims and procedures of the study, and obtaining informed consent. The criteria required to meet as respondents include individuals aged 18-35 years, gestational age in the second or third trimester (14 weeks - 38 weeks), random plasma sugar levels > 140 mg/dL, and the ability to communicate effectively. In addition, respondents were declared ineligible for the study if, during the data collection process, they had other medical conditions such as pre-eclampsia, eclampsia, hypothyroidism or hyperthyroidism, liver disease, were taking other fish oil supplements outside the study, or were habitual smokers or drinkers of alcohol. Informed consent was obtained from the respondents participating in the data collection, and personal information, including age, gestational age, parity, occupation, and education, was collected. Those in the intervention group were informed that they would receive a fish oil supplement in capsule form with a 1000 mg dosage. They were administered once a day in the evening, after dinner, for 14 days. The researcher will check daily by contacting the respondents through online messaging and asking them to send photos or videos of themselves taking the supplements to ensure they are taking them as directed.

The use of an ethical clearance was predicated on four fundamental research ethics principles: decency, or the idea of doing good; respect for others; nonmaleficence, which involves minimizing harm to subjects; and protection of subjects. Justice highlights that each person is entitled to something according to their rights regarding distributive justice and fair distribution. The number of the Ethical Declaration is 000.9/11699/418.100/2024.

Results

This research was done from May to June 2024 at Kediri District Hospital and Aura Syifa Hospital. The study included 60 participants, divided into two groups: 30 in the control group and 30 in the treatment group. Questionnaires were used to collect general data.

Table 1. Characteristics of Respondents

Characteristics	Frequency Control (n=30)		Frequency Intervention (n=30)		*P Value*
	f/M	%	f/M	%	
Age	28.57		30.07		0,281[b]
Gestational age					0,856[a]
Trimester 2	8	73,3	21	70,0	
Trimester 3	22	26,7	9	30,0	
Paritas					0,037[a]
Primigravida	8	73,3	6	20,0	
Multigravida	22	26,7	21	70,0	
Grandemultigravida	0	0	3	10,0	
Latest Education					0,295[a]
Primary	0	0	1	3,3	
Intermediate	29	96,7	29	96,7	
Tertiary	1	3,3	0	0	
Employment Status					0,212[a]
Employed	7	23,3	1	3,3	
Unemployed	23	76,7	29	96,7	

[a] Test of Homogeneity dan [b] Test of Normality

Based on the table above, this means that most of the respondents have an average age of 28-30 years with a p-value of 0.281, the highest percentage of pregnancies is in the third trimester, with a total of 37, the last education of the respondents is mostly intermediate, with a total of 58. As many as 52 respondents do not work. According to the table, this indicates that the data are homogeneous, as the p-value is greater than 0.05.

Table 2. Distribution of Respondents' Anxiety Levels

Variable		Control (n=30)		Intervensi (n=30)	
		f	%	f	%
Anxiety Levels (PRAQ-R2)	Low	18	60,0	16	53,3
	Moderate	12	40,0	13	43,3
	Severe	0	0	1	3,3

From the table above, it is apparent that the distribution of respondents in both groups has an amount that is not significantly different, indicating homogeneous data in both groups.

Table 3. Anxiety Level of the Intervention Group Before and After Treatment

Variable	*Pre-test* (n=30)	*Posttest* (n=30)	*Difference*	*P-Value*
	Mean (± *SD*)	*Mean* (± *SD*)	*Mean* (± *SD*)	
Anxiety Levels (PRAQ-R2)	19.97 (± 6.759)	16.93 (± 5.051)	3.033 (± 2.157)	0,000

***Wilcoxon Test**

It is evident from the preceding table that there is a difference in anxiety levels before and after therapy, with a difference of 3.033 and a P-value of 0.000; the significance value is less than the alpha value (0.05). It can be assumed that in this research, H1 is accepted, which indicates that anxiety levels varied before and after therapy.

Table 4. Anxiety Level of the Control Group

Variable	*Pre-test* (n=30)	*Posttest* (n=30)	*Difference*	*P-Value*
	Mean (± *SD*)	*Mean* (± *SD*)	*Mean* (± *SD*)	
Anxiety Levels (PRAQ-R2)	22.07 (± 5.982)	21.63 (± 6.505)	0.433 (± 1.278)	0,066

***Wilcoxon Test**

It is evident from the preceding table that the control group's anxiety levels differ significantly from those with standard therapy, with a difference of 0.433, and the P value is 0.066, which means the significance value surpasses the alpha value (0.05). In this study, it may be said that H0 is accepted, indicating that the control group's anxiety levels are the same.

Table 5. Comparison of Anxiety Levels of the Two Groups Before and After Intervention

Variable	*Pre-test* (n=30)	*Posttest* (n=30)	*Difference*	*P-Value*
	Mean (± *SD*)	*Mean* (± *SD*)	*Mean* (± *SD*)	
Anxiety Levels (PRAQ-R2	157.40 (± 23.639)	149.50 (± 28.555)	7.900 (± 40.364)	0, 002

***Mann-Whitney Test**

It is evident from the preceding table that the difference in the posttest between the intervention group and the control group is 4.700 with a P-value of 0.002, which means that the sign value is smaller than the alpha value (0.05). In this investigation, it can be inferred that H1 is accepted, indicating a statistically significant difference between the two groups. There is a 4,700 ± 7,415 difference in the means of the two groups.

Discussion

Following the study, the outcomes for the two groups differed. In the intervention group, there was a more significant change in anxiety levels compared to the control group, which did not receive fish oil therapy. In the pre-treatment intervention group, 12 respondents (40%) felt anxious, and in the control group, 13 respondents experienced moderate levels of anxiety, and one respondent (3.3%) experienced high levels of anxiety. After treatment, the intervention group experienced a decrease in anxiety levels from 18 respondents to 27 respondents (90%) experiencing mild anxiety. The outcomes of the paired t-test with sig. (0,000) show this difference. The difference in anxiety levels experienced by respondents in the intervention group may be due to the administration of fish oil.

The fish oil provided to responders includes omega-3 polyunsaturated fatty acids (PUFAs), which are essential nutrients with potential preventive and therapeutic benefits for mental diseases, including depression and anxiety, and contain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (Gian et al., 2021). Some researchers suggest that high doses of n-3 PUFAs may be more effective for depression and anxiety symptoms (Putri et al., 2021). Research indicates that the manufacture of endogenous endocannabinoids (ECs) and bioactive endogenous neuroinflammatory mediators is influenced by polyunsaturated fatty acids (PUFAs). Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the two primary constituents of omega-3 polyunsaturated fatty acids, possess antidepressant properties (Damaiyanti et al., 2023).

A meta-analysis study found that ω-3 fatty acids have significant antidepressant effects in patients diagnosed with major depressive disorder (MDD) or bipolar disorder (Burhani & Rasenick, 2015). Numerous research endeavors have examined the impact of ingesting elevated doses of ω-3 PUFAs via dietary consumption or supplementation, and have discovered decreased anxiety levels across diverse demographic groups, including pregnant women (Verly-Miguel et al., 2015). The content of fish oil increases EPA and DHA in erythrocyte membranes and plasma of patients suffering from unipolar depression, winter seasonal affective disorder, or social anxiety disorder (Larrieu & Layé, 2018).

In addition, gestational age is also among the main factors that can affect the degree of worry that expectant mothers experience, which is consistent with the research conducted (Setiawati et al., 2022), who found that pregnant women in the third trimester experienced more anxiety in mild, moderate, and severe levels. However, in this study, the characteristics of the respondents consisted of the second trimester and trimester 3, which biased the results.

The revised version of the Pregnancy-Related Anxiety Questionnaire (PRAQ-R2) is an instrument for assessing anxiety during pregnancy, with predictors related to childbirth and the baby, and independent of general anxiety. The PRAQ-R2 is a revision of the PRAQ and has undergone psychometric testing (Hanifah, 2019). The instrument comprises ten elements. All of the three categories that these items fall under are (1) dread of the operational procedure (items 1, 2, and 5), (2) worry for fetal abnormalities in items 4, 8, 9, and 10. (3) worry about the physical alterations to items number 3, 6, and 7. (Asih et al., 2021). This questionnaire has been tested for validity by Wardani with an external validity test r value of 0.446-0.837 (r table = 0.444) (Wardani et al., 2018) and tested for Reliability

using the Cronbach alpha statistical test with the PRAQ-R2 overall subscales (α =.77 to.90) and the overall scale (Cronbach's α =.85) had adequate to excellent values. (Mudra et al., 2019).

The use of the PRAQ-R2 questionnaire is consistent with research by Blackmore et al They discovered strong positive associations of generalized anxiety disorder (GAD) symptoms using WaHC (r =.22 to .23) and FoGB (r =.12 to .24) in the second and third trimesters of pregnancy. Huizink and colleagues have altered the PRAQ into a workable 10-item shortened form with three subscales in the PRAQ-R: "fear of childbirth" (FOGB), "worry about having a kid who is physically or mentally handicapped" (WaHC), and "self-appearance concerns"." (Mudra et al., 2019).

Other research also indicates that the PRAQ-R2 and PrAS exhibit a linear relationship between the scale and its related subscales. For instance, a significant correlation was found between the PRAQ-R2 subscales measuring worries about attractiveness and worry about having a child who is physically or cognitively challenged. The PrAS subscales measure infant anxieties and body image issues. Concerns about Childbirth and the PrAS subscales showed modest correlations. Attitudes toward delivery and PRAQ-R2 Fear of Delivery, in addition to PrAS, were also correlated with DASS Anxiety and EPDS. The PrAS overall score and virtually all subscales (except avoidance) had weak negative associations with the BRS. (Weigl et al., 2023).

According to the findings of the Mann-Whitney test, which measured the difference in anxiety levels between the two groups, those in the intervention group reported significantly lower anxiety levels (30%), compared to 0% in the control group.

Omega-3 fatty acids, found in fish oil, support the regulation of the nervous system, blood pressure, blood coagulation, glucose tolerance, and inflammatory processes. It could be beneficial for any inflammatory issue. Taking at least 2000 mg of omega-3 PUFA daily is far more beneficial in reducing symptoms of anxiety. Omega-3 polyunsaturated fatty acids (PUFAs) impact and may even govern neurobiological mechanisms such as inflammation, neurotransmitter systems, and neuroplasticity, all of which are considered to contribute to anxiety and depression. As a result, supplementary PUFAs have the potential to improve mood by reducing hypothalamic-pituitary-gastric axis activity and chronic brain inflammation. (Damaiyanti et al., 2023).

According to the results obtained from the PRAQ-R2 questionnaire administered to pregnant women, most women prefer to select answers in the 'never' column. However, the PRAQ-R2 questionnaire's design results in the lowest value being assigned to the 'ever' column, which suggests that the obtained results indicate mild anxiety. From the results of the posttest Table 7, obtained in both groups, it can be seen that there is a difference between the group of respondents who received the intervention and the control group. The intervention group had a substantial difference in anxiety levels with a mean difference of 4,700 ± 7,415.

Gestational age is one of the primary reasons why expectant mothers experience anxiety. According to the findings of studies on women in their third trimester of pregnancy, as many as 32 mothers (33.36%) experienced anxiety (Setiawati et al., 2022), showing that the closer the time of delivery, the more anxious pregnant women will feel. In addition, parity also affects the occurrence of

anxiety in pregnant women. In the first pregnancy (primigravida), the majority of pregnant women do not understand how to cope with pregnancy until the process of childbirth, so this will affect the anxiety of primigravida women in facing childbirth compared to multi-gravida women who have undergone childbirth before (Anggraeni et al., 2022).

High levels of anxiety and prolonged stress are associated with increased maternal responses to the hypothalamic-pituitary-adrenal axis, as well as increased adrenal cortisol and placental CRH release (Kundarti & Komalyna, 2023). Excessive exposure to glucocorticoid cortisol affects anxiety and mood problems may be attributed to anatomical alterations in the hippocampal area of the brain, which regulates the stress response. (Fiksdal et al., 2017). In addition, gestational age is also among the main factors that may Influence the degree of anxiety in pregnant women, which is consistent with research (Setiawati et al., 2022) that found that third-trimester pregnant women experienced more mild, moderate, and severe levels of anxiety. However, in this study, the characteristics of the respondents consisted of the second trimester and trimester 3, which biased the results.

There are limitations in this study that can be a shortcoming of the study. The researchers are aware of some of these factors and hope to use them as reference data for further research, such as the fact that the respondents did not focus on a single trimester, which could affect the outcome of this research. For example, pregnant women in the third trimester are more likely to possess greater quantities of anxiety, and the time used by the researchers to assess the respondents' consumption of fish oil cannot be done at the same time due to limited space and time to adjust the respondents' rest time.

This trial has several strengths compared to other trials. This study uses supplements with the same dose because it employs capsule preparations, allowing each respondent to receive the same dose, which is easier to consume. In addition, this study used the PRAQ-R2 questionnaire as a measure of anxiety, which measures not only fear about labor but also anxiety about body image and disability of the child.

The research conducted is an experiment, and the results are expected to serve as parameters for consideration or decision-making in the provision of doses that can be used as an alternative treatment for pregnant women with GDM. The study's findings have good consequences for several parties. Variations in blood glucose levels were observed, and anxiety levels in pregnant women after taking fish oil supplements.

Conclusions

Based on the results, it can be concluded that the constituents of fish oil, namely the major components Omega-3 polyunsaturated fatty acids include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) with antidepressant qualities that produces differences in the results of fish oil administration on anxiety in ladies with gestational diabetes mellitus during their pregnancy in both groups, where the intervention group experienced a more significant reduction than the control group.

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