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The Effect of Suplementation Omega-3 on Sputum Conversion, Body Mass Index, Interleukin-6 and Monocyte Lymphocyte Ratio in the Treatment of Pulmonary Tuberculosis

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Abstract

Tuberculosis (TB) is a disease caused by Mycobacteriun Tuberculosis. Its cases continue to increase both in Indonesia, and in the world. Efforts to increase the success rate of TB treatment and reduce the level of transmission need to continue to be developed, one of which is with additional therapy in its treatment. Omega-3 has anti-inflammatory and anti-bacterial potential, which is predicted to increase the success of TB treatment, as seen from sputum conversion, increased body mass index (BMI) and important inflammatory parameters in TB infection namely interleukin-6 (IL-6), monocyte lymphocyte ratio (MLR) values. This study was conducted to determine the effect of Omega-3 addition on sputum conversion, BMI, IL-6 levels and MLR values in pulmonary tuberculosis treatment. Experimental study with consecutive sampling in drug-sensitive pulmonary TB patients who were given additional Omega-3 dose of 1,200 mg (@600mg/capsule), compared with the control group. Each sample was monitored for sputum conversion, BMI, IL-6 levels and MLR values at week 0 (m0), week 4 (m4) and week 8 (m8). In this study, there was a significant effect of adding Omega-3 on reducing IL-6 levels (p= 0.013), reducing MLR values (p= 0.005) and increasing BMI (p= 0.047) but no significant effect on sputum conversion (p= 1,000). The addition of Omega-3 had a significant effect on reducing IL-6 levels, reducing MLR values and increasing BMI, but did not have a significant effect on sputum conversion in pulmonary TB treatment.

Introduction

Tuberculosis (TB) is a disease caused by *Mycobacterium Tuberculosis* (MTB), This disease can infect the lungs and other organs. Tuberculosis is still a health problem in Indonesia which creates very complex health, social, economic and cultural problems. According to the Global *TB Report* In 2022, Indonesia will have the second highest number of tuberculosis cases in the world after India. TB cases in Indonesia are estimated at 969,000 cases. This figure is up 17% from 2020, namely 824,000 cases. The incidence of tuberculosis cases in Indonesia is 354 per 100,000 population.

Data on pulmonary TB cases in 2022 from the South Kalimantan Provincial Health Service is 7,556 cases with 3,861 positive acid-fast bacilli (BTA) (51%), with cases in Banjarmasin City occupying the highest position, 1,768 tuberculosis cases from 719,577 residents of Banjarmasin city with 819 positive BTA cases (46%). The high number of tuberculosis cases in Indonesia requires the government to issue a commitment to fighting tuberculosis by issuing

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Presidential Decree Number 67 of 2021 concerning Tuberculosis Control. Tuberculosis can cause a chronic response. This process causes necrosis, cavitation of lung tissue and also facilitates TB transmission (Nienaber et al., 2021). Anti-inflammatory treatment has been proposed as an adjunct therapy for TB patients as an effort to control excessive inflammation in TB so as to improve TB treatment outcomes and break the chain of TB transmission. One of the proposed anti-inflammatories is Omega-3. Consuming Omega-3 *polyunsaturated fatty acid* (PUFA) changes the phospholipid fatty acid (FA) composition of cell membranes which plays a role in immune and inflammatory responses.

This process is largely mediated by conversion *long chain* PUFA (LCPUFA), ie *eicosapentaenoic acid* (EPA) and *docosahexaenoic acid* (DHA) (Hayford et al., 2021). Omega-3 EPA and DHA serve as substrates for production *pro-resolving lipid mediators* (LM), protectins, maresins and resolvins which help resolve inflammation and reduce the production of anti-inflammatory cytokines (Nienaber et al., 2021). Incorporation of EPA and DHA into cell membranes also increases cell phagocytosis and bacterial apoptosis.Omega-3 supplementation has been shown to be better than diet in terms of weight gain and pneumonia resolution. Therefore Omega-3 can be predicted as an additional supplement in the treatment of tuberculosis (Nienaber et al., 2021).

Research in Uganda shows that Omega-3 supplementation reduces interleukin 6 (IL-6) levels in infections *Human immunodeficiency virus* (HIV) (Coghill et al., 2018). Another study stated that there was a relationship between high levels of IL-6 with the level of acid-fast bacillus (BTA) sputum positivity and the time to conversion of sputum BTA in the treatment of pulmonary TB (Wahyudi, 2022). Research at Persahabatan Hospital showed that pulmonary TB patients with BTA positive had a body mass index (BMI) <18.5 kg/m^2 have a greater cumulative probability of conversion failure than patients with a BMI >18.5 kg/m^2 (Tama et al., 2016).

In the inflammatory process, a number of proinflammatory cytokines, including IL-6, are involved in the MTB infection process and play an important role in the acute and chronic phase response (Domingo et al., 2016). Dysregulation of IL-6 contributes significantly to the pathogenesis of chronic inflammatory diseases, and changes in cytokine levels may reflect disease status and serve as a potential prognostic test for tuberculosis.IL-6 has been identified as a biomarker and should be further investigated as part of monitoring tuberculosis therapy (Zimmer et al., 2022). Immune system status plays an important role in tuberculosis infection. Monocyte cells have been considered as target cells of MTB, and lymphocytes are the main effector cells of TB immunity.As key immune cells, the levels of monocytes and lymphocytes can reflect the state of a person's immunity to infection. Peripheral complete blood count is the most frequently performed test in clinical practice, but the monocyte to lymphocyte ratio/*monocyte to lymphocyte ratio* (MLR), as a simple biomarker is still rarely used in clinical care (Wang et al., 2019).

Based on previous studies, Omega-3 has anti-inflammatory and anti-bacterial effects, so it is predicted to have potential as an additional therapy that can increase the success of tuberculosis treatment and break the chain of tuberculosis transmission. Apart from that, Omega-3 supplements are supplements that are easily available at affordable prices, but are rarely used as adjunct therapy in TB treatment. Based on the things mentioned above, it builds the researcher's interest and interest in conducting this research. The formulation of the problem for this research is: Is there an influence on sputum conversion, body mass index, IL-6 levels and MLR values in patients undergoing pulmonary TB treatment in the group that received additional Omega-3 and those that did not receive additional Omega-3? The aim of this research is to determine the effect of adding Omega-3 as a companion therapy in the treatment of pulmonary tuberculosis on sputum conversion, body mass index, IL-6 levels and MLR values.

The specific objectives of this research are: (1) Carrying out bacteriological examination of the sputum of the control group and treatment group before and after the addition of Omega-3 at week 0, week 4 and week 8 of pulmonary TB treatment; (2) Measuring the BMI of the control group and treatment group before and after adding Omega-3 at week 0, week 4 and week 8 of pulmonary TB treatment; (3) Measuring IL-6 values for the control group and treatment group before and after adding Omega-3 at week 0, week 4 and week 8 of pulmonary TB treatment; (4) Measuring the MLR value of the control group and treatment group before and after adding Omega-3 at week 0, week 4 and week 8 of pulmonary TB treatment; (5) Analyze the effect of adding Omega-3 on sputum conversion in the control group and treatment group at week 0, week 4 and week 8 of pulmonary TB treatment; (6) Analyze the effect of adding Omega-3 on IL-6 levels in the control group and treatment group at week 0 and week 4 of pulmonary TB treatment; (7) Analyze the effect of adding Omega-3 on the MLR values of the control group and treatment group at week 0, week 4 and week 8 of pulmonary TB treatment; (8) Analyzing the effect of adding Omega-3 on the BMI of the control group and treatment group at week 0, week 4 and week 8 of pulmonary TB treatment.

It is hoped that the results of this research will provide scientific literacy regarding the benefits of adding Omega-3 to pulmonary TB therapy. It is hoped that the results of this research can be used as a basis for recommendations to doctors to provide additional Omega-3 in the treatment of pulmonary TB patients in health services. Can provide information and education to the public. The addition of Omega-3 can be used as an accompanying therapy for OAT to increase the success of treatment and break the chain of transmission of pulmonary TB. Providing references or materials for the development of further research to examine interleukin-6 and monocyte-lymphocyte ratios as a prognosis in the treatment of pulmonary TB. Research hypothesis: (1) There is an effect of adding Omega-3 on sputum conversion in the treatment of pulmonary TB; (2) There is an effect of adding Omega-3 on the reduction of IL-6 levels in the treatment of pulmonary TB; (3) There is an effect of adding Omega-3 on reducing MLR in the treatment of pulmonary TB; (4) There is an influence of adding Omega-3 on increasing BMI in the treatment of pulmonary TB.

Methods

This research is an experimental study which aims to analyze the effect of adding Omega-3 supplements on sputum conversion, BMI, IL-6 levels and MLR values in the treatment of pulmonary TB. The research objectives were achieved through intervention in the treatment group and control group.

Population, Sample and Sampling Technique

The population in this study were pulmonary TB patients who were confirmed based on bacteriological examination (sputum BTA) who underwent treatment at the Ulin Banjarmasin Regional Hospital and the Pekauman Community Health Center for the period September 2023 to August 2024.

The research sample was a population of TB patients who met the inclusion and exclusion criteria taken using the method of consecutive *sampling.* Inclusion Criteria: (1) Patients aged over 18 years; (2) The diagnosis of pulmonary TB is made based on bacteriological examination; (3) The patient received pulmonary TB treatment with a standard OAT regimen; (4) Patients who have never received OAT before, do not have relapsed pulmonary TB; (5) Patients whose weight and height can be measured; (6) Pulmonary TB patients who have had routine blood tests before receiving OAT; (7) Willing to sign *informed consent.* Exclusion Criteria: (1) The patient took Omega-3 supplements in the last month; (2) Have a history of allergies to Omega-3, sea fish or sea fish products; (3) The patient is taking immunosuppressant drugs and/or antiplatelet drugs; (4) Patients with comorbid HIV and/or malignancies; (5) Pregnant or breastfeeding patient. In experimental research, not many formulas have been

developed to determine the required sample size. In this study, to determine the required sample size, it was calculated using the Federer formula as follows:[69]

$(n-1)(r-1) \geq 15$

Note: n = sample size for each group

r = number of groups

Based on the results of calculations using the Federer formula above, the sample size for this study was 16 samples in each group.

Research Variables and Operational Definitions

In this study, the independent variable is Omega-3 supplementation, while the dependent variables are sputum conversion, interleukin-6 (IL-6) levels, monocyte-to-lymphocyte ratio (MLR), and intima-media thickness (IMT). Potential confounding variables include daily nutrient intake, the presence of comorbidities, and the severity of pulmonary tuberculosis (TB), all of which could influence the outcomes and must be carefully controlled or accounted for during analysis.

Research Instrument

The equipment used in this study includes personal protective equipment such as N95 masks and examination gloves; sputum examination equipment like sputum pots; blood examination equipment, including purple cap tubes, 5 cc syringes, tourniquets, alcohol swabs, and plasters; and tools for measuring body mass index, such as body scales and height measuring devices. Additionally, IL-6 examination requires red cap tubes, 5 cc syringes, a centrifuge, and test cartridges, while MLR examination uses purple cap tubes, 5 cc syringes, tourniquets, alcohol swabs, and plasters. Omega-3 supplements containing 600 mg (EPA 180 mg and DHA 120 mg) are administered, and a data collection form is used to record all relevant information. The research was conducted at the Ulin Hospital, Banjarmasin and the Pekauman Community Health Center, Banjarmasin. The research period starts from September 2023 – August 2024 or until the sample size is met.

Data Collection Procedures

The research procedures include preparing the study proposal, obtaining approval from the ethics commission, and collecting primary data, which involves conducting direct interviews, gathering anthropometric measurements (height and weight), and performing blood laboratory tests to measure IL-6, monocyte, and lymphocyte levels from pulmonary tuberculosis patients at Ulin Regional Hospital, Banjarmasin, and Pekauman Community Health Center, Banjarmasin, during the period from September 2023 to August 2024.

Data Analysis

The data obtained will be subjected to univariate analysis to assess the distribution of the data and each research variable. Univariate analysis will then be explained through descriptive statistics so that mean, median and standard deviation data can be obtained in the form of tables or graphs. The data obtained will first be tested for normality, if when the normality test is carried out the data obtained is normally distributed, then an unpaired parametric test will be carried out using the *Independent T-test*, if the data distribution is not normally distributed, a non-paired non-parametric test is used *Mann whitney.* Ethical permission was obtained with the approval and consideration of the Ethics Commission of the Faculty of Medicine, Lambung Mangkurat University and the Ethics Commission of the Research and Development Agency of Ulin Hospital, Banjarmasin.

Results and Discussion

Conversion Characteristics, IL-6, MLR and IMT

Table 1. Conversion at Week 4 and Week 8

Variable	Sputum BTA	Total (n=32)		Control (n=16)		Treatment (n=16)	
		n	%	n	%	n	%
Sputum M4	Neg	30	93.75	14	87.50	16	100.0
	Pos	2	6.25	2	12.50	0	0.0
Sputum M8	Neg	31	96.88	15	93.75	16	100.0
	Pos	1	3.12	1	6.25	0	0.0

Table 1 shows the characteristics of sputum conversion at week 4 and week 8. At the 4th week of examination in the control group, it was found that 14 samples (87.50%) experienced negative sputum conversion and 2 samples (12.50%) remained positive, while in the treatment group all samples experienced negative sputum conversion (100%). At the 8th week of examination in the control group, 15 samples (93.75%) had negative conversion and 1 sample (6.25%) remained positive, and in the treatment group all samples had negative sputum conversion (100%).

Table 2. Characteristics of IL-6, MLR and BMI Values

Variable	Total	Control	Treatment
IL-6 (median) (pg/mL)			
Week 0	15.99	11.7	17.8
Week 4	7.93	6.21	8.66
Week 8	5.13	6.36	4.39
MLR (median)			
Week 0	0.64	0.61	0.64
Week 4	0.43	0.40	0.46
Week 8	0.45	0.53	0.37
IMT (median) (kg/m2)			
Week 0	18.23	18.49	17.97
Week 4	18.67	18.82	18.52
Week 8	19.01	19.01	19.02

Table 2 and figure 1 show that IL-6 levels in the control group were 11.7 at week 0, then decreased to 6.21 at week 4 and to 6.36 at week 8. Meanwhile, in the treatment group, IL-6 levels were obtained at 17.8 at week 0, then decreased to 8.66 at week 4 and to 4.39 at week 8.

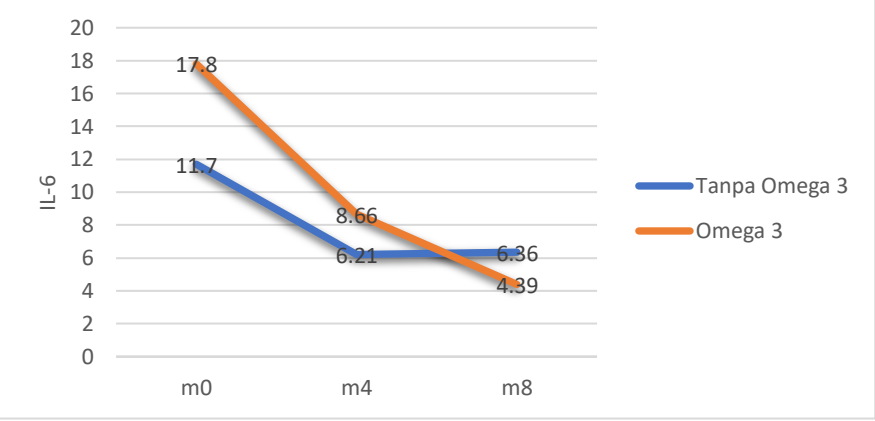

Figure 1. IL-6 Up to Graphics

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Table 2 and figure 2 show that the MLR value in the control group was 0.61 at week 0, then decreased to 0.40 at week 4 and to 0.53 at week 8. Meanwhile, in the treatment group, the MLR value was 0.64 at week 0, then decreased to 0.46 at week 4 and to 0.37 at week 8.

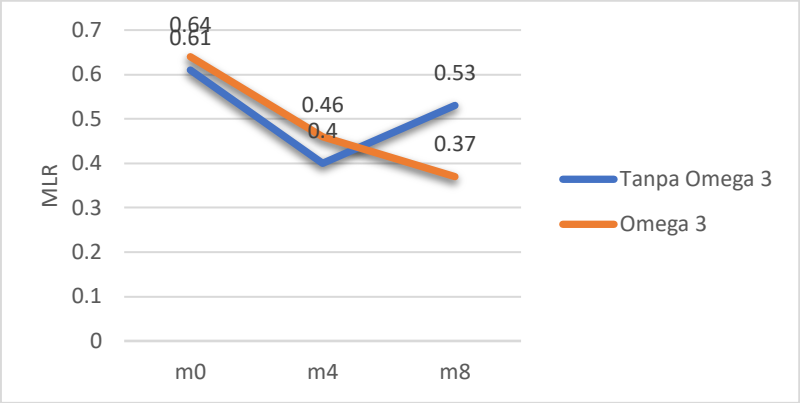

Figure 2. MLR Value Chart

In the BMI variable, the initial examination obtained by the control group was 18.49, then it increased to 18.82 in the 4th week and to 19.01 in the 8th week. Meanwhile, in the treatment group, the initial examination obtained was 17.97, then increased to 18.52 in the 4th week and to 19.02 in the 8th week.

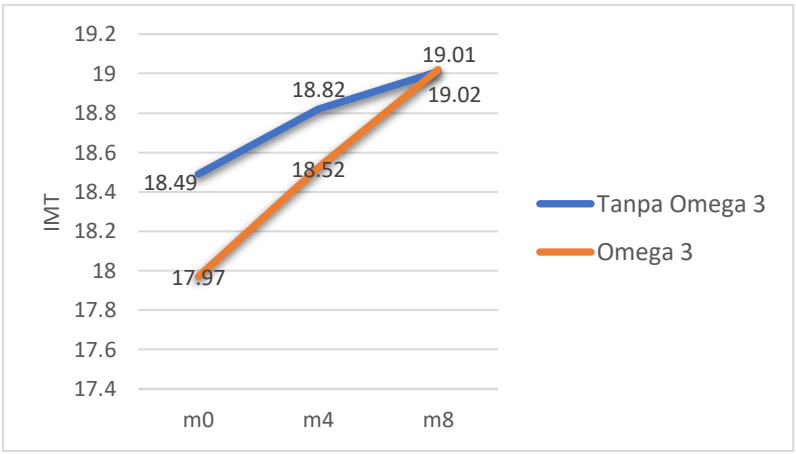

Figure 3. Graphic IMT

Normality Test

Test normality using the method Shapiro Wilk. Data is normally distributed if the significance value is >0.05.

Table 3. Normality Test Results

Variable	Shapiro-Wilk			Information
	Statistics	N	Say.	
IL6 M4	0.621	32	0.000	Not Normally Distributed
IL6 M8	0.795	32	0.000	Not Normally Distributed
MLR M4	0.903	32	0.007	Not Normally Distributed
MLR M8	0.926	32	0.031	Not Normally Distributed
IMT M4	0.941	32	0.081	Normally distributed
IMT M8	0.945	32	0.103	Normally distributed

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The results of the normality test obtained a significance value of <0.05 in the variables of Interleukin-6 (IL-6) levels and monocyte lymphocyte ratio (MLR) values, so that the data were not normally distributed. Therefore, this variable is analyzed by test Mann Whitney. Meanwhile, for the BMI variable, the results of the normality test obtained a significance value of >0.05 so that the BMI data was normally distributed. Therefore, the BMI variable was analyzed using a test Independent T test.

Effect of Additional Omega-3 Therapy on Sputum Conversion

Table 4. Fisher Exact Test of Sputum Conversion Variables

Variable	Control		Treatment		p
	n	%	n	%	
Sputum BTA week 4					
Negative	14	87.5	16	100	0.484
Positive	2	12.5	0	0.0	
Sputum BTA week 8					
Negative	15	93.75	16	100	1.000
Positive	1	6.25	0	0.0	

Table 4 shows statistics using tests Fisher Exact There was no significant effect of the addition of Omega-3 on sputum conversion in pulmonary TB patients both at the 4th week (= 0.484) and 8 weeks (p= 1.000).

Effect of Additional Omega-3 Therapy on IL-6

Table 5. Mann Whitney Test Variable IL-6 Levels

Variable	Control	Treatment	p
Delta IL-6 m0-m4	17.06	15.94	0.734
Delta IL-6 m4-m8	20.63	12.38	0.013

Table 5. shows statistics using tests Mann Whitney there was no significant effect of Omega-3 addition on the decrease of IL-6 in monitoring from week 0 to week 4 (p= 0.734), but there was a significant influence on monitoring from week 4 to week 8 (p= 0.013) pulmonary TB treatment.

Effect of Additional Omega-3 Therapy on MLR

Table 6. Mann Whitney Test Variable Monocyte Lymphocyte Ratio

Variable	Control	Treatment	p
Delta MLR m0-m4	16.34	16.66	0.925
Delta MLR m4-m8	11.84	21.26	0.005

Table 6. shows statistically using Mann Whitney tests there was no significant effect of Omega-3 addition on the decrease of MLR in monitoring from week 0 to week 4 (p= 0.925), but there was a significant influence on monitoring from week 4 to week 8 (p= 0.005) pulmonary TB treatment.

Effect of Additional Omega-3 Therapy on BMI

Table 7. Independent T Test for BMI Variables

Variable	Control	Treatment	p
Delta IMT m0-m4	32.69	54.69	0.047
Delta IMT m4-m8	19.31	49.94	0.452

Table 7 shows statistics using tests Independent T-test there is an influence of the addition of Omega-3 on the increase in IMT during the monitoring from week 0 to week 4 (p= 0.047), but at the 4th week to 8th week monitoring (p= 0.452) there was no effect on increasing BMI.

Effect of Adding Omega-3 on Sputum Conversion

Omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have properties that can overcome inflammation and are able to induce increased bactericidal activity so that they can reduce the number of bacteria and are associated with increasing the phagocytic ability of immune cells (Mahendrani et al., 2020). So it can be assumed that additional administration of Omega-3 can help sputum conversion in tuberculosis patients. In this study, if we look at the sputum conversion data, the treatment group that received the addition of Omega-3 experienced 100% sputum conversion in the 4th week, whereas in the control it was only 87.5%, however statistically there was no significant difference.

(Mahendrani et al., 2020) in his article states that the conversion of BTA sputum to negative at the end of the intensive phase of treatment is influenced by several internal factors such as education and income level, gender, compliance, patient nutritional status, smoking status, and comorbidities. Then external factors can also influence the conversion of BTA sputum in anti-tuberculosis treatment such as environmental conditions, BTA positivity level, medication taking supervisors (PMO), and availability of drugs in health facilities. Apart from that, (Murthy et al., 2018) his research also stated that there are several things that can cause delays in sputum conversion, namely compliance with taking medication, education, initial laboratory tests, comorbidities, nutrition, and unhealthy lifestyles.

In this study, data was not recorded related to the severity of TB, such as chest x-rays and BTA positivity rates. (Murthy et al., 2018) in his research stated that the radiological severity reflects the overall disease severity in pulmonary TB with a positive smear. The proportion of lung fields affected at diagnosis of pulmonary TB was associated with greater AFB smear grade and that the presence of cavitation together with the percentage of lung fields affected on chest radiograph, predicted a positive smear 2 months into treatment. This information provides an explanation that the chest x-ray data and BTA positivity rate which were not recorded in this study may be related to the statistical results which stated that the addition of Omega-3 did not have a significant effect on sputum conversion because the severity of TB may vary in the samples of this study.

Another thing that can cause there to be no significant effect of adding Omega-3 on sputum conversion is comorbidities Diabetes Mellitus (DM) (Inui et al., 2021). From this research data, it is known that the treatment group had more samples with comorbid DM. In addition to being a risk factor for increased incidence of active TB, the concomitant presence of DM worsens treatment outcomes even in already treated patients. In the pre-insulin era, the most common cause of death in DM other than diabetic coma was co-infection with TB. The incidence of DM can increase the risk of treatment failure, death and recurrence (Giorda et al., 2008).

In this study, the entire sample had a BMI below normal, this condition could be a disturbing factor so that the addition of Omega-3 did not significantly affect sputum conversion. Poor nutrition was also significantly associated with treatment failure, including death and longer time to sputum culture conversion (Holtz et al., 2006). Severe pulmonary TB events can lead to the formation of bilateral cavitation in the lung parenchyma, which can be associated with a higher mycobacterial load and increase the likelihood of a longer negative sputum conversion time. Therefore, nutritional counseling and supplementation during TB treatment are associated with improved immune function and bacterial clearance that may promote early sputum conversion (Wagnew et al., 2023).

The Effect of Omega-3 Supplementation on the Reduction of IL-6 Levels

In this study, the results showed that Omega-3 could have a significant effect on reducing IL-6 during the 4th to 8th week of observation of pulmonary TB treatment. The cytokine IL-6 can be pro-inflammatory or anti-inflammatory and is produced around tuberculosis infection. According to Calder (2010), The mechanism for reducing cytokines by Omega-3 fatty acids involves eicosanoid mediators, prostaglandins E1 and E2. The anti-inflammatory effects of EPA and DHA include competitive inhibition of arachidonic acid, a metabolite involved in promoting inflammation and possibly also inhibiting leukocyte migratory activity, through changes in cytoskeletal components. Resolvin and protection are lipid mediators derived from EPA and DHA through the action of lipoxygenase.

Increasing attention has been directed towards the function of Omega-3 PUFA as ligands for peroxisome proliferator activated receptor (PPAR) which regulates genes involved in lipid metabolism and anti-inflammatory responses, Omega-3 PUFA is a PPAR agonist. Inhibition of expression nuclear factor kappa-B (NF-κB), a transcription factor important for the synthesis of inflammatory cytokines and adhesion molecules, has been implicated with Omega 3 PUFA intake (Ramirez et al., 2013). Elevated cytokines can occur in tuberculosis and are a common phenomenon in TB patients. Increased levels of inflammatory cytokines increase significantly in severe TB and this increase in inflammatory cytokines is associated with lung inflammation and further lung damage (Boni et al., 2022). So giving Omega-3 can be predicted to reduce the risk of further lung damage in pulmonary TB in the future (King, 2021).

Omega-3 fatty acids, EPA and DHA, have antibacterial effects and play a role in treating inflammation in tuberculosis (Nienaber et al., 2021). Omega-3 can significantly reduce IL-6 cytokine levels, improve immunoregulation and anti-inflammatory conditions, supporting Omega-3 fatty acids as a potential therapeutic agent for immunodeficiency-related diseases (Alshatwi & Subash-Babu, 2018). Omega-3 fatty acids can also act as an energy source for immune cells to use as a key factor in forming an immune response (Akkerman et al., 2020). IL-6 expression was higher in patients newly diagnosed with tuberculosis. Therefore, IL-6 can be used as a suitable marker to differentiate active and latent TB status and monitor treatment efficiency in tuberculosis (Gunasekaran et al., 2025).

Effect of Adding Omega-3 on MLR

The data from this study shows that the addition of Omega-3 can have a statistically significant effect on reducing the MLR value during the 4th to 8th week of observation of pulmonary TB treatment. Monocytes are leukocytes that can differentiate into macrophages and dendritic cells which have three main functions in the immune system, namely phagocytosis, antigen presentation and cytokine production. After leaving the bone marrow, monocytes circulate in the bloodstream for about 1-3 days, then move to tissues throughout the body where they differentiate into macrophages and dendritic cells. Monocytes are important defense components that play a critical role in the innate immune response (Bieber & Autenrieth, 2015). The heterogeneous nature of monocytes and their ability to differentiate into monocyte-derived macrophages or monocyte-derived dendritic cells enable them to serve as a bridge between innate and adaptive immune responses.

Lymphocytes are found in blood and lymph, which is a colorless fluid in the lymphatic vessels that connect lymph nodes to each other and to the bloodstream. T cells, B cells and natural killer (NK) are different forms of lymphocytes, each of these cells plays a fundamental role in the function of the immune system, influencing the immune system's response to foreign substances such as invading microorganisms. Deviation of the lymphocyte count from the reference value may indicate an abnormal condition. The monocyte to lymphocyte ratio is considered an important criterion for determining a person's immune efficiency during infectious conditions and is easily measured by peripheral blood examination.

In MTB infection, an increase in the monocyte to lymphocyte ratio indicates the severity of active TB. The ratio of monocytes to lymphocytes can also be an indicator of the effectiveness of treatment in tuberculosis. (Meital et al., 2019) states that Omega-3 can help reduce the number of monocytes and increase the activity of lymphocytes, potentially changing this ratio to be more balanced and supporting the healing process. The effects of Omega-3 work by: (a) competing with arachidonic acid (AA) in the biosynthesis of pro-inflammatory mediator molecules, (b) suppressing nuclear factor kappa-B (NF-κB) which is pro-inflammatory through signaling modulation toll-like receptor 4 (TLR4) and activation Peroxisome proliferator-activated receptor gamma (PPAR γ), (c) and metabolism to pro-resolution lipid mediators (resolvin, protectin, maresin).

In general, the results of this study suggest that MLR can be used as a simple examination to help confirm a TB diagnosis and as a tool to monitor the TB treatment process. As in Adane's research et al., which states that MLR is an important biomarker for identifying TB and monitoring the effectiveness of anti-TB therapy. Choudhary et al. 2019, also mentioned that MLR can be a useful diagnostic tool to help establish tuberculosis in settings where microbiological confirmation is not accessible.

Zelmer et al., in his research revealed that although the monocyte to lymphocyte ratio has been shown to be associated with the risk of TB disease, the monocyte to lymphocyte ratio is a nonspecific marker of inflammation in several populations, including HIV-infected pregnant women, people starting antiretroviral therapy, BCG-vaccinated infants, and adolescents latently infected with TB.[109] From this data, it can be concluded that pregnant women, people with HIV and latent TB are not advised to carry out MLR examination as an additional examination to help diagnose tuberculosis and serve as an indicator of the severity of tuberculosis. In this study, the results showed a decrease in MLR values in line with a decrease in IL-6 levels in tuberculosis patients. This opens up opportunities for MLR to become an easier and cheaper examination to help monitor treatment.

Effect of adding Omega-3 on increasing BMI

The results of this study statistically show that there is a significant effect of adding Omega-3 on increasing the BMI of pulmonary TB patients during the 0th to 4th week of monitoring. Research conducted by (Moradi et al., 2022) suggests that Omega-3 supplementation increases the sensation of hunger, which can increase carbohydrate intake. Apart from that, Omega-3 also increases the desire to eat sweet foods. (Damsbo-Svendsen et al., 2013) the research results also show that Omega-3 fatty acids can increase appetite.

These findings are potentially beneficial for patients with compromised nutritional status. A central nervous system that has high levels of Omega-3 can modulate central nervous system function. Several studies have shown that Omega-3 intake can influence monoaminergic neurotransmission involved in appetite regulation. The sensation of hunger is related to long-term energy balance and can be influenced by Omega-3 fatty acids. Omega-3 supplementation for three weeks increased the sensation of hunger (and desire to eat), and also reduced the feeling of fullness. Genetic factors that influence metabolism (including PPARγ) may influence the sensation of hunger and increased appetite.

Increasing the BMI of tuberculosis patients can reduce the mortality rate in tuberculosis. Yen et al., suggested that being overweight was not significantly associated with the risk of death, but that being underweight was significantly associated with a higher risk of TB-specific and non-TB-specific mortality during treatment. These findings suggest that, to reduce TB-specific and non-TB-specific mortality, comprehensive care should be provided to underweight patients during TB treatment.[113] The addition of Omega-3 in this study can significantly increase the BMI of pulmonary TB patients, so that the addition of Omega-3 to pulmonary TB treatment can indirectly reduce the mortality rate from tuberculosis.

Research Limitations

The limitation of this research is that researchers have not been able to fully control disturbing factors that can influence research results, such as age, smoking habits, severity of disease and comorbidities. This limitation needs to be taken into consideration in preparing further research

Conclusion

Based on the analysis of the effect of adding Omega-3 on sputum conversion, IL-6 levels, MLR and BMI values in the treatment of pulmonary TB, the following conclusions can be given : Pertama, There was an effect of adding Omega-3 on sputum conversion at monitoring week 0 to week 4 (100% vs. 87.5%), and monitoring week 4 to week 8 (100% vs. 93.8%) of pulmonary TB treatment, but the statistical test was not significant. Kedua, There was a significant effect of adding Omega-3 on reducing IL-6 levels during monitoring weeks 4 to 8 of pulmonary TB treatment (p= 0.012). Ketiga, There was a significant effect of adding Omega-3 on reducing MLR at week 4 to week 8 of pulmonary TB treatment (p= 0.004). Keempat, There is an effect of adding Omega-3 on the increase in BMI on p during monitoring from week 0 to week 4 of pulmonary TB treatment (p= 0.047).

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