eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Comparison of Omega-3 Serum Level between Hiv-Aids Patients along with Their Clinical Profiles and Healthy Population in Mohammad Hoesin General Hospital Palembang

Lidiawati Handayani[1], Harun Hudari[1*], Eddy Mart Salim[1], Erial Bahar[2], Nova Kurniati[1], Zulkhair Ali[1], Ferry Usnizar[1]

[1]Department of Internal Medicine, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2]Department of Anatomy, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
HIV-AIDS
Healthy population
Omega-3

***Corresponding author:**
Harun Hudari

E-mail address:
Drharunh@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.32539/bsm.v5i4.382

ABSTRACT

Background: Human Immunodeficiency Virus (HIV) infection has been a concerning health problem worldwide. It causes reduction in body immune system and inflammation that can affect its clinical profile. Undergoing ARV therapy patients causes intestine microbiota dysbiosis and translocation that lead to imperfect absorbtion of fatty acid. One way to control microbiota dysbiosis is by controlling the nutritional factor, especially with omega-3. However, different regions upstands different custom in fish consumption especially those of which are rich in omega-3. The purpose of this research is to compare omega-3 serum level between HIV-AIDS patients and healthy population, as well as analyzing the correlation of omega-3 serum level with of HIV-AIDS patient clinical profile. **Methods:** The research will be applying observational analytic study using comparative study approach which will be performed in Tropical Infection Internal Medicine polyclinic and Medical Check-Up Polyclinic in RSMH Palembang starting from April 2020 until January 2021. Sample consisted of 32 HIV-AIDS patients from 20-58 years of age and 16 healthy population from 27-35 years of age on whom will be performed physical examination as well as clinical profile and omega-3 serum level examination. All data processing and analysis will be performed using SPSS v.25 for windows. **Results:** Out of 32 HIV-AIDS patients, we obtained low omega-3 serum level with median value at 3 (2-4) Umol/L, while in healthy population was 4 (3-6) Umol/L. Multivariate analysis inferred that the lower omega-3 serum level correlated with HIV-AIDS stage, duration of ARV therapy, blood pressure, and sex. **Conclusion:** Omega-3 serum levels in HIV-AIDS patients were lower than the healthy population. There was a correlation between omega-3 serum levels and their clinical profile of HIV-AIDS patients in Mohammad Hoesin General Hospital Palembang.

1. Introduction

Human Immunodeficiency Virus (HIV) infection is still a concerning health problem around the world. This viral infection causes acquired immunodeficiency syndromes (AIDS).[1] The HIV specifically infects CD4+ T cells which ultimately causes the death of these cells and severe immune deficiency in infected and inflammatory individuals.[2] If the inflammatory process in the body is allowed to continue without the intervention of anti-inflammatory and anti-oxidant intake in the body has an impact on increasing the risk of complications of HIV-AIDS.[3]

Annually, there is an increase in the number of reported HIV-AIDS cases from 2005 to 2019. The cumulative number of HIV-AIDS from 1987 to June 2019 was 117,064. In South Sumatra province until the end of 2017, there were 2,810 HIV-AIDS patients, making it the province with the fourth-highest number of HIV-AIDS patients in Sumatra after North Sumatra, Riau Islands, and Riau.[1]

The 2019 Ministry of Health Regulation states that

the provision of Anti-retroviral (ARV) therapy to HIV-AIDS patients is considered effective in preventing the reduction of CD4+ T cells levels in the body of people with HIV-AIDS.[9] However, ARV therapy has an impact on the balance of intestinal microbiota production (dysbiosis) in the body. The gut microbiota has an important role in the development of HIV-AIDS because of its role on the translocation of the formation of intestinal bacteria such as lipopolysaccharide in the blood. Lipopolysaccharide can activate CD4+ T cells and HIV-AIDS specifically infects CD4+ T cells. Dinh et al found that ARVs alone have an impact on the dynamism in the gut microbiota, and in chronic HIV-AIDS patients have an increase in intestinal microbiota translocation that can cause systemic inflammation.[4]

Tuddenham et al claimed that patients with chronic HIV-AIDS infection and are having undergoing ARV therapy exhibit intestinal dysbiosis associated with increased microbial translocation and their study found a significant association between an organism and specific markers of microbial translocation and systemic inflammation. Intestinal microbiota dysbiosis also affects the process of fat absorption in the liver, bile, and intestines. This absorption disorder may directly reduce the absorption of macronutrient intake, especially fat.[5]

Several studies[6-8] concluded that the decrease in CD4+ T cells in HIV-AIDS patients would lead to an increase in pro-inflammatory cytokines such as Interleukin-6 (IL-6), Interleukin-8 (IL-8), and nuclear factor Kappa Beta (NFκβ). Acute and chronic systemic infections reinforced with opportunistic infections will potentially cause an increase in oxidative stress accompanied by an increase in Reactive Oxidative Species (ROS). Hence, it needs antioxidant supplementation to reduce free radicals and anti-inflammatory to suppress the growth of excessive pro-inflammatory cytokines in the body. One of the supplements that contain antioxidants and anti-inflammatory is omega-3.[4]

Low omega-3 serum levels in HIV-AIDS patients can be caused by the effects of decreased CD4+ T cells levels. The phenomenon may cause intestinal microbiota dysbiosis and translocation. Eventually, they all have an impact on incomplete fatty acid absorption. On the other hand, people with HIV-AIDS tend to have less nutritional intake because systemic inflammation in the body increases leptin which reduces appetite. Omega-3 (PUFA and MUFA) play an important role as an anti-inflammatory and antioxidant, especially in people with HIV-AIDS.[7,8]

Study by Schwenger et al revealed that there were differences in serum omega-3 levels between HIV-AIDS patients and non-HIV-AIDS individuals with atherosclerosis. Serum omega-3 levels in 60 HIV-AIDS patients were 1.25μmol ±2, whereas non-HIV-AIDS individuals were 2.5 μmol ±1.5. Although both groups had low omega-3 serum levels, HIV-AIDS patients had lower omega-3 serum levels.6 Several studies have also concluded that the level of omega-3 serum levels in HIV-AIDS patients was correlated with their clinical manifestation.[6]

Patients with HIV-AIDS who undergo a decrease in the body's immune system may affect their clinical manifestation. The clinical profile and pattern of opportunistic infections in HIV-AIDS patients vary from one patient to another. Opportunistic infections might come in the forms of oral candidiasis, pulmonary tuberculosis, herpes zoster, carinii pneumocystic pneumonia, or toxoplasmosis cerebri. Rames et al found that the clinical profile significantly correlated with the clinical stage in people with HIV-AIDS.[7]

Although Indonesia is a culture-rich country, not every region has a practice of consuming fish, especially deep-sea fish which has a very high level of omega-3. On the other hand, in Indonesia, there has been no publication of specific research that asseses omega-3 serum levels in HIV-AIDS patients. Based on the preceding background, the researchers would like to compare omega-3 serum levels and clinical profiles between HIV-AIDS patients and the healthy population at Mohammad Hoesin General Hospital Palembang.

2. Methods

This research is an observational analytic study with a comparative study approach which was conducted at the Tropical Infectious Internal Medicine polyclinic and the Medical Check-up polyclinic at

RSMH Palembang between April 2020 to January 2021. The samples were divided into two groups, namely the case group, and the control group. The case group was all HIV-AIDS patients who met the inclusion criteria including all HIV-AIDS patients who had received ARV therapy and routine control to the RSMH Tropical Infection polyclinic, aged over 18 years, and were willing to participate consensually. The control group was a healthy population who did medical check-up at Mohammad Hoesin General Hospital Palembang. Samples of 32 people living with HIV-AIDS and 16 healthy population whom will be performed physical examination, and cheked on clinical profiles, and serum omega-3 levels. All data processing and analysis in this study used the SPSS version 25 for Windows.

3. Results

About 48 samples were obtained of which 32 (66.7%) samples were HIV-AIDS positive and 16 (33.3%) samples were healthy population. Table 1 describes the general characteristics of the research subjects. Chi-square analysis showed that there was a significant difference between omega-3 serum levels in HIV-AIDS patients and the healthy population.

Table 1. Research subjects' general characteristics

Characteristics	Group (n=48)				*P
	HIV-AIDS patients		Healthy population		
	n (%)	Median(min-max)	n (%)	Median(min-max)	
Sex					0,161[a]
Male	25(71,4)		10(28,6)		
Female	7(53,8)		6(46,2)		
Age		31(20-58)		30(27-35)	0,569[b]
<35 years old	24(64,9)		13(35,1)		0,461[a]
≥35 years old	8(72,7)		3(27,3)		
BMI		20(15,2-25,7)		22,9(16,6-27,8)	**0,003[b]**
Normal	14(66,7)		7(33,3)		**0,025[a]**
Underweight	12(92,3)		1(7,7)		
Overweight	6(42,9)		8(57,1)		
Omega-3 (Umol/L)		3 (2-4)		4(3-6)	**0,000[b]**
Normal (≥4)	5(31,3)		11(68,7)		**0,000[a]**
Low (<4)	27(84,4)		5(15,6)		

a) Chi square; b) Mann whitney, p-value sig if <0,05

Omega-3 serum levels in HIV-AIDS patients along with their clinical profiles at RSMH Palembang can be inferred to table 2. The results of the bivariate analysis found that age, duration of ARV therapy, and HIV-AIDS stage were significantly associated with omega-3 serum levels. HIV-AIDS stage was dominated with stage 3, which was as many as 22 (84.6%) samples. Moreover, the higher the stage of the disease also had low omega-3 serum levels.

Table 2. Serum omega-3 level in HIV-AIDS patients and their clinical profiles

Characteristic	Omega 3 (n=32)				p
	Low (<4Umol/L)		Normal (≥4Umol/L)		
	n (%)	Median(min-max)	n (%)	Median(min-max)	
Age					**0,043** [a]
<35 years old	21(87,5)	3(2-3)	3(12,5)	4(4-4)	
≥35 years old	6(75)	3(2-3)	2(25)	4(4-4)	
Sex					0,633 [a]
Male	21(84)	3(2-3)	4(16)	4(4-4)	
Female	6(85,7)	3(2-3)	1(14,3)	4(4-4)	
BMI					0,655 [c]
Normal	11(78,6)	3(2-3)	3(21,4)	4(4-4)	
Underweight	11(91,7)	3(2-3)	1(8,3)	4(4-4)	
Overweight	5(83,3)	3(2-3)	1(16,7)	4(4-4)	
Comorbidities					0,893 [c]

Hypertension	5(83,3)	3(2-3)	1(16,7)	4(4-4)	
Diabetes melitus	2(100)	3(2-3)	0	-	
Absent	20(83)	3(2-3)	4(17)	4(4-4)	
Opportunitic infection					0,536 [c]
Oral Candidiasis	9(75)	3(2-3)	3(25)	4(4-4)	
Tuberculosis (TB)	8(88,9)	3(2-3)	1(11,1)	4(4-4)	
Oral Candidiasis + TB	1(100)	3(2-3)	0		
Oral Candidiasis + PPE	2(66,7)	3(2-3)	1(33,3)	4(4-4)	
Absent	7(100)	3(2-3)	0	-	
Duration of ARV therapy					**0,033[a]**
≤ 1 year	19(95)	3(2-3)	1(5)	4(4-4)	
> 1 year	8(66,7)	3(2-3)	4(33.3)	4(4-4)	
Blood pressure					0,401[a]
Normal	22(81,5)	3(2-3)	5(18,5)	4(4-4)	
High	5(100)	3(2-3)	0(0 %)	-	
HIV-AIDS Stage					**0,042[c]**
2	0	-	1(100)	4(4-4)	
3	22(84,6)	3(2-3)	4(15,4)	4(4-4)	
4	5(100)	3(2-3)	0	-	
Pulse (beats/min)		84(82-96)		82(76-96)	0,361[b]
Respiratory rate (/min)		20(18-29)		20(20-20)	1,000 [b]
Body temperature (°C)		36,7(36,5-37)		36,6(36,2-27,8)	0,268 [b]

[a] Fisher exact, [b] Mann Whitney, [c] Chi square p-value sig if <0,05

Table 3 describes the results of the linear regression of multivariate analysis test. The results of multivariate analysis showed that the duration of ARV therapy, blood pressure, sex, and the stage of HIV-AIDS correlated with omega-3 serum levels in HIV-AIDS patients.

Table 3. Linear regression of clinical profiles correlated with serum omega-3 level in HIV-AIDS patients

Model		Unstandardized Coefficients		Standardized Coefficients	Sig.	95,0% Confidence Interval for B		R
		B	Std. Error	Beta		Lower Bound	Upper Bound	
7	Constant	4.205	.573		.000	3.024	5.385	
	Duration of ARV therapy	-.281	.141	-.219	.057	-.572	.009	**-.370**
	Blood pressure	.341	.173	.196	.060	-.015	.698	**.367**
	Sex	-.281	.134	-.193	.046	-.556	-.005	**-.386**
	Stage of disease	-.778	.136	-.512	.000	-1.058	-.498	**-.753**

Omega-3 serum levels in healthy population can be seen in table 4. Fisher's exact test results showed that there was a significant relationship between age and omega-3 serum levels in healthy population.

Table 4. Serum Omega-3 level in healthy population and their clinical profiles

Characteristic	Omega 3 (n=16)				p
	Low (<4Umol/L)		Normal (≥4Umol/L)		
	n (%)	Median (Min-max)	n (%)	Median (Min-max)	
Age					**0,040[a]**
<35 years old	4(30,8)	3(3-3)	9(69,2)	5(4-5)	
≥35 years old	1(33,3)	3(3-3)	2(66.7)	4(4-4)	
Sex					0,231[a]
Male	4(40)	3(3-3)	6(60)	5(4-6)	
Female	1(16,7)	3(3-3)	5(83,3)	5(4-5)	
BMI					0,1396[c]
Normal	4(57,1)	3(3-3)	3(42,9)	5(4-6)	
Underweight	0	3(3-3)	1(100)	5(5-5)	

Overweight	1(12,5)	3(3-3)	7(87,5)	5(4-6)	
Pulse (beats/min)		70(60-78)		60(54-88)	0,625[b]
Respiratory rate (/min)		20(20-22)		20(20-29)	0,643[b]
Body temperature (°C)		36,7(26,5-36,8)		36,7(36,4-36,8)	0,142[b]

[a] Fisher exact, [b] Mann Whitney, [c] Chi square p-value sig if <0,05

Table 5 presents differences in omega-3 serum levels between HIV-AIDS patients and healthy population. The Chi-square test showed that there was a significant difference in omega-3 serum levels between HIV-AIDS patients and healthy population (p=0.001).

Table 5. Difference and correlation between serum omega-3 level and study group

Group	Omega-3 (n=48)				OR (Lower-upper)	R	P
	Low (<4 Umol/L)		Normal (≥4 Umol/L)				
	n (%)	Median (Min-max)	n (%)	Median (Min-max)			
Healthy population	5(15,6)	3(3-3)	11(68,8)	5(4-6)	**11,8(2,8-49,3)**	**-0,62**	**0,001[a]**
HIV-AIDS patients	27(84,4)	3(2-3)	5(31,2)	4(4-4)			**0,000[b]**

[a]Chi-square, [b]Mann-whitney, p value sig. if <0.05 Odd ratio (OR) with confident interval (CI) 95%, R correlation very weak if r<0,2, weak if r=0,21-0,4, moderate if r=0,41-0,6, strong if r=0,61-0,8 and very strong jika >0,8

Consistent with this, the Mann-Whitney test also showed that there was a significant difference in omega-3 serum levels between HIV-AIDS patients and the healthy population (Tabel 5). Based on the risk analysis test, the odd ratio value and the strength of the strong negative correlation (r=-0.62) concluded that HIV-AIDS patients have the potential to beget omega-3 serum levels 11.8 times lower than the healthy population.

The hypothesis of this study is that Omega-3 serum levels in HIV-AIDS patients are lower than in the healthy population at Mohammad Hoesin General Hospital Palembang. The hypothesis was accepted because the median omega-3 serum level in HIV-AIDS patients was 3(2-4) µmol/L while in the healthy population it was 4(3-6) µmol/L.

4. Discussion

Based on the results of multivariate analysis, HIV-AIDS stage had a strong negative correlation with omega-3 serum levels, whereas ARV therapy duration, blood pressure, and gender had a weak negative correlation with serum omega-3 levels. HIV-AIDS patients were detectable low in omega-3 serum levels (<40% or below 5 µmol/L) and correlates with opportunistic infections.[9] A meta-analysis study conducted by Foggacci et al in 2020 similarly found that low omega-3 serum levels in HIV-AIDS patients correlated with their blood pressure. Filipovic et al in 2019 observed omega-3 serum levels on blood pressure in a healthy population and found that individuals with high omega-3 serum levels tend to have lower blood pressure.[10]

The lower the omega-3 serum levels, the more severe the clinical profile of HIV-AIDS patients. The patients may experience conditions with various kinds of acute and chronic inflammation which produce various kinds of pro-inflammatory cytokines and even ended with cytokine storms. EPA and DHA in omega-3 are anti-inflammatory that can suppress NFKβ, substances which produce pro-inflammatory cytokines. ALA is an antioxidant that can eradicate free radicals and oxidative stress, which in turn controls the production of reactive oxygen species (ROS). Excessive ROS will disrupt endothelial and mitochondrial function and the dysfunction may cause systemic inflammation that leads to systemic disease and complications, reflected in the clinical profile.[11-13]

There was a significant relationship between age and omega-3 serum levels in healthy population. This

study is in line with Filipovic's research which assumed that in a healthy population, the older the age the lower the omega-3 serum level.

There was a significant difference in omega-3 serum levels between HIV-AIDS patients and the healthy population (p=0.001). In line with this study, Schwenger et al (2019) described the differences in omega-3 serum levels between group with HIV-AIDS and group without HIV-AIDS with atherosclerosis. Serum omega-3 levels in 60 HIV-AIDS patients were 1.25 µmol ±2 while the group without HIV-AIDS with atherosclerosis was 2.5 µmol ±1.5. Although both groups had low omega-3 serum levels, in HIV-AIDS patients the omega-3 serum levels were much lower.6 Waymack et al in 2019 concluded that the percentage of omega-3 serum levels in HIV-AIDS patients also correlated with their clinical profiles.[3]

Tuddenham et al (2020) in their meta-analysis concluded that patients who have chronic HIV-AIDS infection and are undergoing ARV therapy exhibit intestinal dysbiosis associated with increased microbial translocation. The study also mentioned there was a significant association between specific markers of microbial translocation and systemic inflammation. Intestinal microbiota dysbiosis also affects the process of fat absorption in the liver, bile, and intestines. This absorption disorder may directly reduce the absorption of macronutrient intake, especially fat.[5]

The low level of serum omega-3 in HIV-AIDS patients can be caused by the effect of decreased CD4+ T cells levels which causes intestinal microbiota dysbiosis and translocation and then consequently cause incomplete fatty acid absorption. On the other hand, HIV-AIDS patients tend to have less food intake because systemic inflammation in ther body increases leptin which reduces appetite. Omega-3 (either PUFA and MUFA) play an essential role as an anti-inflammatory agent and antioxidant, especially in people with HIV-AIDS.[7,8]

Several studies[6-8] concluded that the decrease in CD4+ T cells in HIV-AIDS patients would lead to an increase in pro-inflammatory cytokines such as Interleukin-6 (IL-6), Interleukin-8 (IL-8), and nuclear factor Kappa Beta (NFκβ). Acute and chronic systemic infections coupled with opportunistic infections may cause an increase in oxidative stress accompanied by an increase in Reactive Oxidative Species (ROS). Omega-3 with its antioxidant trait can reduce free radicals and as an anti-inflammatory agent is able to suppress the growth of excessive pro-inflammatory cytokines in the body.[4]

5. Conclusion

Omega-3 serum levels in HIV-AIDS patients are lower than the healthy population at RSMH Palembang. Omega-3 serum levels in a healthy population are related to age. There is a weak correlation between omega-3 serum levels and their clinical profile of HIV-AIDS patients in Mohammad Hoesin General Hospital Palembang.

6. References

1. Harahap, Syaiful W. HIV/AIDS Tertinggi di 10 Provinsi. Situs Berita Online Tagar ID. Juni 2019, https://www.tagar.id/penyebaran-hivaids-tertinggi-di-10-provinsi diakses pada 25 Februari 2020
2. Ersha, Riry Febrina; Ahmad, Armen. Human Immunodeficiency Virus–acquired immunodeficiency syndrome with Kaposi Sarcoma. Jurnal Kesehatan Andalas, 2018, 7: 131-134.
3. Waymack, James R.; Sundareshan, Vidya. Acquired immune deficiency syndrome (AIDS). In: StatPearls [Internet]. StatPearls Publishing, 2019.
4. Dinh, Duy M., et al. Intestinal microbiota, microbial translocation, and systemic inflammation in chronic HIV infection. The Journal of infectious diseases, 2015, 211.1: 19-27.
5. Tuddenham, Susan A., et al. The Impact of human immunodeficiency virus infection on gut microbiota α-diversity: An Individual-level Meta-analysis. Clinical Infectious Diseases, 2020, 70.4: 615-627.

6. Schwenger, Katherine JP, et al. Relationships between atherosclerosis and plasma antioxidant micronutrients or red blood cell polyunsaturated fatty acids in people living with HIV. Nutrients, 2019, 11.6: 1292.
7. Ramesh, K.; Gandhi, Sangeetha; Rao, Vishwas. Clinical profile of human immunodeficiency virus patients with opportunistic infections: A descriptive case series study. International Journal of Applied and Basic Medical Research, 2015, 5.2: 119.
8. Sepkowitz.KA. AIDS-The first 20 Years. The New England Journal Medicine.2001;344(23):1764-72
9. Godoy, Guilherme, et al. Decreased Docosahexaenoic acid levels in serum of HIV carrier patients. Journal of Medicinal Food, 2020.
10. Filipovic, Mark G., et al. Whole blood omega-3 fatty acid concentrations are inversely associated with blood pressure in young, healthy adults. Journal of hypertension, 2018, 36.7: 1548.
11. Fava, Maurizio. Omega-3 fatty acids for MDD with high inflammation: A Personalized Approach Principal Investigators: Mark H. Rapaport, MD, Emory University David Mischoulon, MD, PhD and. 2020.
12. Lorke, Malin, et al. Effect of antioxidants, mitochondrial cofactors and omega-3 fatty acids on telomere length and kinematic joint mobility in young and old shepherd dogs–A randomized, blinded and placebo-controlled study. Research in Veterinary Science, 2020.
13. Farood, Muhammad A., et al. Intake of omega-3 formulation EPA: DHA 6: 1 by old rats for 2 weeks improved endothelium-dependent relaxations and normalized the expression level of ACE/AT1R/NADPH oxidase and the formation of ROS in the mesenteric artery. Biochemical Pharmacology, 2020, 173: 113749.