

# Correlation of Vitamin B12 and D with Neurocognitive Function in HIV/AIDS Patients in H. Adam Malik General Hospital Medan

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## ABSTRACT

**Objective:** To analyze the correlation between levels of vitamins B12 and D with neurocognitive function in HIV/AIDS patients who are outpatients at the PUSYANSUS polyclinic, H. Adam Malik General Hospital Medan.

**Method:** Data were analyzed using Shapiro-Wilk test statistics to evaluate the normality distribution of numerical variables, Pearson correlation test if data were normally distributed or Spearman correlation test if data were not normally distributed.

**Results:** From the research subjects were 30 people, it was found that the majority of respondents were 17 women, with the most education status being SMA 14 people. The mean age of the patients was 34.8 6.86 years, with the median BMI of respondents being 25.2 kg/m<sup>2</sup>. Vitamin B12 levels had a median value of 511.5 ng/mL, where the majority of respondents had normal levels of 25 people. Neurocognitive function has a median score for the MMSE is 28.5, with the majority of respondents showing a normal score of 27 people.

Otherwise, the mean MoCA-Ina score was 24.17 4.28, with the majority of respondents showing an abnormal score of 18 people.

**Conclusion:** There was no significant correlation between vitamin B12 and D levels

with neurocognitive function based on MMSE and MoCA-Ina scores ( $p > 0.05$ ) in HIV/AIDS patients.

**Keywords:** HIV/AIDS, vitamin B12, vitamin D, neurocognitive function, MMSE, MoCA-Ina

## INTRODUCTION

Human Immunodeficiency Virus (HIV) is a type of virus that attacks human immune system and can acquired immunodeficiency syndrome (AIDS).<sup>[1]</sup> Based on WHO data in 2018, there are an estimated 640,000 people living with HIV /AIDS in Indonesia.<sup>[2]</sup> Data from Ministry of health in North Sumatra recorded that there were 9,362 people who had HIV/ AIDS in North Sumatra Province in 2018.

Infection of HIV causes a many neurological complications including a cognitive deficit called HIV-Associated Neurocognitive Disorders (HAND). The involvement of HIV in the Central Nervous System (CNS), interferes daily activities and causes poorer quality of life. Some subclassification of HAND are: Asymptomatic Neurocognitive Impairment (ANI), HIV-related Mild Neurocognitive Disorder (MND), and HIV-Associated Dementia (HAD).<sup>[3]</sup>

The high prevalence of HAND forms of ANI and MND was also found in patients undergoing a the combination of Antiretroviral Therapy (cART).<sup>[4,5]</sup> A study conducted by Fitri and Aldy Rambe in determining the correlation between Cluster of Differentiation 4 (CD4) lymphocytes and cognitive function in HIV/AIDS patients with a cross-sectional method and involved 48 HIV/AIDS patients who undergo physical, neurological and Montreal Cognitive Assessment-Indonesian version (MoCA-Ina).<sup>[6]</sup> Other study conducted by Fitri and Aldy Rambe in determining found a correlation between plasma Cluster of Differentiation 4 (CD4) lymphocytes and duration of antiretroviral (ARV) treatment, opportunistic infection and cognitive function in HIV/AIDS patients.<sup>[7]</sup>

Vitamin B12 affects metabolism of homocysteine. Vitamin B12 and/or folate deficiency is a marker of increased homocysteine levels.<sup>[8]</sup> A study on HIV-negative populations in older adults without dementia found higher vitamin B12 levels and lower homocysteine levels were associated with reduced rates of brain volume loss over 6 years.<sup>[9]</sup> Several recent studies showed a significant correlation between decreased vitamin B12 ( $378.5 \pm 151.8$ ) and neurocognitive disorders specifically in impaired executive function and the speed of psychomotor processes.<sup>[10]</sup> Another study also showed 13.7% of HIV/AIDS patients with mild neurocognitive disorders with a Mini Mental State Examination (MMSE) score of <24 had low levels of vitamin B12, which was interestingly dominated by women (62.4%) with an older age range of >55 years (67.8%). Levels of vitamin B12 are mild deficiencies (200-350 pg/mL; 28.7%), moderate deficiency (100-200 pg/mL; 56%) and severe deficiency (50-100 pg/mL;

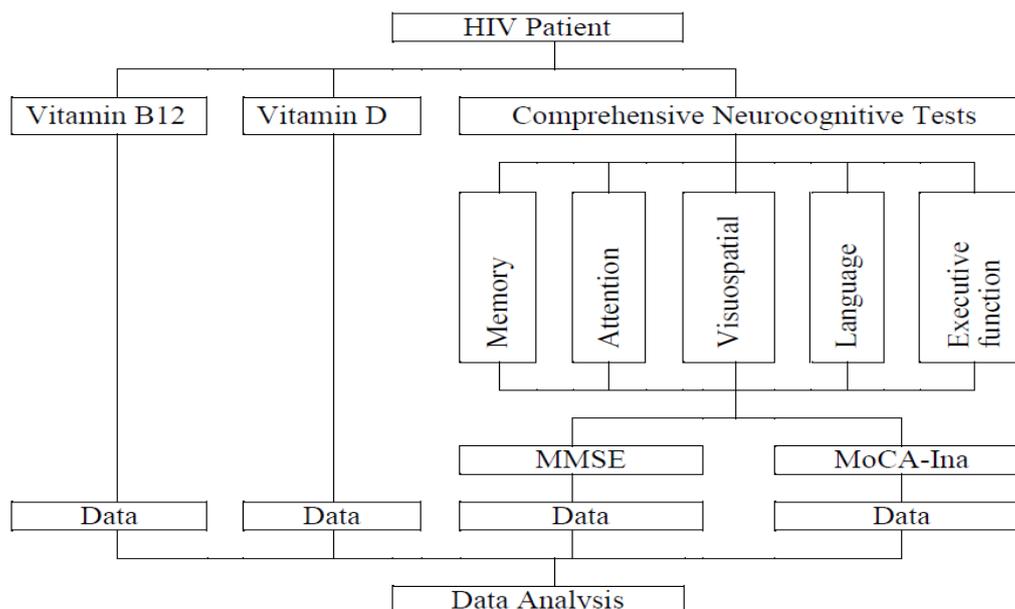
15.3%) with minimum vitamin B12 levels being 51 pg/mL.<sup>[11]</sup> Even though more research is needed to confirm this data.<sup>[12]</sup>

Population of HIV/AIDS who were in middle age had risk of various concomitant diseases typically seen in the elderly population, including weakness, metabolic syndrome, osteoporosis and pathological fractures, insulin resistance, diabetes, cardiovascular disease, and cognitive impairment which have also been associated with deficiency of vitamin D. Some recently studies showed deficiency of Vitamin D had a correlation HIV/AIDS infection and certain antiretroviral therapies. The purpose of the study was to analyze the correlation between vitamin B12 and D levels with neurocognitive function in HIV/AIDS patients who were treated at the Haji Adam Malik Medan

## **MATERIAL AND METHODS**

This study is an analytical study to determine the correlation between vitamin B12 and D levels with neurocognitive function in HIV / AIDS patients conducted at Haji Adam Malik Hospital after receiving approval from the Health Research Ethics Commission.

The samples of the study were HIV/AIDS patients who underwent treatment at Haji Adam Malik Hospital Medan during sampling time. All data were categorized into independent variables, namely vitamin B12 and D levels and dependent variables for neurocognitive function. Pearson test was used to see the correlation of vitamin B12 and D levels with neurocognitive function disorders if the data was normal and Spearman correlation tests if the data was not distributed normally. A value of  $p < 0.05$  with a 95% confidence interval was considered statistically significant.



Picture 1. Flowchart of the Study

## RESULTS

### Research Characteristics

Thirty patients who met the inclusion and exclusion criteria. The educational status of the most research subjects was high school 14 people (46.7). The average age of the patients in the study was  $34.8 \pm 6.86$  years. The median BMI value of respondents was 25.2 (20.0-40.5) kg/m<sup>2</sup>.

Table 1. Characteristics of the study

Characteristics	n (%)
Gender	
Male	13 (43,3)
Female	17 (56,7)
Education	
SD	2 (6,7)
SMP	1 (3,3)
SMA	14 (46,7)
SMK	1 (3,3)
D-3	3 (10,0)
S-1	9 (30,0)
Age (Years)	$34,8 \pm 6,86^a$
BMI (kg/m <sup>2</sup> )	$25,2 (20,0-40,5)^b$

BMI: Body Mass Index

### Vitamin B12 levels in HIV/AIDS patients

Vitamin B12 levels in HIV/AIDS patients who had a median value of 511.5 (204.0-2640.0) ng/mL, where the majority of study subjects had normal levels of 25 people (83.3%), followed by an excess of 5 people (16.7%), and none had vitamin B12 deficiency (0.0%).

Vitamin B12 levels in HIV/AIDS patients.

Table 2 Vitamin B12 levels HIV/AIDS patients

Variable	n (%)
Vitamin B12 (ng/mL)	511,5 (204,0-2640,0) *
Deficiency (<187)	0 (0,0)
Normal (187-883)	25 (83,3)
Excess (>883)	5 (16,7)

Median (Min-Max)

### Vitamin D Levels in HIV/AIDS Patients

Vitamin D levels in HIV/AIDS patients with an average of  $21.18 \pm 6.76$  ng/mL, where the study subjects experienced the most insufficiency of 26 people (86.7%), followed by normal 3 people (10.0%), deficiency 1 person (3.3%), and none of them experienced vitamin D toxicity (0.0%).

Table 3. Vitamin D levels in HIV/AIDS patients

Variable	n (%)
Vitamin D (ng/mL)	$21,18 \pm 6,76^*$
Deficiency (<10)	1 (3,3)
Insufficiency (10-30)	26 (86,7)
Normal (30-100)	3 (10,0)
Toxicity (>100)	0 (0,0)

\* Mean  $\pm$  SD

### Neurocognitive Function in HIV/AIDS Patients

Neurocognitive function in HIV/AIDS patients with a median score for MMSE was 28.5 (21-30), the majority of respondents showed a normal score of 27 people (90.0%), followed by probable 3 people (10.0%), and no patient received a definite score for MMSE (0.0%). In contrast, the average MoCA-Ina score was  $24.17 \pm 4.28$ ,

with the majority of respondents showing an abnormal score of 18 people (60.0%), and 12 people (40.0%) getting normal score of Moc-Ina.

Table 4. Neurocognitive function in HIV/AIDS patients

Variable	n (%)
MMSE	28,5 (21-30) <sup>a</sup>
Normal (24-30)	27 (90,0)
Probable (17-23)	3 (10,0)
Definite (<17)	0 (0,0)
MoCA-Ina	24,17 ± 4,28 <sup>b</sup>
Normal (≥26)	12 (40,0)
Not Normal (<26)	18 (60,0)

<sup>a)</sup> Median (Min-Maks)

<sup>b)</sup> Mean ± SD

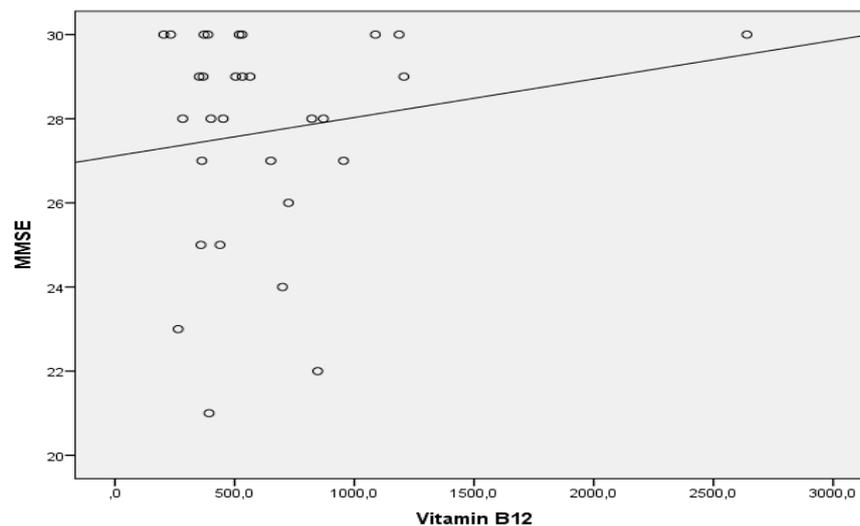
### Correlation of Vitamin B12 with Neurocognitive Function in HIV/AIDS Patients

Table 5 Demonstrated the correlation of vitamin B12 with neurocognitive function in HIV/AIDS patients. An analysis of vitamin B12 levels showed that vitamin B12 did not correlate significantly to MMSE values ( $p = 0.862$ ;  $r = 0.033$ ) or MoCA-Ina ( $p = 0.419$ ;  $r = -0.153$ ).

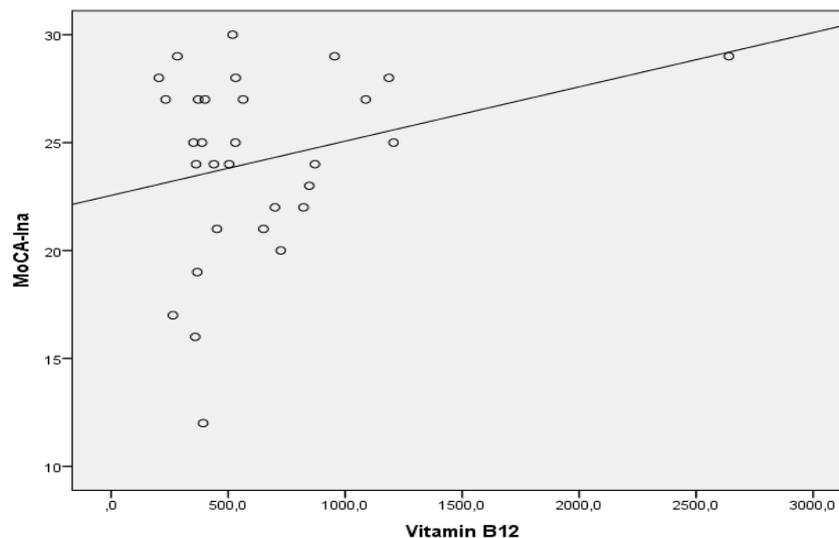
Table 5. Correlation of vitamin B12 level with neurocognitive function in HIV/AIDS patients.

	MMSE		MoCA-Ina	
	<i>p</i>	<i>R</i>	<i>p</i>	<i>R</i>
Vitamin B12 *	0,862	0,033	0,419	-0,153

\* Spearman's Rho



Picture 4.1. Correlation between Vitamin B12 and MMSE scatterplot



Picture 2. Correlation between Vitamin B12 and MoCA-Ina scatterplot

### Correlation of Vitamin D with Neurocognitive Function in HIV/AIDS Patients

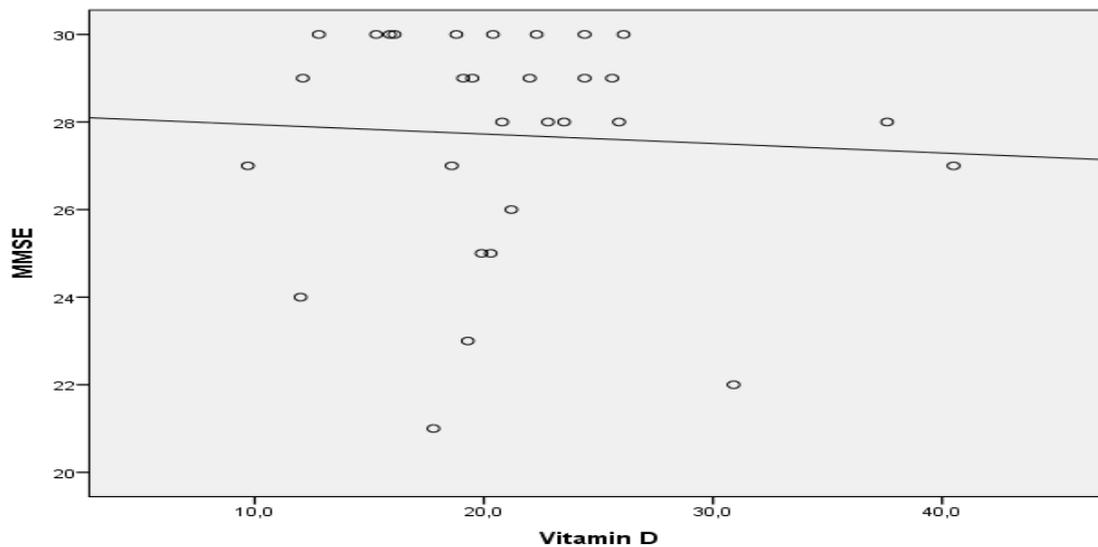
The analysis of vitamin D levels showed that vitamin D did not correlate significantly to MMSE values ( $p = 0.757$ ;  $r = -0.059$ ) or MoCA-Ina ( $p = 0.605$ ;  $r = -0.099$ ). The correlation of vitamin D with

neurocognitive function in HIV/AIDS patients is presented in table 4.7. below.

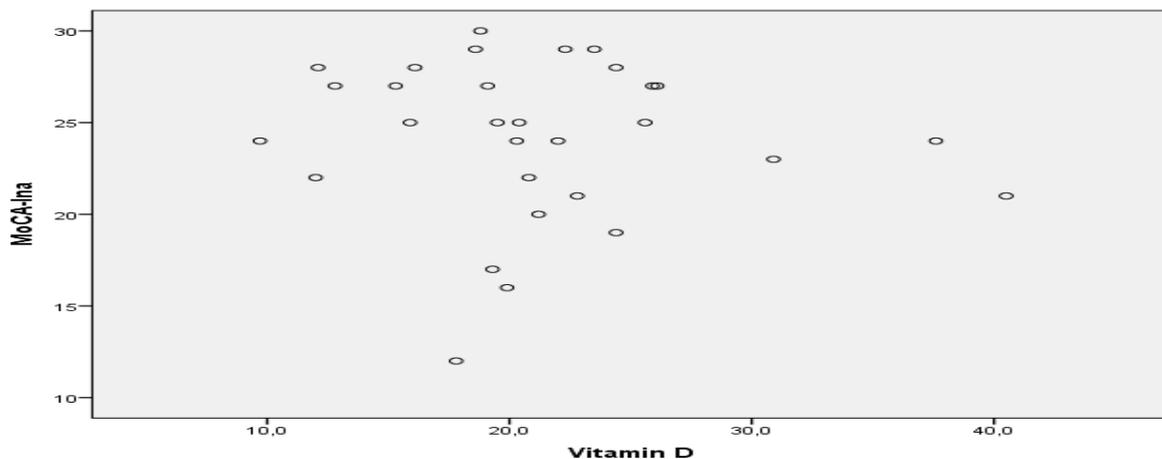
Table 6. Correlation of vitamin D with neurocognitive function in HIV/AIDS patients.

	MMSE		MoCA-Ina	
	<i>P</i>	<i>r</i>	<i>p</i>	<i>R</i>
Vitamin D*	0,757	-0,059	0,605	-0,099

\* Pearson



Picture 3. Correlation between Vitamin D and MMSE scatterplot



Picture 4. Correlation between Vitamin D and MoCA-Ina scatterplot

### DISCUSSION

There were more common in female 17 people (56.7%) than male. The results of this study are relevant to several previous studies, namely the Okafor et al which found the most HIV / AIDS patients in women (64.4%) and study by Jumare et al also found the highest incidence of HIV/AIDS in women (41.8%). (13,14)

Average age of the study was  $34.8 \pm 6.86$  years. This was relevant to various studies that report almost the same result, Suyanto et al found the age of HIV/AIDS patients between 30 - 39 years (35.92%), Jumare et al found the average age of HIV / AIDS patients was  $35 \pm 9$  years in and sumonu et al found the average age of HIV/AIDS patients was  $36.44 \pm 8.22$  years. (13,15,16)

In this study, the age of the study subjects was younger compared to studies which showed that HIV/AIDS was associated with neurocognitive disorders that gained an average of older age (>45 years). (16,17) Patients with HIV/AIDS infection perform poorly in the domains of language, memory, orientation, attention/calculation and practical relative to control ( $p < 0.05$ ). (13) The study has excluded subjects who were previously diagnosed with neurocognitive disorders before being diagnosed with HIV/AIDS. The neurocognitive function assessment in this study showed a MoCA-Ina score of the majority was abnormal in 18 people (60%). Although based on MMSE scores show probable neurocognitive disorders only in 10.0% of subjects. This can happen because the subjects of this study are stage 1 and 2 HIV/AIDS patients, where the advanced clinical stage is the main predictor of HIV/AIDS-related neurocognitive disorders. (18)

Viral load and host factors are thought to interfere with the brain's glutamate metabolism and nerve transmission which potentiates the toxicity of neurotransmitters that play an important role in the development of *HIV-Associated Neurocognitive Disorders* (HAND). In HIV/AIDS patients, the levels of glutamate are five times greater. Recent studies in patients receiving cART showed selective increases of glutamate levels in patients with HAND compared to patients without neurocognitive disorders. (19)

In addition there was also a disruption of vitamin B12 utilization that causes abnormal production of major methyl group donors in the nervous system. Immunoreactivity reactions are characterized by increased levels of the TGF- $\beta$  protein that inhibits macrophages, T lymphocytes and NK cells found in the frontal cortex of *HIV-Associated Dementia* (HAD) patients and detected in reactive astrocytes and white matter mononuclear cells in CNS of HIV/AIDS patients. (20) In advanced immunosuppression is more

commonly reported with neurocognitive disorders especially HAD. (21) Dementia is a clinical manifestation in 4-15% of patients with HAND. (22)

This study did not show a significant correlation between vitamin B12 and neurocognitive function based on MMSE or MoCA-Ina scores but some studies showed the importance of vitamin B12 in this condition, there is a methylation reaction disorder that causes neurological and psychological dysfunction. Recent research shows a link between loss of neurocognitive function and vitamin B12 deficiency especially at levels of  $< 150$  ng/mL. (23) Previous studies have shown low serum vitamin B12 levels in HIV/AIDS patients ( $154 \pm 37$  ng/mL). (24)

The average of vitamin D levels in this study was also decreased by  $21.18 \pm 6.76$  ng/mL with the majority of subjects experiencing insufficiency compared to deficiency (86.7% vs. 3.3%), although the average age of the study subjects  $< 45$  years. This confirms that decreased vitamin D levels are indeed associated with HIV/AIDS infection, although it does not show a significant correlation between low vitamin D and neurocognitive disorders.

This decrease in vitamin D levels is in line with previous research by Falasca et al with the level of vitamin D  $26.8 \pm 9.3$ . (25)

## CONCLUSION

No significant correlation was found between vitamin B12 and vitamin D levels with neurocognitive function based on MMSE and MoCA-Ina scores ( $p > 0.05$ ) in HIV/AIDS patients.

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**Conflict of Interest:** None

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