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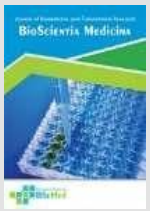

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The Relationship between Plasma Glutamate Levels and Sleep Quality in HIV Patients

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A B S T R A C T

Background: Disturbance sleep quality is often found in sufferers of human immunodeficiency virus (HIV). Disturbed sleep quality can affect immunity, which ultimately can increase patient morbidity and mortality. Impaired sleep quality in HIV sufferers is related to neurotoxicity due to the HIV virus, which damages sleep architecture. HIV infection can cause an increase in brain extracellular glutamate. Elevated glutamate plays a role in neuronal and glial damage and death. This study aimed to assess the relationship between plasma glutamate levels and sleep quality in HIV sufferers. **Methods:** The research uses a cross-sectional design. The samples were HIV sufferers in a polyclinic voluntary counseling test (VCT) internal medicine of Dr. M. Djamil General Hospital Padang, who met the inclusion and exclusion criteria. Samples are selected by consecutive methods. Sleep quality was assessed using a questionnaire called the Pittsburgh sleep quality index (PSQI). Plasma glutamate levels were measured using the ELISA method. Statistical analysis using SPSS with a p-value <0.05 was considered statistically significant. **Results:** The research sample consisted of 82 people. The median plasma glutamate level was 16.39 µg/mL. Impaired sleep quality was found in 45 (54.9%) HIV sufferers. There was no significant relationship between plasma glutamate levels (p= 0.506), age (p=0.795), gender (p=0.547), education (p=0.358), occupation (p=0.255), disease duration (p=0.348), stage (p=0.309) and type of ARV therapy (p=0.791) with sleep quality in HIV sufferers. From this research, a significant relationship was found between sleep quality, body mass index (BMI) (p= 0.015), and marital status (p= 0.039). **Conclusion:** There is no relationship between plasma glutamate levels and sleep quality in HIV sufferers. There are other factors that influence sleep quality, namely BMI and marital status.

1. Introduction

Human immunodeficiency virus (HIV) is a single-stranded RNA virus that is included in the family Retroviridae, genus Lentivirus. This virus attacks the immune system in humans, which in the long term can cause acquired immune deficiency syndrome (AIDS).[1] Impaired sleep quality is a condition often experienced by HIV sufferers.[2-4] Sleep quality is defined as an individual's satisfaction with all aspects of the sleep experience. Sleep quality has four attributes: sleep efficiency, sleep latency, sleep duration, and awakening after sleep onset.[5] Disturbed sleep quality has been shown to increase the risk of inflammation. Conversely, inflammation also causes increased sleep quality disorders.[6] The increased risk of inflammation will certainly have an impact on reducing the quality of life and increasing the morbidity and mortality of HIV sufferers.

The exact mechanism that causes sleep disturbances in HIV sufferers is not fully known, but

it is associated with neurotoxicity due to the HIV virus, which progressively destroys sleep architecture.[7] The neurotoxic effect of the HIV virus ultimately causes an increase in brain extracellular glutamate levels.[4] The accumulation of extracellular glutamate in the brain triggers an excitotoxicity cascade that leads to neuronal and glial damage and death.[8,9] Glutamate is a neurotransmitter, the main excitatory and important intermediate in brain cellular metabolism. Under normal conditions, glutamate is needed for communication between neurons. Glutamate also has neuroprotective effects by increasing factor release neurotrophic, including brain-derived nerve factor (BDNF), which is an endogenous molecule that supports the survival of neurons and promotes the growth and differentiation of new neurons and synapses.[8-10] Glutamate is also known to play a role in the regulation of the sleep-wake cycle.[11]

The role of glutamate in the pathophysiology of various diseases associated with neuronal and glial death has long been known. Hayashi, in 1954, reported that injection of glutamate into the brain or carotid arteries can cause seizures (convulsion). Research conducted by Lynch in 1997 found that excessive activation of glutamate receptors (NMDA and AMPA) plays an important role in the mechanism of amnesia. Likewise, research conducted by Gotti in 1990, Grotta in 1995, and Bordi in 1997 found glutamate hyperexcitation conditions in stroke sufferers. Other studies also found an increase in glutamate levels in sufferers with traumatic brain injury, as found in research by Toulmond in 1993, Mukhin in 1996, Scmutz in 1997, Okiyama in 1997, and Faden in 1997.[12] The importance of understanding the role of glutamate in neurological diseases is believed to provide potential insight as an antagonistic treatment for glutamatergic transmission.[8] Research on the role of glutamate in sleep disorders in HIV sufferers has never been conducted before. Based on this background, a problem formulation was formulated as to whether there is a relationship between plasma glutamate levels and sleep quality in HIV sufferers.

2. Methods

This research is research by design cross-sectional. The population of this study was HIV sufferers who were admitted to the internal medicine VCT polyclinic at Dr. M. Djamil General Hospital Padang and who met the inclusion and exclusion criteria. Inclusion criteria include patients who have been diagnosed with HIV at all stages based on WHO clinical criteria, are aged over 18 years, and are willing to take part in the research and sign informed consent, while the exclusion criteria are HIV sufferers with a history of opportunistic infections of the central nervous system, cerebrovascular disease, head trauma, and intracranial tumors, HIV sufferers undergoing hemodialysis and HIV sufferers who have not taken ARVs. The research was conducted from December 2022 to March 2023. The sample size was set at 84 people, who were divided into 2 groups, namely the group who experienced sleep quality disorders and the group without sleep quality disorders.

Examination for sleep disorders was carried out with instruments Pittsburgh sleep quality index (PSQI) on each subject. Then, a 2 cc venous blood sample was taken. The blood sample is then centrifuged to obtain a plasma sample. Examination of plasma glutamate levels using the ELISA technique was carried out at the Infectious Disease Diagnostic and Research Center Laboratory, Faculty of Medicine (FK) Universitas Andalas (Unand). This research was approved by the research ethics committee of the Faculty of Medicine, Universitas Andalas, Padang, Indonesia. Data analysis was carried out using SPSS version 25 software. Data analysis was carried out univariate and bivariate, where $p<0.05$.

3. Results

This research was conducted on 82 research samples divided into 2 groups. There were 45 samples in the group that experienced sleep quality problems and 37 samples in the group with good sleep quality. The median age of the sample was 33.5 (19-61) years. There were more men in the sample (78.0%, n= 64) than women. From measurements, Body mass index

(BMI) obtained 42% (n=35) of the sample classified normoweight, 26.8% (n=22) obese, 15.9% (n= 13) overweight, and the rest underweight. The majority of the samples in this study had quite high levels of education, namely 41 samples (50%) from tertiary institutions and 34 samples from high school (41.5%). From marital status, it is known that 43 samples (52.4%) are not married. This research sample generally already has a job (78.1%, n= 64). Based on stage, the distribution of samples was quite even, with the highest number of samples in stage 2 (35.4%, n=29). From the duration of the disease, it is known that the majority of the sample suffered from HIV for 1-<5 years (41.5%, n= 34). The median plasma glutamate level in this study sample was 16.39 µg/mL (0.34-127.59).

Table 1. Basic characteristics of research subjects.

Characteristics	**Description (n= 82)**
Age (years), median (min-max)	33,50 (19-61)
Gender, n (%)	
Male	64 (78,0%)
Female	18 (22,0%)
BMI, n (%)	
Underweight	12 (14,6%)
Normoweight	35 (42,7%)
Overweight	13 (15,9%)
Obesity I	17 (20,7%)
Obesity II	5 (6,1%)
Education level, n (%)	
Primary school	2 (2,4%)
Junior high school	5 (6,1 %)
Senior high school	34 (41,5%)
College	41 (50,0%)
Marital status, n (%)	
Single	43 (52,4%)
Divorced	8 (9,8%)
Married	31 (37,8%)
Employment status	
Not working	18 (21,9%)
Working	64 (78,1%)
Sleep quality, n (%)	
Disturbed	45 (54,9%)
Normal	37 (45,1%)
HIV stages, n (%)	
1	27 (32,9%)
2	29 (35,4%)
3-4	26 (31,7%)
Duration of disease, n (%)	
< 1 year	20 (24,4%)
1-<5 years	34 (41,5%)
5-<10 years	22 (26,8%)
≥ 10 years	6 (7,3%)
ARV therapy	
Efavirenz base	43 (52,4%)
Non-efavirenz base	39 (47,6%)
PSQI score, median (min-max)	5,00 (2-11)
Glutamate level, median (min-max)	16,39 (0,34-127,59)

The basic characteristics of the study sample were then grouped based on the presence or absence of sleep quality disorders. There were no statistically significant differences in the basic characteristics of age, gender, disease duration, disease stage, employment status, and education level between

samples with sleep quality disorders and samples without sleep quality disorders. However, statistically significant differences were seen in the characteristics of body mass index (BMI) with a value of p= 0.015 and marital status with p= 0.039 on sleep quality in HIV sufferers. There was no significant difference in plasma glutamate levels between groups with and without sleep quality disorders (p = 0.506) (OR 0.744, IK 95%, 0.311-1.779).

Table 2. Relationship between basic sample characteristics and sleep quality disorders.

Characteristics	Disturbed sleep quality (n=45)	Normal sleep quality (n=37)	OR (I 95%)	P
Age			1,179 (0,341-4,075)	0,795*
≥ 50 years, n (%)	7 (58,3%)	5 (41,7%)		
< 50 years, n (%)	38 (54,4%)	32 (45,7%)		
Gender			1,387 (0,477-4,031)	0,547*
Female, n (%)	11 (61,1%)	7 (38,9%)		
Male, n (%)	34 (53,1%)	30 (46,9%)		
BMI				0,015*
Underweight, n (%)	11 (91,7%)	1 (8,3%)		
Normoweight, n (%)	20 (57,1%)	15 (42,9%)		
Overweight, n (%)	3 (23,1%)	10 (76,9%)		
Grade I obesity	9 (52,9%)	8 (47,1%)		
Grade II obesity	2 (40%)	3 (60,0%)		
Education			2,188 (0,399-11,991)	0,358*
< 12 years	5 (71,4%)	2 (28,6%)		
≥ 12 years	40 (53,3%)	35 (46,7%)		
Marital status				0,039*
Single	25 (58,1%)	18 (41,9%)		
Divorced	1 (12,5%)	7 (87,5%)		
Married	19 (61,3%)	12 (38,7%)		
Employment status			1,879 (0,628-5,620)	0,255*
Not working	12 (66,7%)	6 (33,3%)		
Working	33 (51,6%)	31 (48,4%)		
Duration of the disease				0,348*
< 1 year, n (%)	14 (70,0%)	6 (30,0%)		
1-<5 years, n (%)	17 (50,0%)	17 (50,0%)		
5-<10 years, n (%)	12 (54,5%)	10 (45,5%)		
≥10 years, n (%)	2 (33,3%)	4 (66,7%)		
Disease stage				0,309*
Stage 3-4, n (%)	17 (65,4%)	9 (34,6%)		
Stage 2, n (%)	16 (55,2%)	13 (44,8%)		
Stage 1, n (%)	12 (44,4%)	15 (55,6%)		
ARV therapy			0,889 (0,372-2,124)	0,791*
Efavirenz base	23 (53,5%)	20 (46,5%)		
Non-efavirenz base	22 (56,4%)	17 (43,6%)		

Analysis after this was carried out on the variables BMI and marital status. Analysis results after this using the Tukey HSD test on the BMI variable, it was found that there were differences in sleep quality disorders in the groups overweight compared to the group underweight (p=0.005), but differences were not found when comparing other groups, whereas from the marital status variable it was known that statistically significant differences in sleep quality disturbances were found in the married group with the unmarried group (p= 0.045) and the group married and those who experienced divorce (p=0.035), but there was no difference between the unmarried group when compared with the divorced group.

Provisions regarding the normal value of glutamate in HIV sufferers are not yet available. Therefore, this study carried out calculations of cut-off point (COP) plasma glutamate levels, which are associated with

impaired sleep quality in HIV sufferers. From the analysis results, it was found that the COP of plasma glutamate levels was 16.39 µg/mL. Based on the COP value, the sample was divided into two groups. In this study, there were 41 people (50%) with plasma glutamate levels that were below the cut-off point and 41 people (50%) with plasma glutamate levels equal to or above the cut-off point. In the group with sleep quality disorders, there were 21 people (51.2%) who had plasma glutamate levels above the cut-off point. Meanwhile, in the group without sleep quality disorders, there were 20 people (41.5%) who had plasma glutamate levels above the cut-off point. The results of the Chi-square test showed that there was no significant difference in plasma glutamate levels between groups with and without sleep quality disorders (p = 0.506), as well as odds ratio (OR) equal to 0,744, CI 95%, 0,311-1,779.

Table 3. The relationship between plasma glutamate levels and the incidence of sleep quality disorders in HIV sufferers.

Variable	Sleep quality (PSQI)		P-value	OR (CI95%)
	Disturbed (n= 45)	Normal (n= 37)		
Plasma glutamate levels			0,506*	0,744 (0,311-1,779)
≥ cut-off point	21 (51,2%)	20 (48,8%)		
< cut-off point	24 (58,5%)	17 (41,5%)		

4. Discussion

This research was conducted on 82 samples of HIV sufferers, of which 45 samples (54.9%) experienced sleep quality problems. This is in line with the results of research by Bedaso in 2020, which found the prevalence of sleep disorders in HIV sufferers was 57.6%. Previous research by Gamaldo in 2013 on the HIV population in the United States found that 56% of HIV sufferers experienced sleep quality problems. Similar results were also found by Estrada in 2018 in the HIV population in Mexico, where 58.6% of sufferers experienced sleep quality problems.[13-15] The prevalence of sleep quality disorders in HIV sufferers is much higher compared to that in the general population, which is only around 10%.[4,16]

Analysis of the age variable in this study showed that 58.3% of HIV sufferers aged the same or more than 50 years experienced sleep quality problems. Research by Bedaso in 2020 on the HIV population in Ethiopia found that the risk of sleep disorders increased with increasing age. The risk of sleep disorders in HIV sufferers aged between 55-64 years is 5.7 times, while for those aged ≥ 65, it is 6.6 times when compared to younger age groups.[15]

Neurophysiological and neurochemical changes involving the brainstem ARAS system, thalamus, and hypothalamus, along with certain cortical regions, contribute to age-related sleep disorders. The main promoter for the initiation and maintenance of sleep involves a small group of cells in the preoptic region of the hypothalamus, which produce the inhibitory neuropeptide galanin. The number of galanin-expressing neurons within the preoptic area of the hypothalamus significantly decreases with age. The severity of loss of these cells at post-mortem examination predicts the severity of sleep fragmentation in old age. The main promoters for wakefulness are found in the brainstem ARAS system and the lateral hypothalamic area, which expresses orexin/hypocretin. These two areas, which collectively help maintain a stable waking state, also experience age-related decline. This may be partly responsible for the worsening instability between sleep-wake cycles. Beyond changes in sleep-wake regulation, reduced nighttime sleep time in older individuals is associated with thinning gray matter in the superior temporal and

frontolateral cortex.[17]

Several factors contribute to age-related sleep disorders, including obesity, decreased immunity, medical comorbidities, and psychological and socio-economic factors, including retirement from work, resulting in poor sleep quality. Types of age-related sleep disorders include earlier bedtimes, shorter duration of nighttime sleep, increased frequency of naps, increased number of nighttime awakenings and time spent awake at night, and decreased slow-wave sleep.[15,18-20] The results of bivariate analysis of the age factor in this study did not show significant results between groups with and without sleep quality disorders. This condition is caused by uneven sample proportions where the research sample is dominated by sufferers aged <50 years.

Based on gender, the largest proportion of sleep quality disorders in this study were experienced by women (61.1%) compared to men (53.1%). Research by Valero in 2017 on the general population obtained the same results where gender differences also influence a person's sleep quality, where women are more at risk of experiencing sleep quality disorders than men. This difference can be caused by hormonal changes experienced by women during puberty, pregnancy, and menopause, which cause physical and psychological changes that can increase the incidence of sleep-related problems.[19,21] Previous research conducted by Krishnan in 2006 found that gender differences in sleep became clear after puberty. The menstrual cycle, pregnancy, and menopause can change sleep architecture. The types of sleep disorders that are commonly found related to gender differences are obstructive sleep apnea (OSA), insomnia, and restless leg syndrome.[22] No significant relationship was found between gender and sleep quality disorders in this study due to the small number of female samples compared to male samples.

From this research, it was found that there was a significant influence of BMI on sleep quality. An increase in BMI is associated with the risk of occurrence of obstructive sleep apnea (OSA).[23] Najafi's 2021 research on the HIV patient population in Tehran found that BMI had a significant influence on the incidence of obstructive sleep apnea (OSA) in HIV sufferers. The study stated that compared with normal weight, obesity (BMI ≥ 30 kg/m^2) increased the risk of OSA (OR [95% CI]: 2.54 [1.10–5.89]). A cross-sectional study, which Gutierrez conducted in 2019 on the HIV population in Philadelphia, United States, also obtained similar results. More than half of the participants in their study had moderate to high risk for OSA, which was also associated with more metabolic correlates, including hypertension, diabetes, and higher BMI.[24,25]

The effect of obesity on sleep disorders is two-way where being overweight can cause sleep quality problems, whereas sleep quality disorders increase the risk of obesity. OSA is the most common sleep disorder found in obese sufferers. In obese sufferers, fat deposits in the upper respiratory tract make it difficult to breathe during sleep, causing OSA.[23] Research by Beccuti in 2011 showed that poor sleep quality can increase the risk of obesity. The association between sleep and obesity is likely mediated by the role of the orexin system, which is inhibited by sleep-inducing neurons in the ventrolateral preoptic area (VLPO) containing GABA. Orexigenic neurons, located in the lateral hypothalamic (LHA) and posterior hypothalamic (PH) regions, play a major role in the maintenance of arousal by activating the ARAS and the entire cerebral cortex and modulating central nervous system nuclei and other structures involved in sleep-wake regulation. Orexin activity is also involved in the regulation of feeding by increasing the drive for homeostatic and non-homeostatic food intake.[26]

There was no statistically significant difference in education level between groups with and without sleep quality disorders in this study sample. This result is in accordance with what was obtained from a study of a large population of HIV patients in Brazil conducted by Allavena 2015, where the level of education did not affect the quality of sleep of sufferers. Different results were obtained by Cunha in 2022, who conducted research on 385 HIV patients.

This research found a relationship between low levels of education (<8 years) and sleep disorders. Previous research by Ren in 2018 on a population of HIV sufferers in China also found a significant relationship between education level and sleep quality. This research concluded that the lower the level of education, the more susceptible one is to experiencing sleep disorders.[27-29]

The relationship between education level and sleep quality is associated with several factors, such as economic stress, limited access to health care, lack of knowledge about sleep hygiene, and an environment that does not support good sleep. Low education levels are associated with lower economic status and income, longer working hours, physically demanding jobs, stressful work environments, limited access lack of quality health services, delays in the treatment of chronic medical conditions that can cause sleep disorders, as dirty and crowded living environments that do not support good sleep.[30-34] The difference in results in this study occurred because the majority of the study sample (91.4%, n= 75) had studied for ≥ 12 years. Although not statistically significant, in this study, it appears that 71.4% of patients with less than 12 years of education experienced problems with sleep quality. Sufferers in this group were 2.18 times more likely to experience problems with sleep quality compared to HIV sufferers with education. ≥12 years.

From this study, there was no significant relationship between work and sleep quality disorders. These results are in accordance with Nokes' research in 2001, which stated that the sleep quality of HIV sufferers was not influenced by age, occupation, and mode of HIV transmission.[35] Different results were found from Najafi's research in 2021, which found that employment status was an independent factor influencing sleep quality in HIV sufferers, whereas unemployed sufferers tend to have poor sleep quality. Unemployment in HIV sufferers is related to social factors and demographics, including younger age, lower education levels, and the presence of stigma in society. Poverty is also a chronic stressor that can disrupt a person's physical and mental health, affecting the quality of life and the quality of sleep.[24] Previous research by Jabbari in 2015 found that sleep quality in HIV sufferers was influenced by education and employment status.[24,36]

In this study, it was found that there was a statistically significant influence of marital status on sleep quality disorders in HIV sufferers. A large population cohort study of HIV patients conducted by Allavena in 2015 found the same thing, where marital status had a significant influence on sleep quality. This study found that unmarried HIV sufferers had poorer sleep quality. Contradictory results were obtained by Najafi in 2021, who found no significant relationship between marital status and sleep quality in the HIV population in Tehran, Iran. Various studies have found that married patients have better sleep quality. The presence of a supportive partner can provide emotional and psychological comfort, which can be a positive influence on sleep. Divorced or unmarried individuals may experience poorer sleep quality due to increased feelings of loneliness, stress, and emotional distress. The absence of a partner can lead to a lack of emotional support.[24,27,37]

Based on the duration of the disease, the largest proportion of sleep quality disorders in this study were experienced by sufferers who were diagnosed < 1 year (n = 70%). This proportion tends to decrease over time. the more the length of duration of HIV experienced by the sufferer. Research by Adane in 2022 found that patients with an HIV diagnosis <12 months were 4.02 times more likely to have poor sleep quality compared to those with a longer diagnosis [OR = 4.02, 95% CI: (1.604-10.070)]. Previous research by Oshinaike in 2014 and Mengistu in 2021 obtained similar results where a shorter duration of HIV diagnosis was significantly associated with poor sleep quality compared to a longer duration of diagnosis. The possible reason is that HIV-positive patients experience psychological stress and emotional disorders due to negative stigma in society. These factors may contribute to higher rates of sleep disturbance in the early months after HIV diagnosis. Impaired sleep quality is also associated with the time

when ARV drugs are initially administered, where one of the side effects of ARVs at the start of use is disturbances in sleep quality. The emergence of side effects when using ARVs also has an impact on the patient's psychology in the form of increasing the patient's concern about their health.[38-40] Different results were obtained by Ren in 2018, who found no relationship between the duration of the disease and the occurrence of sleep disorders.[28] The results obtained in the current study were not significant. It is thought to be due to the presence of other risk factors that have a greater influence on sleep quality disturbances in the early stages of the disease, such as immunity status and viremia levels.

There was no significant difference between stages and the occurrence of sleep quality disorders in HIV sufferers in this study. These results are in accordance with research conducted by Nokes in 2001 and Lee in the same year. Their research stated that there was no significant relationship between the HIV stage and disturbances in the sufferer's sleep quality. These results contradict previous research conducted by Moeller in 1991 and Darko in 1992, which found a relationship between stage and sleep disorders occurring at more advanced stages (stages 3 and 4). The advanced stage is characterized by decreased immunity and an increasing number of medical comorbidities that can interfere with sleep quality.[35,41-43] Although no significant relationship was found, in this study, it appeared that the percentage of sufferers who experienced sleep disorders increased along with the higher stage of the disease.

From this study, there was no significant relationship between ARV use and sleep quality disorders. Research on 300 HIV sufferers in Nigeria by Osiyemi in 2022 also found no significant association between factors related to HIV, one of which was the type of ARV and sleep disorders. Previous research in a large population involving 4103 HIV patients in China did not find a significant relationship between the use of ARV regimens, including efavirenz, and the occurrence of sleep quality disorders in sufferers.[43] There are differences in results with research conducted by Nunez in 2001, which found that plasma efavirenz levels ≥ 3.5 µg/ml were an independent predictor of insomnia in HIV sufferers (OR 6.3 [95% CI 1.2-32.9] p= 0.03).[44,45] Research by Fumaz in 2001 on 100 HIV patients found that sleep disturbances due to the effects of efavirenz appeared to decrease with time. In the efavirenz group, 35% reported difficulty sleeping after four weeks of therapy, 7% reported difficulty sleeping after week 24, and no subjects reported sleep problems at week 48, whereas in the placebo group, the rate of sleep disturbance was 4% at all time points studied.[46]

Neurological and neuropsychiatric reactions are the most frequent manifestations experienced by sufferers treated with efavirenz, one of the side effects being sleep disturbances. This side effect is associated with the ability of efavirenz to penetrate the BBB. Efavirenz is thought to cause neurotoxic effects, but the mechanism responsible for efavirenz-induced neurotoxicity is not yet clear, although growing evidence is associated with disturbances in mitochondrial function and bioenergetics of neurons and glia.[47] The insignificant effect of efavirenz on sleep disorders in this study is thought to be because sufferers have been taking efavirenz for quite a long time, so the side effects of sleep disorders due to the use of this drug have reduced over time.

The median plasma glutamate level in this study was 16.39 (min-max 0.34-127.59) µg/mL. There was no significant relationship between glutamate levels and sleep quality disorders in HIV sufferers in this study. This may be because the samples in this study, both in the groups with and without sleep quality disorders, were patients who regularly took ARVs and had fairly good clinical conditions. ARVs are known to suppress the development of HIV infection, increase patient immunity, prevent the emergence of neuropsychiatric symptoms such as depression and anxiety, and prevent the emergence of medical comorbidities that can disrupt the patient's sleep quality.[47]

Glutamate is an excitatory neurotransmitter that is found in abundant amounts in the brain. Glutamate is involved in various aspects of normal brain function, including cognition, learning, and memory.[8-10] Glutamate also plays a role in the initiation and maintenance of sleep and wakefulness through its role in the brainstem, lateral and basal hypothalamus forebrain. Glutamate in the brain stem regulates brain activity and maintains muscle tone during wakefulness, as well as regulating changes in the EEG and causing muscle weakness during the REM phase of sleep. Glutamate in the lateral hypothalamus participates in the system arousal by activating orexin neurons. Glutamatergic neurons in the basal forebrain take part in EEG synchronization and cause sleep deprivation. Glutamatergic neurons in the cerebral cortex are not the only target system arousal but also contribute to regulation arousal. Meanwhile, glutamatergic neurons can regulate sleep stages through interactions with other neurons, forming a complex sleep-wake regulatory network in the brain. This suggests that transitions between different phases of sleep and wakefulness have different neural circuits.[48]

There are several limitations to this research. Research is of a nature cross-sectional, so it cannot determine the causal relationship between various variables. Another limitation is that assessing sleep quality is a subjective examination. An objective examination (such as polysomnography) is needed to obtain more valid research results. This study did not assess which aspects of sleep quality were disturbed, but rather assessed sleep quality in general and there was no data regarding sleep quality before suffering from HIV. This study did not examine several HIV-related factors that may be associated with impaired sleep quality, such as CD4 levels, viral load, incidence of anxiety and depression, as well as drug abuse in the form of alcohol and other illegal substances. This study only assessed glutamate levels in plasma, while glutamate levels in CSF were not assessed. The study also did not assess other factors that could influence plasma glutamate levels, such as plasma platelet levels and increased liver enzyme levels.

5. Conclusion

From this study, it was found that the median plasma glutamate level in HIV sufferers was 16.39 µg/mL. Impaired sleep quality was found in 45 people (54.9%) of people with HIV. No significant relationship was found between plasma glutamate levels, stage and duration of disease, and the type of ARV used and sleep quality disorders in HIV sufferers. There is a meaningful relationship between values of body mass index (BMI) and marital status with sleep quality disorders in HIV sufferers.

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