GENERALIZED ANXIETY DISORDER AMONG PEOPLE LIVING WITH HIV RECEIVING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY

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Abstract: Generalized anxiety disorder is the most prevalent anxiety disorder that may worsen psychological well-being and physical conditions of people living with Human Immunodeficiency Virus (PLHIV). There is sparse knowledge on factors contributing to this mental illness for preventive measures and evidence-based interventions. The study aimed to determine the prevalence of generalized anxiety disorder or GAD and its contributing factors among PLHIV receiving Highly Active Antiretroviral Therapy (HAART). This was a cross-sectional study of 210 PLHIV who sought treatment at the Infectious Disease Clinic in one of the public hospitals in Malaysia. Patients who fulfilled the inclusion criteria and consented were assessed for socio-demographic characteristics and clinical factors using Pro Forma questionnaires and face-to-face interviews, supplemented with data from medical records. Visual analogue scale, Hospital Anxiety Depression Scale and Multidimensional Scale of Perceived Social Support were used to determine adherence to treatment, level of anxiety and level of support system, respectively. Mini International Neuropsychiatric Interview was used to diagnose GAD. 28 (13%) participants had GAD. After controlling for confounders, multivariate analysis indicated that illicit substance used in the past (AOR=4.17; p=0.003; 95% CI=1.56-9.44) and a low and moderate level of social support from significant others (AOR=3.73; p=0.002; 95% CI=1.66-10.04) were the significant contributing factors to GAD among PLHIV. In conclusion, low level support systems and illicit substance use were profound contributing factors for GAD among PLHIV. Hence, addressing these two factors, in addition to conventional HAART treatment, is crucial to ensure optimum care of this group of patients.

Keywords: Anxiety, HIV, substance use, support system

1. Introduction

HIV or human immunodeficiency virus is a virus that causes HIV infection. It attacks the body's immune system by destroying infection-fighting cells, CD4 cells. CD4 cells or cluster differentiation 4 cells are white blood cells that are important in immune systems. In advanced stage, if HIV infection is untreated, it can progress into acquired immunodeficiency syndrome (AIDS) (Centre for Disease Control and Prevention (CDC), 2019). In Malaysia, about 20% of people living with Human Immunodeficiency Virus (PLHIV) suffer from anxiety and depression, while 29% of the HIV-infected patients meet the criteria of likely anxiety disorder (Hasanah et al., 2011). This disorder predisposes PLHIV to develop challenging psychological complications such as psychosis, early dementia and suicide (Tyree et al., 2019). Considering the major negative effects of anxiety in PLHIV, it is important that this mental disorder be identified and treated early so that PLHIV patients will have better quality of life when enduring multiple difficulties with this stigmatizing disease.

Anxiety is an emotion that is characterized by anxious feelings, worried thoughts and physical changes such as increased heart rate, shortness of breath and elevated blood pressure. Those with anxiety typically have recurrent or persistent thoughts or fears. Individuals with anxiety may have difficulty controlling his or her worry and are preoccupied with overwhelming uncertainties. Impaired concentration, irritability, muscle aches and sleep problems are common symptoms of anxiety. According to globally recognized standard criteria; the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), this emotional disturbance is considered as a psychiatric disorder when

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it disturbs individual's routine functions and the symptoms continue for more than six months. Generalized Anxiety Disorder is one of the anxiety disorders manifested with free floating anxiety. Not uncommon, in serious cases, physical symptoms may become severe and manifest as panic attacks (American Psychological Association, n.d.).

Mental health professionals believe that anxiety disorder occurs as a result of multifaceted factors; intercalated between genetic and environmental factors. Focusing on PLHIV, a previous study showed that female PLHIV may have a higher risk of developing anxiety in comparison to men (Ngum et al., 2017). Other key contributing factors to anxiety were low levels of education, unemployment and marital status of being a widow/divorcee or not living with a spouse (Zeng et al., 2019). In Malaysia, non-Malay patients with HIV have lower chances of anxiety compared to the Malays (Radzniwan et al., 2016). A study conducted in a state of Kelantan, however, found that Malay patients who practice Islam have a low risk of developing anxiety (Othman et al., 2015). Perhaps, using religion as part of coping with stress may reduce the anxiety among those patients.

HIV infections damage the immune system and weaken protective mechanisms against diseases and other types of cancer in humans. Infected individuals gradually become immunodeficient as the virus destroys the immune cells and impairs their function. In general, immune function is determined by the number of CD4 cells (Word Health Organization (WHO), 2019). The associations between CD4 cells and anxiety have not been well established. In two local studies, the authors found insignificant associations between CD4 counts with anxiety (Radzniwan et al., 2016; Yee et al., 2009). Other than that, the number of HIV viral particles or viral load has also been documented as one of the important predictors for depression (Radzniwan et al., 2016) but not for anxiety disorder (Levy et al., 2019).

Having a good social support has also been found to be an essential coping mechanism for adjustment and acted as a buffer towards stress in mental and physical health among PLHIV (Hostinar & Gunnar, 2015). A previous study in Malaysia found that support system, particularly financial support, as one of the factors that contribute to common psychological disorders in patients with HIV (Yee et al., 2009). However, the study did not explore further the level of support from their families, friends and others received by the patients. There are limited local studies that investigate the support systems among PLHIV to understand proper interventions.

Patients who use illicit substance is at risk of GAD (Prior et al., 2017). Elsewhere, researchers suggested that the misuse of substances such as cannabis, amphetamine, opiate, and alcohol may associate with anxiety disorder (Pandey et al., 2017; Saye et al., 2017; Sharma et al., 2019; Turna et al., 2019). In Malaysia, alcohol consumption has been proven to be one of the factors that contribute to common psychological disorders in patients with HIV (Yee et al., 2009). However, there is limited data available to show the associations between misuse of other substance with anxiety disorder.

There are clear gaps of knowledge that local evidence on anxiety disorder among PLHIV and its contributing factors due to inadequate data. Hence, this study aims to determine the prevalence of GAD among PLHIV and investigate its contributing factors including the sociodemographic factors, clinical factors, adherence to treatment, substance misuse as well as the level of support by families, friends and significant others given to PLHIV.

2. Methodology

2.1 Study design, setting and data collection

This was a cross-sectional study to determine the prevalence of the GAD among PLHIV receiving Highly Active Antiretroviral Therapy (HAART) and its associated factors. It was carried out at the Infectious Disease Clinic of one of the public hospitals in Selangor, which provides specialised treatment for infectious diseases in Malaysia. It is a tertiary and reference hospital for infectious disease cases from the north region of Selangor. There are about 1000 patients who receive HAART per month turning up at this infectious disease clinic.

2.2 Data collection and assessment tools

Participants were selected using systematic random sampling. The inclusion criteria included PLHIV aged 18 years old and above, who came to the outpatient clinic and received HAART, and were

able to communicate in English or Bahasa Malaysia. Those who had been diagnosed with severe mental illness and had underlying malignancy were excluded from the study. Only PLHIV who voluntarily gave informed consent were enrolled in the study.

Their feelings of anxiety were screened using the Hospital Anxiety Depression Scale (HADS) (Yahya & Othman, 2015). Participants who scored eight and above for HADS were listed as cases of anxiety and considered as 'probable anxiety'. This group of participants were interviewed further using the Mini International Neuropsychiatric Interview (MINI) to confirm the diagnosis of GAD. The MINI has been used worldwide and validated locally as a structured diagnostic interview instrument. It follows the criteria of the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) (Mukhtar et al., 2012). Sociodemographic characteristics (including age, gender, ethnicity, level of education, employment status, occupation, total household income, marital status and living companion) and clinical factors (including viral load, CD4 count, adherence to medication, treatment regime, side effects of medications, co-morbid substance and duration of illness) were assessed directly from face-to-face interviews or retrieved from medical records from the hospital electronic record system. Furthermore, the visual analogue scale (VAS) and the Multidimensional Scale of Perceived Social Support (MSPSS) were used to measure adherence to treatment and level of social support from family, friends and significant others) respectively.

2.3 Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) version 23. The factors associated with GAD among PLHIV patients were analysed with simple logistic regression (SLogR) followed by multiple logistic regression (MLogR) as the data consisted of categorical variables. The sociodemographic factors, clinical factors, adherence to treatment and level of supports from family, friends and significant others were the independent variables entered into the SLogR. Variables with a p-value of less than 0.05 from the SLogR were then included in the MLogR analysis. A p-value of less than 0.05 was considered statistically significant in the MLogR. Model fitness was checked using Hosmer-Lemeshow goodness of fit test. Confounders were adjusted; interactions, multicollinearity and assumptions were also checked. The p-value of less than 0.05 with a confidence interval of 95% was taken as statistically significant.

2.4 Ethics

Ethical approval was obtained from the Medical and Research Ethics Committee of National Clinical Research Center (CRC) Ministry of Health, Medical and Research Ethics Committee (Protocol no NMRR-18-3891-44221), Faculty of Medicine Universiti Teknologi MARA Research Committee, Medical and Research Ethics Committee, Universiti Teknologi MARA, 600-IRMI 5/1/6, REC/47/19 and Medical and Research Ethics Committee of the Clinical Research Center (CRC) of the respective hospital prior to commencing the study.

3. Findings

3.1 Background of participants

Of 210 participants, the mean age of was 29.72 ± 9.98 years and more than three-quarter of the participants were male (186; 88.6%). More than half of the participants (116; 55.2%) were Malays, while the rest were Chinese (71; 33.8%), Indians (21; 10%) and others (2; 1%). Most of the participants received tertiary education (113; 53.8%), completed secondary school (86; 41%), and only less than 10% completed primary school, at (11; 5.2%). Among the participants, 134 were employed, and 16 (7.6%) were unemployed. More than half of the participants (134; 63.8%) were in the Bottom 40 economic group (B40) with the total household income of less than RM 3860; less than one-third (45; 21.4%) were in the Middle 40 economic group (M40) with the household income of between RM 3860 and RM 8319 and others (31; 14.8%) were in the Top 20 group (T20) with the income of more than RM 8319. They were mostly single (134; 63.8%) and others had a spouse (76; 36.8%) (Refer to Table 1).

3.2 Prevalence of generalized anxiety disorder

Findings showed 52 (24%) participants with probable anxiety, and among them, 28 participants were recognized to have GAD. Among cases of probable anxiety, 34 (16.2%) of PLHIV indicated mild anxiety, 15 (7.1%) moderate, and 3 (1.4%) severe level of anxiety (Refer to Figure 1).

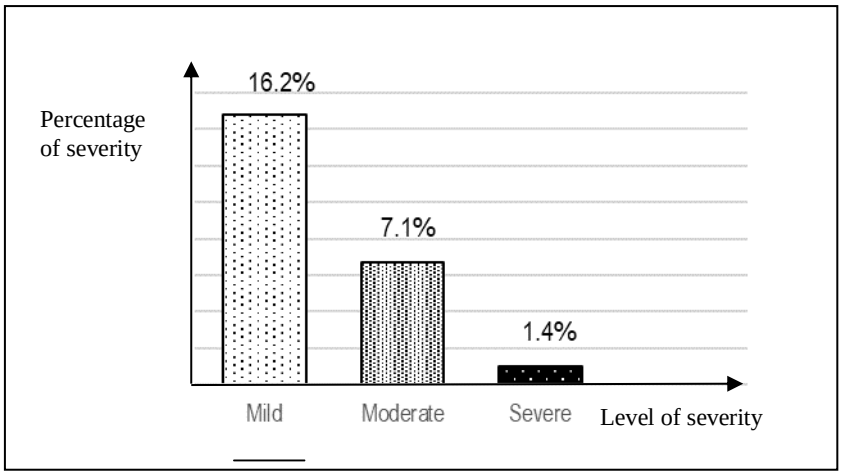

Figure 1: Severity of anxiety

3.3 Sociodemographic factors and generalized anxiety disorder

The sociodemographic factors of gender, ethnicity, religion, education level, employment status, marital and living status were categorised into two groups based on the previous studies (Radzniwan et al., 2016; Hasanah et al., 2011). The age domain was grouped into <45 and ≥ 45 years old as incidence of medical comorbidities such as hypertension, cardiovascular disease and heart failure increases in adults age 45 years and above (Yazdanyar & Newman, 2009). A study done in Malaysia about emotional state found that happiness was associated with high income level (Boo et al., 2016), thus the three levels of household income were categorised into two groups.

There were no significant association between sociodemographic factors and PLHIV who were generalised as anxiety disorder. However, Table 1 shows that more than half of the PLHIV who had GAD were less than 45 years old, male, completed primary school, single or living with a companion, and with household income of B40 and M40.

Table 1: Association of Sociodemographic Factors and GAD

Sociodemographic Factors	Generalized Anxiety Disorder				
	No (n=182)	Yes(n=28)	B	p-value	OR (95% CI)
Age					
<45 years old	122(67.0%)	24(85.7%)	0.49	0.32	1.62(0.62-4.23)
≥45 years old	60(38.0%)	4(14.3%)			
Gender					
Male	161(88.4%)	25(89.0%)	0.08	0.90	1.09(0.30-3.91)
Female	21(11.9%)	3(11.0%)			
Ethnicity					
Malay	98(53.8%)	18(64.2%)	0.43	0.30	1.54(0.68-3.53)
Non-Malay	84(46.2%)	10(35.8%)			
Religion					
Islam	101(55.5%)	19(67.8%)	0.53	0.22	1.69(0.72-3.94)
Others	81(44.5%)	9(32.2%)			
Education					
Primary school	10(5.5%)	1(3.6%)	0.45	0.67	1.57(0.19-12.76)
Secondary to tertiary	172(94.5%)	27(96.4%)			
Employment					
Employed	158(86.8%)	25(89.2%)	-0.24	0.72	0.79(0.22-2.81)
Unemployed	24(13.2%)	3(10.8%)			

Table 1: Association of Sociodemographic Factors and GAD

Sociodemographic Factors	Generalized Anxiety Disorder				
	No (n=182)	**Yes(n=28)**	**B**	**p-value**	**OR (95% CI)**
Total Household income					
B40 & M40	154(84.6%)	25(99.2%)	0.42	0.52	1.52(0.43-5.36)
T20	28(15.4%)	3(10.8%)			
Marital Status					
Single/ Widow/Separated/Divorce	130(71.4%)	22(78.5%)	0.38	0.43	1.47(0.56-3.82)
Married	52(28.6%)	6(21.5%)			
Living companion					
With companion	140(76.9%)	21(75.0%)	-0.11	0.82	0.90(0.36-2.26)
Alone	42(23.1%)	7(25.0%)			

*The Bottom 40 group (B40) = total household income less than RM 3860; the Middle 40 group (M40) = total household income between RM 3860 and RM 8319; the Top 20 group (T20) = total household income of more than RM 8319. Univariate analysis used simple logistic regression; B-beta value; p value; OR-Odds Ratio; CI-confidence interval; *significant p value <0.05; **significant p value <0.01*

3.4 Contributing factors of generalized anxiety disorder

The associations between independent variables and GAD among PLHIV were analysed using SLogR. Results revealed that the significant factors were low and moderate social support from significant others, illicit substance use in the past, having more than two side effects of the medications, CD4 counts ≥ 350 cells/ul, viral load ≥ 20 copies/ml, history of taking cannabis, illicit substance use for the past 3 months and overall low and moderate social support. Illicit substance use in the past include cannabis, inhalants (e.g., glue), amphetamine-type stimulants such as methamphetamine and ecstasy (Chie et al., 2015; Wickersham et al., 2016). MLogR generated two significant factors that predicted GAD among PLHIV. Patients with low and moderate social support from significant others had 4-times higher risk to develop GAD (AOR=4.09; p=0.002, 95%CI= 1.66-10.04). Patients with past illicit substance use had about 4-times higher risk of having GAD (AOR=3.84; p=0.003, 95%CI= 1.56-89.44). Refer table 2 for further information.

Table 2: Logistic Regression of Factors Associated with Generalized Anxiety Disorder

Variables	Simple Logistic Regressions					Multiple Logistic Regressions				
	B(df)	**p-value**	**OR[a]**	**95% CI**		**B(df)**	**p-value**	**AOR[b]**	**95% CI**	
LMSS from significant other	1.32(1)	0.003	3.73	1.65	8.93	1.41(1)	**0.002***	4.09	1.66	10.04
Illicit substance use in the past	1.25(1)	0.005	3.41	1.45	8.04	1.35(1)	**0.003***	3.84	1.56	89.44
More than 2 side effect of medications	1.27(1)	0.02	3.55	1.22	10.28	0.88(1)	0.13	2.41	0.78	7.44
CD4 counts ≥ 350 cells/ul	-0.83(1)	0.04	0.44	0.19	0.98	-0.61(1)	0.16	0.54	0.23	1.28
Viral load ≥ 20 copies/ml	0.96(1)	0.03	2.60	1.01	6.34	0.46(1)	0.93	1.59	0.55	4.59
History of taking cannabis	1.43(1)	0.03	4.17	1.14	15.30	0.98(1)	0.25	2.66	0.49	14.32
Illicit substance use for the past 3 months	1.97(1)	0.02	7.61	1.37	37.43	1.60(1)	0.11	4.97	0.70	35.20
LMSS overall	0.97(1)	0.03	2.63	1.13	6.13	-0.35(1)	0.66	0.70	0.15	3.39

Notes: *[a]Simple logistic regression; [b]Multiple logistic regression; B=beta value; CI=confidence interval; df- degree of freedom; AOR=adjusted odds ratio; OR=Odds Ratio; *significant p value <0.05; **significant p value <0.01; ATS=Amphetamine-type stimulant; LMSS=Low and moderate social support*

4. Discussion

PLHIV have to deal with many obstacles in their lives, including jobs, family relationships, and others. They require support from the family members as a source of safety, acceptance and dignity so that they feel less fear of rejection and ostracised by the family members (Tuan Abdullah et al., 2019). Therefore, acceptance and adequate support from the family members could minimise their pessimism and encourage PLHIV to cope well with stress as well as reduce the risk of having psychological disorder which is crucial for proper treatment adherence (Dejman et al., 2015). The significant others are one's closest and most trusted individuals that can be mothers, fathers, relatives and friends (Cheng & Starks, 2002). HIV is a manageable chronic condition subject to a variety of psychosocial problems.

Therefore, PLHIV need a great deal of help from others, especially closed ones. This starts at the very first moment when they receive the unfortunate news that they are infected with HIV.

Social support is an essential component for the PLHIV who have higher risk of developing GAD, especially when they live in the environment lacking social support. The lack of social support from significant ones may induce fear for PLHIV to disclose their illness which will further cause them to experience excessive worries (Evangeli & Wroe, 2017). Thus, they need reassurance and support from the significant others to reduce their anxiety (Riahi, Aliverdinia, & Pourhossein, 2011). Positive social support is a protective factor from stress and alleviates the feeling of insecurity which will reduce the risk of anxiety (Harandi et al., 2017).

Substance use in the past has a significant association with GAD. During multivariate analysis, this factor consistently showed a significant association with the odds of developing GAD increased by almost 4-times. This finding supports the previous study of the association between substance history and development of GAD in PLHIV (Chen et al., 2018). This outcome emphasizes that the use of illicit substance in the past strongly contributes to GAD. Previous systemic review and meta-analysis did not find any significant association between amphetamine use with anxiety disorder (McKetin et al., 2019) and one of the previous studies also determined that exposure to cannabis had no risk in developing anxiety disorder (Elkington et al., 2016).

There is no significant association between socio-demographic factors and GAD. However, we found that 85% of the patients with GAD were in the age group of less than 45 years old. In the study on prevalence of anxiety in chronic disease of irritable bowel syndrome, it was found that the increasing years of age has 5% less chances to develop anxiety (Byrne et al., 2017). Another study also indicated that anxiety is more prevalent in younger age compared to older age (Flint et al., 2010). The high number of anxiety disorder in patients with younger age could be related to HIV disclosure concern (Evangeli & Wroe, 2017). They face fear of being rejected and discriminated upon disclosure of the illness. Hence, exploration of the roots of anxiety among the patients with HIV would be beneficial to reduce the possibility of developing anxiety. Besides, young adults might be having ineffective coping skills compared to older individuals (Leppink et al., 2016).

Among PLHIV with GAD, 89% of them were from the household income level of B40 and M40. It is known that low-income level is associated with anxiety among people living with HIV (Duko et al., 2019) probably due to increase of financial commitment as they need to go frequently to the hospital and spend much money on transportation and other expenses. The other possible causes of anxiety among patients from B40 group could be job instability and a decline in work performance due to frequent medical leaves.

Other than that, 89% of PLHIV with GAD were single. Single patients has increased odds of having anxiety by 3.6 times compared to the patients who are married (Ngocho et al., 2019) and similar studies showed that being unmarried had 2-times higher risk to develop anxiety (Olagunju et al., 2012). HIV-infection is a chronic disease which needs endless support as patient face various social challenges.

5. Conclusion

This study suggests that the use of substance in the past and receiving only low to moderate social support from significant others increase the risk of PLHIV patients developing GAD. The findings may inform clinicians on the needs for early intervention, including counselling and increasing support system for PLHIV who are abusing drugs. Early psychological intervention such as supportive therapy, behavioural or cognitive therapy among PLHIV with a history of illicit substance use may alleviate the symptoms and reduce the risk of developing GAD. Addressing these psychological aspects is essential so that the detrimental effects of GAD such as suicide can be prevented early. Minimising the psychological consequences of this chronic and stigmatising illness can help them optimise their quality of life. Moreover, enhancing their adherence to the HAART may improve the CD4 counts to ≥350 cells/ul, which could lessen the odds of getting GAD.

In addition, endless support, listening to the needs and frustrations, and providing encouragement for adherence are important for the patients to achieve their treatment goal as well as healthy psychological well-being. This research provides insights to the contributing factors of GAD among PLHIV. Nevertheless, we would like to suggest more robust prospective studies, and broader sample sizes to establish the causal factors for GAD among PLHIV as this study is limited by its design. We

are aware that there are also many other factors such as physical, personal and environmental factors that could influence GAD among PLHIV.

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