

# Common Psychological Disorder among Patients with Retroviral Disease

## Nor Hidayah Jaris<sup>1</sup>, Suresh Kumar Chidambaram<sup>2</sup>, Semran Kaur<sup>3</sup>, Salmi Razali<sup>1,4</sup>

<sup>1</sup>Department of Psychiatry, Faculty of Medicine, Universiti Teknologi MARA, Malaysia <sup>2</sup> Department of Medicine, Faculty of Medicine, Universiti Teknologi MARA, Malaysia <sup>3</sup> Department of Psychiatry, Hospital Sungai Buloh, Selangor, Malaysia <sup>4</sup>Institute of Pathology, Laboratory and Forensic Medicine (I-PPerForM) Universiti Teknologi MARA, 47000 Sungai Buloh, Selangor, Malaysia

norhidayahjaris@gmail.com, chikku.suresh@gmail.com, semran\_badeshae@msn.com, drsalmi@gmail.com Tel.: +603-61265000

#### **Abstract**

Major depressive disorder (MDD) and generalized anxiety disorder (GAD) increases further morbidity and mortality of patients with retroviral disease (RVD). This study aimed to determine the prevalence and the contributing factors of MDD and GAD. The symptoms were screened using the Hospital Anxiety Depression Scale (HADS), MDD and GAD was diagnosed with the Mini International Neuropsychiatric Interview (MINI). 27(12.9%) patients had MDD and 28(13.0%) had GAD. The contributing factors include illicit drug use in the past, social support system, and CD4 count. Interventions for RVD patients should include counselling for those abusing drugs, increasing support system and adherence to treatment.

Keywords: Retroviral Disease, Anxiety, Depression, Support system

eISSN 2514-7528 © 2021 The Authors. Published for AMER ABRA CE-Bs by E-International Publishing House, Ltd., UK. This is an open-access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). Peer-review under responsibility of AMER (Association of Malaysian Environment-Behaviour Researchers), ABRA (Association of Behavioural Researchers on Asians / Africans / Arabians) and cE-Bs (Centre for Environment-Behaviour Studies), Faculty of Architecture, Planning & Surveying, Universiti Teknologi MARA, Malaysia.

DOI: https://doi.org/10.21834/jabs.v6i18.380

#### 1.0 Introduction

Common psychological disorders often defined as instability state of mood, which presented by emotional and psychological symptoms of depression and anxiety (Ross, 2017). In Malaysia, about 20% of those patients with RVD have anxiety and depression while 29% of the HIV-infected patients met criteria for likely anxiety disorder (Hasanah et al., 2011). MDD among patients with the retroviral disease (RVD) or human immunodeficiency virus (HIV) infection is prevailing. To date, 39% of them have been identified to have depression (Tran et al., 2019). MDD is a debilitating mental illness that may increase further morbidity and mortality of RVD patients (Todd et al., 2017). RVD patients with MDD have poor adherence to Highly Active Antiretroviral Therapy (HAART) (Tull, Berghoff, Bardeen, Schoenleber, & Konkle-Parker, 2018) increasing their susceptibility for symptoms of Acquired immunodeficiency syndrome (AIDS) and other complications. Moreover, this disorders also predispose RVD patients to devastating psychological complications such as psychosis, early dementia and suicide (Tyree, Vaida, Zisook, Mathews, & Grelotti, 2019). Considering the major negative effects of the depression and anxiety in patients with RVD, it is important that this mental disorder be identified and treated early so that patients with RVD can have the best quality of life when enduring multiple difficulties with this stigmatizing disease.

#### 2.0 Literature Review

Depression has an adverse effect on how you feel, how you think and how you act. However, it's a treatable illness. Depression induces feelings of frustration, lack of interest in once enjoyed activities. It can result in a variety of emotional and physical problems and can diminish the ability of a person to function at work and at home (American Psychiatric Association (APA), 2017). Anxiety is an emotion that is characterized by anxious feelings, worried thoughts and physical changes such as elevated blood pressure. Those with anxiety disorders typically have recurrent or persistent thoughts or fears. They can avoid such worrying situations. They can also experience physical symptoms such as sweating, shaking, dizziness or a fast heartbeat (American Psychological Association, n.d.). Mental health professionals considered those who have feelings of depression and anxiety as a 'case' of MDD and GAD when patients fulfilled the criteria of depression in DSM-5.

RVD 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). Previous studies have indicated many factors which could lead to depression in patients with RVD. It has been shown, in terms of sociodemographic influences, that younger RVD patients have a higher tendency for MDD (Deshmukh, Borkar, & Deshmukh, 2017). In terms of gender, female RVD patients may have a higher risk to develop depression and anxiety in comparison to men (Ngum, Fon, Ngu, Verla, & Luma, 2017). Other key contributing factors to depression and anxiety were low levels of

education, unemployment and marital status of being a widow or not living with spouse (Zeng et al., 2019). In Malaysia, non-Malays patients with RVD have lower chances of anxiety compared to Malays (Radzniwan et al., 2016). A study conducted in a state of Kelantan, however found that Malay patients who are more likely to practice Islam have a low risk of developing anxiety (Othman et al., 2015).

Clinically, an important parameter that indicates the strength of the immune system, i.e. CD4 count is an essential predictor for depression in RVD patients. Scientists indicated that the level of CD4 count of less than 200 cells/ul might lead to depression among RVD patients (Tesfaye & Bune, 2014). However, two local studies found insignificant association between CD4 counts with depression and 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). Another factor vital for increasing their risk of depression is concurrent drug abuse. A cohort study at AIDS Center in the United States found that amphetamine use by RVD patients within three months resulted in significant depressive symptoms, while cannabis use alone increased the risk of depression (Mimiaga et al., 2013).

The social support system is acting in conjunction with sociodemographic and clinical factors in predisposing RVD patients to depression. Patients with RVD face difficulties in their jobs and relationships that may increase their susceptibility to depression and affect their everyday activities (Tuan Abdullah et al., 2019). Thus, having good support was found to be an essential coping mechanism for adjustment and act as a buffer towards stress in mental and physical health (Hostinar & Gunnar, 2015). Positive social support lowered the risk of getting depression and in contrast, less support associated with a higher score of depressive symptoms (Fawzi et al., 2012; Seffren et al., 2018).

While substantial studies have been carried out to investigate contributing factors for depression among RVD patients, there are still gaps of knowledge that need to be fulfilled to inform effective intervention of RVD. Given the feelings of sadness or depression is very subjective, accurate diagnosis, i.e. Major depressive disorder or MDD is crucial so that correct treatment can be offered. Many previous researchers have evaluated depression among RVD patients by screening for the illness only, but yet to diagnose this mental illness properly. Hence, the findings of those studies only informed the results of 'caseness', not the 'case' of depression (Ostergaard et al., 2010). Furthermore, locally, there is sparse of data and research investigating illicit substance use and social support system among RVD patients. Previous studies in Malaysia found that female gender, financial support and alcohol consumption were the factors that contribute to common psychological disorders in patients with HIV (Yee et al., 2009). Shane and Koh's research postulated an association between CD4 counts and Hepatitis B co-infection with depression (Shane et al., 2010). A high perceived social support was identified by Terence et al. to lower the risk of depressive disorder among this vulnerable group (Terence et al., 2017). Thus, this study aimed to determine the prevalence of the diagnosis of major depressive disorder (MDD) and generalized anxiety disorder (GAD) among RVD patients and investigate its contributing

factors including the sociodemographic factors, clinical factors, adherence to treatment as well as the level of support by family, friends and significant others given to patients with RVD.

## 3.0 Methodology

### 3.1 Study design, setting and data collection

This was a cross-sectional study to determine the prevalence of the MDD and GAD among RVD patients receiving Highly Active Antiretroviral Therapy (HAART) and its associated factors. It was carried out in the Infectious Disease Clinic, Hospital Sungai Buloh which is one of the public hospitals in Selangor. It provides specialized treatment for infectious disease in Malaysia. It is tertiary and a reference for infectious disease cases from the north region of Selangor. There were about 1000 patients receiving HAART in a month attending this infectious disease clinic.

#### 3.2 Data collection and assessment tools

Participants were selected using systematic random sampling. The inclusion criteria include RVD patients aged 18 years old and above, attending an outpatient clinic and receiving HAART, was 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 RVD patients who gave informed consent voluntarily without coercion were enrolled in the study.

The symptoms of depression and anxiety were screened with the Hospital Anxiety Depression Scale (HADS)(Yahya & Othman, 2015). The participants who scored eight and above for HADS were identified as 'caseness' of depression anxiety and considered as 'probable depression and anxiety'. This group of participants were interviewed further using the Mini International Neuropsychiatric Interview (MINI) to confirm the 'case' of MDD or 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 with the RVD patients or retrieval of 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.

## 3.3 Statistical Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) version 23. The factors associated with MDD and GAD among RVD 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 that 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.

#### 3.4 Ethics

Ethical approval was obtained from the Medical Research Ethics Committee, Ministry of Health (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 Medical and Research Ethics Committee of the Clinical Research Center (CRC) of the respective hospital prior to commencing the study.

#### 4.0 Results

## 4.1 Background of participants

Of the total 210 participants, the mean age of the participants was  $29.72 \pm 9.98$  years and more than three-quarter of the participants were male (186; 88.6%). More than a half of the participants (116; 55.2%) were Malay, and others were Chinese (71; 33.8%), Indian (21; 10%) and others (2; 1%). Most of the participants received tertiary education (113; 53.8%) and completed secondary school (86; 41%). Less than 10% went to primary school only (11; 5.2%). Among the participants, 134 were employed, and 16(7.6%) were unemployed. More than half of participants (134; 63.8%) were in Bottom 40 group (B40) with total household income less than RM 3860, less than one-third (45; 21.4%) were in the Middle 40 group (M40) with household income 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%) (Table 1).

## 4.2 Prevalence of Major depressive disorder and Generalized anxiety disorder

There were 47 (22%) with probable depression cases and 52 (25%) cases with probable anxiety. Among these cases, 27 participants were established to have MDD (13%) and 28 had GAD (13%). Figure 1 shows the prevalence of MDD and GAD and figure 2 exhibits different level of depression and anxiety severity with 31 (14.8%) of RVD patients had mild depression, 14 (6.7%) had moderate, and 2(1%) had a severe level of depression. There were 34 participants (16.2%) who had a mild degree of anxiety and 15 (7.1%) of them had moderate level and three (1.4%) had a severe level of anxiety.

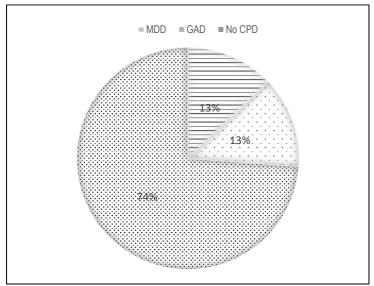


Fig 1: Prevalence of MDD and GAD among Patients with Retroviral Disease

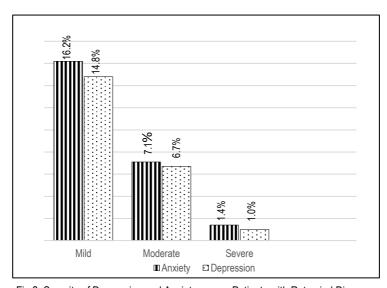


Fig 2: Severity of Depression and Anxiety among Patients with Retroviral Disease

## 4.3 Sociodemographic factors and Common Psychological Disorder

There was no variable of sociodemographic characteristics that had a statistically significant association with MDD and GAD among RVD patients receiving HAART. However, more than two third of the patients with RVD who had MDD and GAD were single and less than 50% of them were living alone. Refer Table 1 and 2 for further information.

Table 1. Background Socio-demography of Patients with RVD and Major Depressive Disorder

Sociodemographic	Major depressive disorder							
Factors	No (n=182)	Yes(n=28)	В	p-value	OR (95% CI)			
Age								
<45 years old	125(68.3%)	21(77.8%)	1.08	0.05	2.95(0.98-8.89)			
≥45 years old	58(31.7%)	6(22.2%)						
Gender								
Male	160(87.4%)	26(96.3%)	-1.32	0.21	3.737(0.48-28.88)			
Female	23(12.6%)	1(3.7%)						
Ethnicity								
Malay	98(53.6%)	18(66.7%)	0.55	0.21	1.74(0.74-4.06)			
Non-Malay	85(46.4%)	9(33.3%)						
Religion								
Islam	102(55.7%)	18(66.7%)	0.46	0.29	1.59(0.68-3.72)			
Others	81(44.3%)	9(33.3%)						
Education								
Primary school	8(4.4%)	3(11.1%)	1.01	0.16	2.73(0.68-11.02)			
Secondary to tertiary	175 (95.6%)	24 (88.9%)						
Employment								
Employed	161(87.0%)	22(81.5%)	-0.51	0.35	0.60(0.20-1.75)			
Unemployed	22(12.0%)	5(18.5%)						
Total Household income								
B40 & M40	154(84.2%)	25(92.6%)	0.86	0.26	2.35(0.53-10.49)			
T20	29(15.8%)	2(7.4%)						
Marital Status								
Single/	128(69.9%)	24(88.9%)	1.24	0.05	3.44(0.99-11.89)			
Widow/Separated/Divorce								
Married	55(30.1%)	3(11.1%)						
Living companion								
With companion	142(77.6%)	19(70.4%)	-0.38	0.41	0.69(0.28-1.68)			
Alone	41(22.4%)	8(29.6%)						

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; Cl-confidence interval; \*significant p value <0.05; \*\*significant p value <0.01

Table 2. Background Socio-demography of Patients with RVD and Generalized Anxiety Disorder

Sociodemographic										
Factors	No (n=182)	Yes(n=28)	В	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%)	80.0	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%)								
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/	130(71.4%)	22(78.5%)	0.38	0.43	1.47(0.56-3.82)					
Widow/Separated/Divorce										
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;  $\rho$  value; OR-Odds Ratio; Cl-confidence interval; \*significant  $\rho$  value <0.05; \*\*significant  $\rho$  value <0.01

## 4.4 Contributing factors to Major Depressive Disorder

The significant associations between independent variables and MDD among RVD patients analysed using SLogR include amphetamine-type stimulant (ATS) use for the past three months, history of taking an illicit substance, receiving low to moderate support from family, friends, and significant others, and overall support, CD4 counts (≥ 350 cells/ul), side effects of medications and viral load (≥ 20 copies/ml)(Table 3). Multiple logistic regression (MLogR) indicated the four significant predictors for MDD among RVD patients including ATS use for the past three months, receiving low to moderate support from family and significant others, and level of CD4 counts (≥ 350 cells/ul). The use of ATS for the past three months markedly increased the odds of having MDD by 40.23 times (AOR= 40.23:

p=0.01; 95% CI=3.61-447.86). RVD patients who received only low to moderate social support from family and significant others had about 5.65 and 4.36 odds of having RVD (AOR= 5.65; p=0.01; 95% CI=1.43-22.38 and AOR=4.36; p=0.02; 95% CI=1.22-15.64) respectively. Furthermore, having the level of CD4 count of more than 350 cells/ul protected RVD patients from MDD (AOR=0.31; p=0.03; 95% CI= 0.11-0.86). The Omnibus test for model coefficient showed that the model was significant (X² (5) = 46.08; p<0.001; the Nagelkerke R²=0.368; Cox & Snell R²=0.197) and the predictive accuracy of the model for the training sample was 85.10%. There was no multicollinearity exist between independent variables; the values for tolerance were more than 0.1, and VIF was less than 10 for each variable.

Table 3. Logistic Regression of Factors Associated with Major Depressive Disorder

Variables	Simple Logistic Regressions				Multiple Logistic Regressions					
	B(df)	p- value	ORª	95% CI		B(df)	p- value	AORb	95% CI	
ATS use for the past three months	3.13(1)	0.008	22.75	2.27	227.56	5.16(1)	0.001	40.23	3.61	447.86
LMSS from family	2.07(1)	0.000	7.92	2.63	23.83	1.73(1)	0.01*	5.65	1.43	22.38
LMSS from significant others	1.94(1)	0.000	6.94	2.51	19.16	1.47(1)	0.02*	4.36	1.22	15.64
CD4 counts ≥ 350 cells/ul	-1.26(1)	0.003	0.28	0.12	0.65	-1.19(1)	0.03*	0.31	0.11	0.86
Side effects of medications	1.61(1)	0.002	4.99	1.76	14.12	1.10(1)	0.09	3.03	0.86	10.57
LMSS overall	1.53(1)	0.002	4.61	1.78	11.95	0.49(1)	0.59	1.63	0.27	9.91
Viral load ≥ 20 copies/ml	1.42(1)	0.001	4.15	1.74	9.94	1.10(1)	0.59	3.01	0.96	9.49
History of taking illicit substance	0.89(1)	0.04	2.45	1.01	5.96	0.34(1)	0.63	1.36	0.39	4.62
LMSS from friends	1.02(1)	0.03	2.78	1.07	7.21	0.32(1)	0.70	1.38	0.26	7.19

Simple logistic regression; bMultiple logistic regression; B=beta value; Cl=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</p>

## 4.5 Contributing factors to Generalized Anxiety Disorder

We analysed the associations between independent variables and GAD among RVD patients using SLogR and revealed 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  $\geq$  350 cells/ul, viral load  $\geq$  20 copies/ml, history of taking cannabis, illicit substance use for the past 3 months and overall low and moderate social support. MLogR yielded two significant factors that predicting GAD among patients with RVD. Patients with low and moderate social support form significant others had 4-times higher risk to develop GAD (AOR=4.09; p=0.002, 95%Cl= 1.66-10.04). Patients with illicit substance use in the past has about 4-times higher risk to have GAD (AOR=3.84; p=0.003, 95%Cl= 1.56-89.44).

Table 4. Logistic Regression of Factors Associated with Generalized Anxiety Disorder

Veriables Circulate Democratics Multiple Legistic Democratics											
Variables	Simple Logistic Regressions					Multiple Logistic Regressions					
	B(df)	p- value	ORª	95% CI		B(df)	p- value	AOR <sup>b</sup>	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	

<sup>o</sup>Simple logistic regression; <sup>b</sup>Multiple logistic regression; <sup>B</sup>=beta value; Cl=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

## 5.0 Discussion

The main contributing factors of MDD are the use of ATS for the past three months, the low and moderate social support from family and significant others as well as a CD4 count less than 350 cells/ul. ATS drugs include amphetamine, methamphetamine and ecstasy or 3,4-methylenedioxyethylamphetamine (MDMA) (Massaro et al., 2017). The ATS recent use increases about 40-fold of chances for RVD patients to get MDD. Researchers indicated that ATS directly damages the brain, suppresses the immune system and increases cytokine levels of RVD patients (Schuster & Gonzalez, 2012). Its neurotoxicity increases the risk of depression among the RVD patients (Zeng et al., 2018). Furthermore, abstinent from ATS among those who had already dependent on this drug can manifest with symptoms of MDD, including a dysphoric state and low motivation (Amiri et al., 2016). In view of that, the awareness of the consequences of taking illicit substances must be emphasised continuously as well as the encouragement of living a healthy lifestyle without drugs.

In particular, our research showed the significance of the support from family and significant others in the life of RVD patients. Complementary messages and family expectations may reduce the rumination of hopelessness and boost self-esteem in continuing care among chronic disease patients (Pernice-Duca, 2010). Patients with RVD face many obstacles in their lives, including jobs, family relationships, and others. They need protection from the family members as a source of safety, acceptance and dignity,

hence, this group of patients will feel lack of fear of rejection and being marked by the family members (Tuan Abdullah et al., 2019). Therefore, lack of rejection and adequate support from the family could lessen the pessimism and encourage RVD patients to cope well with the stress as well as reduce the risk of having psychological disorder which leads to proper treatment adherence (Dejman et al., 2015). Higher perceived social support from family, especially emotional or informational, reduce the risk of having depression among RVD patients (Matsumoto et al., 2017). The significant others are one's closest and most trusted individual that could be mothers, fathers, relatives and friends (Cheng & Starks, 2002). RVD is a manageable chronic condition subject to a variety of psychosocial problems. Therefore, RVD patients need a great deal of help from others, especially near ones. This starts at the very first moment when they got the unfortunate news that they were infected with HIV.

CD4 is a type of white blood cells, named T-cells which is also known as regulatory T cells which acts by reducing the excessive immune response and regulate immune tolerance (Workman, Szymczak-Workman, Collison, Pillai, & Vignali, 2009). CD4 stimulates the production of anti-inflammatory cytokines such as interleukin-10 and subsequently regulate inflammatory responses (Miyara et al., 2009). Our study indicated that the level of CD4 is a crucial determinant for MDD among RVD patients. Those who have CD4 counts more than 350 cells/ul are protected from having MDD. This result supported the findings of other researchers elsewhere (Terloyeva et al., 2018). HIV may infect and kill CD4 cells which cause the failure of the immune system (Aavani & Allen, 2019). Therefore, CD4 cells play a critical role to inhibit the worsening of the inflammatory process before developing depression that occurs during stressful experiences. On the other hand, when the immune system is low due to reduced CD4 counts, it may lead to abnormality in the cascade of neurohormonal changes at the Hypothalamus-Pituitary-Adrenal Gland (HPA) resulted in depletion of the precursor of serotonin which can lead to depression (Masih & J.M.I. Verbeke, 2018). The level of CD4 count is negatively correlated with MDD among RVD patients, therefore, it is recommended that the physicians to strengthen the education on adherence of HAART to achieve the optimal CD4 counts more than 350 cells/ul and to ensure optimum immunity in reducing the risk of getting depression.

Social support is an essential component for the patients with RVD who had had higher risk to develop GAD when they are living in environment of lack social support. The lack of social support from significant ones may induce the fear in patients with RVF to disclose about their illness which further causing excessive worries in them (Evangeli et al., 2017). They need reassurance and support from the significant others to reduce the anxiety (Riahi et al., 2011). Positive social support is a protective factor from the stress and alleviates the feeling of insecurity which reduce the risk of having anxiety (Harandi et al., 2017).

Substance use in the past had 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 supported the previous study of the association between substance history and RVD management efficacy (Chen et al., 2018). This outcome emphasizes that the use of illicit substance in the past strongly contributed to GAD.

The severity level of common psychological disorders as measured by HADS showed that 16.2% of the participants had mild level of anxiety, 7.1% of them had moderate level and 1.4% had severe level of anxiety. For depression, 14.8% of them had mild depression 6.7% had moderate and 1% had severe level of depression.

This findings were in accordance with other study investigated on the severity level of depression which demonstrated the mild level of depression was 9%, moderate 16% and severe was 3% (Othman et al., 2015) which comparable with another study that revealed less than 10% of the patients had severe depression (Hadi; et al., 2019).

We found no significant association between socio-demographic factors with MDD in the univariate analysis. However, few points could be discussed. This study demonstrated that more than three-quarter of the patients who had been diagnosed with MDD were from the age group of less than 45 years old, male, household income of B40 and M40 and single.

There was 78% of the patients with MDD from the age group less than 45 years old. A study of depression and its correlation with other factors found that 58% of patients with HIV had depression and the odds of having depression was 1.7-2.5 times among the patients less than 49 years old (Duko et al., 2019). Other study found that 76% of HIV patients diagnosed with MDD were from the age of 25-44 years old (Deshmukh et al., 2017) and 2-times higher risk with the age less than 40 years old (Ngum et al., 2017). This could be due to different coping skills and resiliency compared to older age and still have a lack of knowledge about the illness.

96% of the patients with MDD belongs to the male group. Although not significantly associated, there was a study found that being male had a risk of 1.6-times in developing depression (Mohammed et al., 2015). This finding contrary to the findings in previous studies which revealed being female had higher risk to develop depression (Ngum et al., 2017; Saadat et al., 2015). The inability to provide the family needs and decline in social status would probably increase the risk of male to have depression (Mufukari, 2011).

Patients with a household income of B40 and M40 predominated the participants who had diagnosed with MDD (93%). A local study before found that patients with low household income less than RM 1000 a month had odds of having depression by 5-times compared to higher-income (Radzniwan et al., 2016). Some of the patients might be having loss of income in view of lack of capacity of working especially when they are in the unstable stage of illness and this could be worse if they are the breadwinners of the families.

Patients with HIV who were single and on HAART had a high prevalence of MDD (89%) compared to married patients. This is in line with a study of frequency and risk factors among HIV-patients which found that being single increased the prevalence of depression (Anagnostopoulos; et al., 2015) and being widow or widower also higher the prevalence (Bhatia et al., 2014). However, another study found no significant association between being single and depression among HIV-patients (Duko et al., 2019). Upon receiving the news of the HIV-positive diagnosis, patients face a lot of challenges such as grief, stigma, continuous treatment and follow up and possible relationship as well as work issues.

For GAD, there was no significant association between socio-demographic factors and GAD. However, we found that 85% of the patient with GAD were in the group of age less than 45 years old. In the study on prevalence of anxiety in chronic disease of irritable bowel syndrome, it found that the increasing years of age have 5% less chances to develop anxiety (Byrne et al., 2017) and there was a study indicated that the 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 et al., 2017). They felt fear 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 be addressed and managed 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 the patients with generalized anxiety disorder, 89% of them were from the household income level of B40 and M40. It was known that low-income level was associated with anxiety among people living with HIV (Duko et al., 2019) probably due to increase of financial commitment as they need to come frequently to the hospital and spent a high amount of money for transportation and other expenses. The other possible factor could be patients from B40 group had the job instability and due to frequent medical leaves, it would lead to a decline in work performance and would possibly cause anxiety among them.

Other than that, 89% of patients with HIV who were diagnosed to have GAD were single. Single patients had increased odds of having anxiety by 3.6 times compared to the patients who were married (Ngocho et al., 2019) and similar studies showed that being unmarried had 2-times higher risk to develop anxiety (p=0.002) (Olagunju et al., 2012). HIV-infection is a chronic disease which needs endless support as they face various social challenges.

#### 6.0 Conclusion and Recommendations

This study indicated that the use of ATS for the past three months, receiving only low to moderate social support from family and significant others as well as having CD4 count less than 350 cells/ul increase the risk of RVD patients for MDD. The findings may inform clinicians on the needs for early intervention, including counselling for RVD patients who are abusing drugs and increasing support system for them. Addressing these psychological aspects is essential so that the detrimental effects of MDD such as premature dementia, psychosis and suicide can be prevented early. Minimising the psychological consequences of this chronic and stigmatising illness can help them to have optimum 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 MDD.

In addition, endless support, listening to the needs and frustration and encouragement for adherence were important for the patients to achieve treatment goal as well as healthy psychological well-being. Early psychological intervention such as supportive therapy,

behavioural or cognitive therapy among patients with RVD with a history of illicit substance use may alleviate the symptoms and reduce the risk of developing GAD.

This research provides insights to the contributing factors of MDD and GAD among the RVD patients; nevertheless, we would like to inform that the study was limited by its design and suggest a more robust prospective study, and broader sample sizes to establish the causal factors for MDD and GAD among the RVD patients. We are aware that many other physical, personal and environmental factors that could influence MDD and GAD among them

## Acknowledgement

We would like to thank the Director-General of Health Malaysia for his permission to publish this article and to express our appreciation to all the study participants who had volunteered to participate in this study. We would like to express our gratitude to the senior lecturer and consultant of public health medicine, Dr Ikhsan Selamat, and Prof. Dr Mohd Razali Salled, a consultant psychiatrist in Universiti Telnologi MARA, Faculty of Medicine, Sungai Buloh Campus who were directly involved in this study. The authors received no financial support for the research, authorship or publication of this article and declared no conflict of interest.

#### References

Aavani, P., & Allen, L. J. (2019). The role of CD4 T cells in immune system activation and viral reproduction in a simple model for HIV infection. *Applied Mathematical Modelling*, 75, 210-222.

Amiri, S., Alijanpour, S., Tirgar, F., Haj-Mirzaian, A., Amini-Khoei, H., Rahimi-Balaei, M., Zarrindast, M.-R. (2016). NMDA receptors are involved in the antidepressant-like effects of capsaicin following amphetamine withdrawal in male mice. *Neuroscience*, 329, 122-133.

Anagnostopoulos;, Ledergerber, Jaccard, Shaw, Stoeckle, Bernasconi, Barth, Calmy, Berney, & Jenewein. (2015). Frequency of and risk factors for depression among participants in the Swiss HIV Cohort Study (SHCS). *PLoS ONE, 10*(10), e0140943

Bhatia, & Munjal. (2014). Prevalence of depression in people living with HIV/AIDS undergoing art and factors associated with it. *Journal of Clinical and Diagnostic Research*, 8(10), WC01-WC04. doi:10.7860/JCDR/2014/7725.4927

Byrne, Rosenfeld, Leung, Qian, Raudzus, Nunez, & Bressler. (2017). Prevalence of Anxiety and Depression in Patients with Inflammatory Bowel Disease. Can J Gastroenterol Hepatol, 2017, 6496727. doi:10.1155/2017/6496727

Chen, Shiu, Yang, Li, Wang, Zhang, Zhang, Bao, Aung, Chen, Zhao, & Lu. (2018). Substance use, anxiety, and self-management efficacy in HIV-positive individuals: A mediation analysis. *J Subst Use*, 23(4), 408-414. doi:10.1080/14659891.2018.1436603

Cheng, S., & Starks, B. (2002). Significant Others on students' educational expectations. *Sociology of Education*, 75(4), 306-327.

Dejman, M., Ardakani, H. M., Malekafzali, B., Moradi, G., Gouya, M. M., Shushtari, Z. J., . . . Mohraz, M. (2015). Psychological, social, and familial problems of people living with HIV/AIDS in Iran: A qualitative study. *Int J Prev Med.* 6.

Deshmukh, N. N., Borkar, A. M., & Deshmukh, J. S. (2017). Depression and its associated factors among people living with HIV/AIDS: Can it affect their quality of life? *J Family Med Prim Care*, *6*(3), 549-553. doi:10.4103/2249-4863.222016

Duko, Toma, Asnake, & Abraham. (2019). Depression, Anxiety and Their Correlates Among Patients With HIV in South Ethiopia: An Institution-Based Cross-Sectional Study. Front Psychiatry, 10, 290. doi:10.3389/fpsyt.2019.00290

Evangeli, & Wroe. (2017). HIV Disclosure Anxiety: A Systematic Review and Theoretical Synthesis. *AIDS Behav*, 21(1), 1-11. doi:10.1007/s10461-016-1453-3

Fawzi, M. C. S., Eustache, E., Oswald, C., Louis, E., Surkan, P. J., Scanlan, F., Mukherjee, J. S. (2012). Psychosocial support intervention for HIV-affected families in Haiti: implications for programs and policies for orphans and vulnerable children. *Social science & medicine*, 74(10), 1494-1503.

Flint, Peasley-Miklus, Papademetriou, Meyers, Mulsant, Rothschild, Whyte, & Group. (2010). Effect of age on the frequency of anxiety disorders in major depression with psychotic features. *The American Journal of Geriatric Psychiatry*, 18(5), 404-412.

Hadi;, Mustapha;, & Hafidzi. (2019). Depression Anxiety Stress among HIV Patients in East Coast Malaysia. Depression, Anxiety, Stress, Community, Malaysia.

Harandi, Taghinasab, & Nayeri. (2017). The correlation of social support with mental health: A meta-analysis. *Electronic physician*, 9(9), 5212

Hostinar, C. E., & Gunnar, M. R. (2015). Social Support Can Buffer against Stress and Shape Brain Activity. *AJOB Neurosci*, 6(3), 34-42. doi:10.1080/21507740.2015.1047054

Leppink, Odlaug, Lust, Christenson, & Grant. (2016). The Young and the Stressed: Stress, Impulse Control, and Health in College Students. *J Nerv Ment Dis*, 204(12), 931-938. doi:10.1097/NMD.000000000000586

Masih, J., & J.M.I. Verbeke, W. (2018). Immune System Function and its Relation to Depression: How Exercise can Alter the Immune System-Depression Dynamics. *Journal of Depression and Anxiety*, 07(04). doi:10.4172/2167-1044.1000325

Massaro, Abdalla, Laranjeira, Caetano, Pinsky, & Madruga. (2017). Amphetamine-type stimulant use and conditional paths of consumption: data from the Second Brazilian National Alcohol and Drugs Survey. *Braz J Psychiatry*, 39(3), 201-207. doi:10.1590/1516-4446-2015-1894

Matsumoto, S., Yamaoka, K., Takahashi, K., Tanuma, J., Mizushima, D., Do, C. D., . . . Oka, S. (2017). Social Support as a Key Protective Factor against Depression in HIV-Infected Patients: Report from large HIV clinics in Hanoi, Vietnam. *Sci Rep*, 7(1), 15489. doi:10.1038/s41598-017-15768-w

Mimiaga, M. J., Reisner, S. L., Grasso, C., Crane, H. M., Safren, S. A., Kitahata, M. M., . . . Mayer, K. H. (2013). Substance use among HIV-infected patients engaged in primary care in the United States: Findings from the centers for AIDS Research Network of Integrated Clinical Systems Cohort. *American Journal of Public Health*, 103(8), 1457-1467. doi:10.2105/AJPH.2012.301162

Miyara, M., Yoshioka, Y., Kitoh, A., Shima, T., Wing, K., Niwa, A., . . . Valeyre, D. (2009). Functional delineation and differentiation dynamics of human CD4+ T cells expressing the FoxP3 transcription factor. *Immunity*, 30(6), 899-911.

Mohammed, Mengistie, Dessie, & Godana. (2015). Prevalence of depression and associated factors among HIV patients seeking treatments in ART clinics at Harar Town , Eastern Ethiopia. *J AIDS Clin Res, 6*(6), 1-6. doi:10.4172/2155-6113.1000474

Mufukari. (2011). Gender related factors that lead to depression after diagnosis with HIV/AIDS. Stellenbosch: Stellenbosch University,

Mukhtar, F., Bakar, A. K. A., Junus, M. M., Awaludin, A., Aziz+, S. A., Midin, M., . . . Kaur, J. (2012). A preliminary study on the specificity and sensitivity values and inter-rater reliability of mini international neuropsychiatric interview (MINI) in Malaysia. *ASEAN Journal of Psychiatry*, 13(2).

Ngocho, Watt, Minja, Knettel, Mmbaga, Williams, & Sorsdahl. (2019). Depression and anxiety among pregnant women living with HIV in Kilimanjaro region, Tanzania. *PLoS ONE*. 14(10).

Ngum, A., Fon, P. N., Ngu, R. C., Verla, V. S., & Luma, H. N. (2017). Depression Among HIV/AIDS Patients on Highly Active Antiretroviral Therapy in the Southwest Regional Hospitals of Cameroon: A Cross-Sectional Study. *Neurology and Therapy*, 6(1), 103-114. doi:10.1007/s40120-017-0065-9

Olagunju, Adeyemi, Erinfolami, & Ogundipe. (2012). Factors associated with anxiety disorders among HIV-positive attendees of an HIV clinic in Lagos, Nigeria. *Int J STD AIDS*, 23(6), 389-393.

Ostergaard, S. D., Foldager, L., Allgulander, C., Dahl, A. A., Huuhtanen, M.-T., Rasmussen, I., & Munk-Jørgensen, P. (2010). Psychiatric caseness is a marker of major depressive episode in general practice. *Scandinavian journal of primary health care*, 28(4), 211-215.

Othman, Fadzil, Zakaria, Jaapar, & Husain. (2015). Religiosity in Malay patients with HIV/AIDS: correlation with emotional distress. *Middle-East Journal of Scientific Research*, 23(2), 170-174.

Pemice-Duca, F. (2010). Family network support and mental health recovery. *Journal of Marital and Family Therapy*, 36(1), 13-27.

Radzniwan, R., Alyani, M., Aida, J., Khairani, O., Nik Jaafar, N. R., & Tohid, H. (2016). Psychological status and its clinical determinants among people living with HIV/AIDS (PLWHA) in Northern Peninsular Malaysia. *HIV & AIDS Review, 15*(4), 141-146. doi:10.1016/j.hivar.2016.11.002

Riahi, Aliverdinia, & Pourhossein. (2011). Relationship between social support and mental health

Saadat, Behboodi, & Saadat. (2015). Comparison of depression, anxiety, stress, and related factors among women and men with human immunodeficiency virus infection. *J Hum Reprod Sci, 8*(1), 48.

Shane, Koh, & Cheah. (2010). Psychiatric morbidity among HIV patients in Hospital Tuanku Jaafar, Seremban, Malaysia. HIV/AIDS Prevention, Treatment and Care: The Way Forward. *Universiti Sains Malaysia, Penang, AIDS Action & Research Group.*, 85-101.

Schuster, R. M., & Gonzalez, R. (2012). Substance abuse, hepatitis C, and aging in HIV: common cofactors that contribute to neurobehavioral disturbances. *Neurobehavioral HIV Medicine*, 2012(4), 15. doi:10.2147/NBHIV.S17408

Seffren, V., Familiar, I., Murray, S. M., Augustinavicius, J., Boivin, M. J., Nakasujja, N., . . . Bass, J. (2018). Association between coping strategies, social support, and depression and anxiety symptoms among rural Ugandan women living with HIV/AIDS. *AIDS Care*, 30(7), 888-895. doi:10.1080/09540121.2018.1441969

Terence, Sidi, Choy, & Mahadevan. (2017). Prevalence of Depressive Disorder and Its Association With Perceived Social Support Among Patients With Human Immunodeficiency Virus (Hiv) in Hospital Tuanku Jaafar, Seremban (Htjs), Malaysia. *ASEAN Journal of Psychiatry*, 18(1), 10-19.

Terloyeva, D., Nugmanova, Z., Akhmetova, G., Akanov, A., Patel, N., Lazariu, V., . . . McNutt, L. A. (2018). Untreated depression among persons living with human immunodeficiency virus in Kazakhstan: A cross-sectional study. *PLoS ONE*, *13*(3), e0193976. doi:10.1371/journal.pone.0193976

Tesfaye, S. H., & Bune, G. T. (2014). Generalised psychological distress among HIV-infected patients enrolled in antiretroviral treatment in Dilla University Hospital, Gedeo zone, Ethiopia. 1, 1-9.

Todd, J. V., Cole, S. R., Pence, B. W., Lesko, C. R., Bacchetti, P., Cohen, M. H., . . . Mack, W. (2017). Effects of antiretroviral therapy and depressive symptoms on all-cause mortality among HIV-infected women. *American journal of epidemiology*, 185(10), 869-878.

Tran, B. X., Ho, R. C. M., Ho, C. S. H., Latkin, C. A., Phan, H. T., Ha, G. H., . . . Zhang, M. W. B. (2019). Depression among Patients with HIV/AIDS: Research Development and Effective Interventions (GAPRESEARCH). *Int J Environ Res Public Health*, *16*(10). doi:10.3390/ijerph16101772

Tuan Abdullah, Mat Min, Hossain, & Abdullah. (2019). Relationship and career challenges faced by people infected with HIV in Malaysia. F1000Research. 8. doi:10.12688/f1000research.21079.1

Tull, M. T., Berghoff, C. R., Bardeen, J. R., Schoenleber, M., & Konkle-Parker, D. J. (2018). An initial open trial of a brief behavioral activation treatment for depression and medication adherence in HIV-infected patients. *Behavior modification*, 42(2), 196-209.

Tyree, G. A., Vaida, F., Zisook, S., Mathews, W. C., & Grelotti, D. J. (2019). Clinical correlates of depression chronicity among people living with HIV: What is the role of suicidal ideation? *Journal of affective disorders*, 258, 163-171.

Workman, C. J., Szymczak-Workman, A. L., Collison, L. W., Pillai, M. R., & Vignali, D. A. (2009). The development and function of regulatory T cells. *Cellular and Molecular Life Sciences*, 66(16), 2603.

Word Health Organization (WHO). (2019). HIV/AIDS. Retrieved from <a href="https://www.who.int/news-room/fact-sheets/detail/hiv-aids">https://www.who.int/news-room/fact-sheets/detail/hiv-aids</a>

Yahya, F., & Othman, Z. (2015). Validation of the Malay version of the hospital anxiety and depression scale (HADS) in Hospital Universiti Sains Malaysia. *Int Med J.* 22(2), 80-82.

Yee, Gee, Guan, Teong, & Kamarulzaman. (2009). Identifying depression among the human immunodeficiency virus (HIV) patients in University Malaya Medical Centre, Kuala Lumpur, Malaysia. *Asian J Psychiatry*, 10(2), 1-13.

Zeng, C., Guo, Y., Hong, Y. A., Gentz, S., Zhang, J., Zhang, H., . . . Cai, W. (2019). Differential effects of unemployment on depression in people living with HIV/AIDS: a quantile regression approach. *AIDS Care*, 1-8. doi:10.1080/09540121.2019.1587366

Zeng, X.F., LI, Q., LI, J., Wong, N., LI, Z., Huang, J., . . . Lu, G. (2018). page: HIV-1 Tat and methamphetamine co-induced oxidative cellular injury is mitigated by N-acetylcysteine amide (NACA) through rectifying mTOR signaling.