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Depression and anxiety were low amongst virally suppressed, long-term treated HIV-infected individuals enrolled in a public sector antiretroviral program in Thailand*

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ABSTRACT

HIV/AIDS and anxiety/depression are interlinked. HIV-infected patients suffering from depression may be at risk for poor adherence which may contribute to HIV disease progression. Additionally, an HIV diagnosis and/or using certain antiretroviral agents may trigger symptoms of anxiety/depression. The objective of the study was to assess the prevalence and factors associated with anxiety and depression in HIV-infected patients from the Thai National HIV Treatment Program. This cross-sectional study was performed from January 2012 to December 2012 in HIV-infected out-patients, aged ≥18 years, from three HIV referral centers. Symptoms of anxiety and depression were measured using the Thai-validated Hospital Anxiety and Depression Scale (HADS). A score of ≥11 was defined as having anxiety and depression. Associated factors were assessed by multivariate logistic regression. Totally 2023 (56% males) patients were enrolled. All patients received antiretroviral therapy (ART) for a mean duration of 7.7 years. Median CD4 was 495 cells/mm^3. Ninety-five percent had HIV-RNA < 50 copies/ml. Thirty-three percent were currently on efavirenz (EFV)-based ART. The prevalence of anxiety and depression were 4.8% and 3.1%, respectively. About 1.3% had both anxiety and depression. In multivariate logistic models, the female sex [OR = 1.6(95%CI 1.1–2.3), $p = .01$], having adherence <90% [OR = 2.2(95%CI 1.5–3.4), $p < .001$], fair/poor quality of life (QOL) [OR = 7.2 (95%CI 3.6–14.2), $p < .001$] and EFV exposure [OR = 1.6(95%CI 1.1–2.3), $p = .01$], were independently associated with having anxiety or depression. Our findings demonstrated that prevalence of depression and anxiety was low amongst virally suppressed, long-term antiretroviral-treated HIV-infected individuals. Some key characteristics such as the female sex, poor adherence, poor/fair QOL and EFV exposure are associated with anxiety and depression. These factors can be used to distinguish who would need a more in-depth evaluation for these psychiatric disorders.

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Introduction

In low–middle income countries depression and anxiety are common in people living with HIV (Gonzalez, Batchelder, Psaros, & Safren, 2011; Lowther, Selman, Harding, & Higginson, 2014). For the Asia Pacific region, the rates for major depression were 1.7–6.6% (Chiu, 2004). In Thailand, depression prevalence ranges from 3.2% to 32.3% (Buathong, Hiransuthikula, Tangwongchaib, & Komoltri, 2009; Pumpradit et al., 2010; Wongpakaran et al., 2014) and anxiety prevalence ranges from 1.27% to 37.5% (Lotrakul & Saipanish, 2006; Siriwanarangsan, Kongsuk, Arunpongpaisal, Kittiratanapaibul, & Charatsingha, 2004). Depressive symptoms are associated with poor adherence (Gonzalez et al., 2011), faster disease progression(Villes et al., 2007), and poorer quality of life (QOL) (Selvaraj, Ross, Unnikrishnan, & Hegde, 2013). More than 50% of HIV-infected patients with depression are never diagnosed (Asch et al., 2003).

HIV infection itself can cause cognitive changes and depression, but these problems often improve after starting combination antiretroviral therapy (cART) (Gibbie et al., 2006). However, efavirenz (EFV), which is a preferred component of WHO recommended first-line

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ART regimens, can cause neuropsychiatric side effects (Clifford et al., 2009). Female sex can be associated with psychiatric problems and suicidal ideation (Kinyanda et al., 2012; Kinyanda, Hoskins, Nakku, Nawaz, & Patel, 2011). Some studies report that HIV-infected women have poorer adherence and more depression than men (Turner, Laine, Cosler, & Hauck, 2003). Nevertheless, men have higher suicidal rates than women, which suggests undetected and unmanaged poor mental health.

There are few studies from Thailand of adequate sample size (Nuesch et al., 2009; Pumpradit et al., 2010). Therefore, we investigated the prevalence and factors associated with anxiety and depression among HIV/AIDS patients receiving cART in a prospective cohort from three large HIV referral centers in Thailand.

Material and methods

Subjects and procedure

This cross-sectional study was conducted from January to December 2012, at Bamrasnaradura Infectious Disease Institute, Sanpatong Hospital, and HIV-NAT. All potential patients who came for their regular HIV treatment and care during the study period were approached. This study was approved by each site's Ethical Committee. All patients gave written informed consent.

Instruments used

The Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983), commonly used in HIV-infected patients (Rabkin, 2008), was used. A total anxiety or depression score ≥11 is defined as abnormal; anxiety has 100% sensitivity and 86% specificity; depression has 86% sensitivity and 91% specificity. Internal consistency by Cronbach's alpha coefficient is 0.86 for anxiety and 0.83 for depression (Lotrakul & Sukanich, 1999).

Data collection

Subjects completed HADS and World Health Organization QOL-BREF Thai version (WHOQOL-BREF) questionnaires to obtain data on QOL and anxiety/depression (WHO, 2002). Demographic factors, HIV disease, CD4/HIV-RNA, treatment-related factors and adherence data at the same patient visits were retrieved from site clinical databases.

Statistical analysis

Stata version 11 (Statacorp, College Station, TX, USA) was used. Descriptive statistics summarized demographic, HIV-related characteristics, anxiety and depression. Logistic regression was used to assess factors associated with anxiety/depression, defined as a score ≥ 11. Predictor covariates were age, sex, current employment status, marital status, health benefit scheme, current CD4, viral load (VL), cART exposure, EFV exposure, adherence and QOL. The universal health coverage scheme is a national HIV program, offering free cART, CD4/HIV-RNA and safety parameters. Covariates with $p < .10$ were adjusted in multivariate models while retaining terms that were significant ($p \leq .15$).

Results

The characteristics of the patients at the time of the HADS assessment are given in Table 1. Age, marital status, educational levels, cART duration, CD4 count and HIV-RNA levels were not associated with anxiety or depression in univariate analysis; sex was associated with anxiety but not depression. In a multivariate logistic regression model, anxiety was associated with female sex, adherence <90%, "fair or poor" QOL, and health benefit coverage other than the universal health coverage (Table 2). Multivariate analysis showed that "fair or poor" QOL level and EFV use were independently associated with depression (Table 3).

Discussion

We found the prevalence of anxiety, depression, and both anxiety and depression were lower among those already on cART compared to previous reports conducted in treatment-naïve subjects (Gonzalez et al., 2011; Kaharuza et al., 2006; Nogueira Campos, De Fatima Bonolo, & Crosland Guimaraes, 2006; Olley, Seedat, Nei, & Stein, 2004; Olley, Seedat, & Stein, 2006; Pumpradit et al., 2010; Siriwanarangsan et al., 2004). A possible explanation may be that the HIV-infected people have acquired skills to adapt to living with HIV resulting in overall better well-being (Carvalho, Morais, Koller, & Piccinini, 2007; De Santis, Florom-Smith, Vermeesch, Barroso, & DeLeon, 2013; Fang et al., 2015; Farber, Schwartz, Schaper, Moonen, & McDaniel, 2000; Kelly et al., 2000; Russell et al., 2016). People are no longer afraid of dying from HIV (Bedingfield, Kipp, Kaler, & Rubaale, 2014).

Factors associated with anxiety in our study were female sex (Kaharuza et al., 2006; Liu et al., 2013), no access to universal health coverage (Bunjoungmanee, Chunloy, Tangsathapornpong, Khawcharoenporn, & Apisarnthanarak, 2014; Himakalasa, Grisurapong, & Phuangsaichai, 2013; Li, Lee, Wen, et al., 2010), poor adherence (Nel & Kagee, 2011; Panigrahi, Swain, &

Table 1. Demographic characteristics, and HIV disease and treatment information for 2,023 study participants.

Characteristics	All patients (*N* = 2023)	Anxiety			Depression		
		Non-anxious (*N* = 1926)	Anxious (*N* = 97)	*p*	Not depressed (*N* = 1961)	Depressed (*N* = 62)	*p*
Female, sex	880 (44%)	824 (43%)	56 (58%)	.004	849 (43%)	31 (50%)	.29
Mean (SD) age	48.9 (7.8)	43.9 (7.8)	42.8 (7.7)	.17	43.8 (7.8)	45.0 (8.2)	.25
Currently employed	1845 (91%)	1756 (91%)	89 (92%)	.84	1792 (91%)	53 (86%)	.11
Married or in a relationship	962 (48%)	917 (48%)	45 (46%)	.97	929 (47%)	33 (53%)	.41
Health benefit coverage				.10			.99
Universal coverage (UC) scheme	685 (34%)	662 (34%)	23 (24%)		664 (34%)	21 (34%)	
Social security scheme	812 (40%)	763 (40%)	49 (51%)		786 (40%)	26 (42%)	
Civil servant benefits scheme	387 (19%)	370 (19%)	17 (18%)		376 (19%)	11 (18%)	
Self-supported	139 (7%)	131 (7%)	8 (8%)		135 (7%)	4 (7%)	
Self-reported adherence <90% (vs. ≥90%)	279 (14%)	247 (13%)	32 (33%)	<.001	266 (13.6%)	13 (21.0%)	.10
cART regimen				.40			.71
NNRTI-based	1545 (76%)	1476 (77%)	69 (71%)		1500 (76%)	45 (73%)	
PI-based	474 (23%)	446 (23%)	28 (29%)		457 (23%)	17 (27%)	
Other	4 (1%)	4 (1%)	0 (0)%		4 (1%)	0 (0%)	
Mean (SD) years on cART	7.7 (2.9)	7.7 (2.9)	7.5 (3.0)	.28	7.7 (2.9)	8.1 (3.2)	.64
Currently using EFV	671 (33%)	638 (33%)	33 (34%)	.86	645 (33%)	26 (42%)	.14
Exposed to EFV	914 (45%)	864 (45%)	50 (52%)	.20	877 (45%)	37 (60%)	.02
Median (IQR) years on EFV	4.4 (1.8–7.5)	4.4 (1.9–7.5)	3.9 (1.3–7.8)	.31	4.4 (1.8–7.5)	5.2 (2.0–8.8)	.02
Mean (SD) QOL Score	89.9 (12.5)	90.5 (12.0)	76.6 (13.4)	<.001	90.4 (12.0)	73.1 (14.8)	<.001
Total QOL categories				<.001			<.001
Poor (score 26–60)	25 (1.2%)	14 (0.7%)	11 (11.3%)		16 (0.8%)	9 (14.5%)	
Fair (score 61–95)	1343 (66.4%)	1264 (65.6%)	79 (81.5%)		1293 (65.9%)	50 (80.7%)	
Good (score 96–130)	655 (32.4%)	648 (33.7%)	7 (7.2%)		652 (33.3%)	3 (4.8%)	
Median (IQR) CD4 cell count; cells/mm^3	495 (363–645)	495 (363–637)	498 (357–715)	.26	496 (363–639)	485 (364 –733)	.59
CD4 count ≥ 350 cells/mm^3	1102 (78%)	1043 (78%)	59 (79%)	.85	1068 (78%)	34 (77%)	.94
HIV-RNA <50 copies/mL	1287/1360 (95)	1219/1286 (95)	68/74 (92%)	.28	1247/1319 (95%)	40/41 (98%)	.4

Notes: Data are reported as *N* (%) unless otherwise specified. Categorical covariates were compared by a chi-square or Fisher's exact test, and continuous covariates by a *t*-test or Wilcoxon rank sum test as appropriate.

Mohanty, 2015), and bad or fair QOL (Margalho, Pereira, Ouakinin, & Canavarro, 2011; Nuesch et al., 2009). Factors associated with depression were exposure to EFV (Apostolova et al., 2015; Cavalcante et al., 2010; Mothapo et al., 2015) and bad or fair QOL (Bengtson et al., 2015; Pedersen et al., 2015).

It is possible that women have higher anxiety because their needs are ignored (Carosi et al., 2009; Lechner et al., 2003; Loutfy et al., 2013; Sullivan, McNaghten, Begley, Hutchinson, & Cargill, 2007), while there are more public health campaigns targeting men who have sex with men (Allison, Adams, Klindera, Poteat, & Wolf, 2014; Anand et al., 2015). Thai women generally have higher levels of societal obligations compared to men and expected to carry the burden of being caretakers (Songwathana, 2001). Working women are more vulnerable to the effects of occupational stressors compared to men with the same level of stress (Roxburgh, 1996). However, we did not detect any significant difference in the prevalence of depression between women and men in this present study. Typical Thai families have a strong bond and great family social support which may

Table 2. Factors associated with anxiety from logistic regression models done in 2023 HIV-infected patients.

Characteristic		Univariate		Multivariate	
	N	Crude OR (95%CI)	*p*	Adjusted OR (95%CI)	*p*
Sex					
Male	1143	1 (ref)	<.01	1	<.01
Female	880	1.83 (1.21–2.76)		1.93 (1.26–2.94)	
Health benefit coverage			.09		.05
Universal coverage (UC) scheme	685	1 (ref)		1	
Social security scheme	812	1.85 (1.11–3.07)		1.98 (1.18–3.32)	
Civil servant benefits scheme	387	1.32 (0.70–2.51)		1.71 (0.89–3.29)	
Self-supported	139	1.76 (0.77–4.02)		1.92 (0.82–4.45)	
Adherence (%)			<.001		<.001
≥90%	1744	1 (ref)		1	
< 90%	279	3.35 (2.15–5.22)		3.21 (2.04–5.05)	
QOL level			<.001		<.001
Good	655	1 (ref)		1	
Fair or poor	1368	6.51 (3.00–14.15)		6.42 (2.94–14.02)	

Table 3. Factors associated with depression from logistic regression models done in 2023 HIV-infected patients.

		Univariate		Multivariate	
Characteristic	*N*	Crude OR (95%CI)	*p*	Adjusted OR (95%CI)	*p*
Level of total QOL			<.001		
Good	655	1 (ref)		1 (ref)	<.01
Fair or poor	1368	9.8 (3.06–31.34)		10.25 (3.2–32.87)	
Ever exposed to efavirenz			.02		
Never	1109	1 (ref)		1 (ref)	
Yes	914	1.83 (1.09–3.06)	<.001	1.98 (1.18–3.32)	<.001

help decrease the rate of depression (Li, Lee, Jiraphongsa, et al., 2010).

In addition, having a good healthcare system can help patients deal better with disease (Lohse, 2016) and have good adherence (Bunjoungmanee et al., 2014; Himakalasa et al., 2013; Li, Lee, Wen, et al., 2010). In this study, only 7% of them had to pay for ART by themselves. Hence, it is not surprising that patients in the universal health coverage program (ILO, 2008) had less anxiety because they receive good quality care which does not incur any out of pocket expenses (WHO, 2012). Consistent with other studies, the odds of anxiety were approximately three times higher in patients with poor adherence (Ammassari et al., 2002; Campos, Guimaraes, & Remien, 2010; Gonzalez et al., 2011; Ingersoll, 2004; Nilsson Schonnesson, Williams, Ross, Bratt, & Keel, 2007). Patients who are not adherent to their medications may have more anxiety prior to the clinic visit because they fear being criticized by their healthcare providers if their CD4 and their HIV VL results are not good.

Furthermore, we found that good QOL was significantly associated with lower levels of anxiety and depression. These findings are consistent with previous studies that showed emotional status and neurocognitive performance were also associated with the levels of the QOL (Osowiecki et al., 2000; Pappin, Wouters, & Booysen, 2012).

Also, patients exposed to EFV had a significantly higher odds of depression which concurs with previous studies (Clifford et al., 2009; Fumaz et al., 2005; Lochet et al., 2003; Parienti et al., 2004; Poupard et al., 2007; Rihs et al., 2006). EFV exposure for at least three months yielded more cognitive and mood disorders (Lochet et al., 2003; Poupard et al., 2007).

Our study has several limitations. First, data may not be representative of all HIV-infected Thais. Second, the patients were already on cART for more than six months which may be different to those initiating cART. It is unknown whether anxiety/depression will improve or worsen over time. Third, the psychiatric symptoms were based on the patients' self-reported scores so may not be accurate. Also, HADS has not been validated for use in Thai HIV-infected population but is considered to be one of the best, currently available tool to assess anxiety and depression in HIV-infected patients (Rabkin, 2008; Savard, Laberge, Gauthier, Ivers, & Bergeron, 1998) and validated in the general Thai population (Lotrakul & Sukanich, 1999). Cronbach's alpha coefficients for internal consistency for anxiety and depression were well above the threshold of 0.70 (0.8551 and 0.8259, respectively) (Lotrakul & Sukanich, 1999), indicating that the scale is reliable in Thai HIV-infected Thais. Last, we did not collect the data about alcohol use and substance abuse. Anecdotal evidence suggests many of our patients stopped smoking, drinking alcohol and using recreational drug upon their HIV diagnosis. However, we cannot completely discard the potential effects of alcohol, smoking and substance abuse on anxiety and depression (Bellos et al., 2013; Moylan, Jacka, Pasco, & Berk, 2013).

In conclusion, we found a low prevalence of anxiety and depression in Thai HIV-infected patients on long-time cART with well-suppressed VL. Healthcare providers should carefully assess psychiatric comorbidities in women, those with poor adherence and those patients who are on EFV-based regimens.

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(Governmental pharmaceutical organization). The rest of the authors declare no conflict of interest.

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