# Chapter 10
# Psychiatric Aspects of HIV Infection in Sub-Saharan Africa

**Etheldreda Nakimuli-Mpungu**

**Abstract** Psychiatric assessment should always be incorporated into any assessment of patients with HIV/AIDS. To begin the process of HIV care, routine HIV testing coupled with pre- and post-test counseling should be offered to patients accessing outpatient and inpatient mental health services. Referral networks to other healthcare facilities should be put in place so that medical assessments to rule out organic causes can be treated. Mental health care providers should be equipped with skills and tools to provide prevention interventions for persons living with mental disorder and HIV/AIDS. Likewise, HIV healthcare personnel need to be equipped with skills and tools to be able to carry out routine mental health assessments/screening for the common mental health problems in HIV/AIDS.

Lastly, HIV infection causes significant brain degeneration with resultant affective (depression, mania), psychotic, anxiety and cognitive disorders, the latter commonly referred to as HIV-Associated neurocognitive disorders or HAND. These neuropsychiatric disorders occur in both children and adults. Untreated, they will compromise adherence to treatment initiatives and pose significant HIV-infection risk behavior. All this calls for integration of mental health care in any HIV-care program for their early detection and treatment for better outcomes and improved quality of life for PLWHA and for prevention strategies if we are to stem the epidemic.

**Keywords** HIV depression • HIV related secondary mania • Severe mental illness • People living with HIV AIDS (PLWHA) • Bipolar disorder co-morbid with HIV/AIDS

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## Introduction

Psychiatric disorders have been reported among people at risk for or infected by HIV worldwide. Addressing co-occurring psychiatric disorders is a necessary step in control of the HIV epidemic [1, 2]. The psychiatric sequelae of HIV infection have etiologies that involve biological, psychological and social factors. These include the natural and expected grief response to being diagnosed with a terminal illness, later reactions to disability and illness as well as exacerbation of pre-existing psychiatric illness. On the other hand new psychiatric symptoms and syndromes may occur as a result of direct effect of the HIV virus on the brain, or as a consequence of HIV-related opportunistic diseases and as side effects of HIV-related treatments. Despite the impressive reduction of HIV-related morbidity and mortality where antiretroviral therapy (ART) is available, reports of psychiatric repercussions of HIV disease are on the increase [3].

The consequences of untreated psychiatric disorders among those with HIV infection include reduced coping capacity at the time of HIV diagnosis, poor HIV-related disease prognosis, failure to access HIV care and treatment, erratic adherence to antiretroviral regimens, diminished quality of life, greater social burden, increased health-care costs and higher mortality [4–7]. Among persons living with HIV, there is a documented mental health treatment gap that needs to be addressed. This gap is large for both severe and common mental disorders worldwide [2], but more pronounced sub-Saharan Africa.

Understanding psychiatric disorders among people living with HIV and AIDS (PLWHA) in sub-Saharan Africa can help better define priorities and needed resources to reduce the incidence, the prevalence and the burden of HIV disease on individuals with these disorders and on the communities in which they receive care. In this chapter we review published epidemiology of mental disorders among PLWHA in sub-Saharan Africa. We begin with the most described HIV related-psychiatric disorders among people with HIV: depression; mania; anxiety (including PTSD); and psychosis. We also discuss sero-prevalence of HIV and risk behaviors in individuals with severe mental illness (SMI) as well as the impact of SMI on HIV treatment outcomes in sub-Saharan Africa.

## Depression

A systematic review of the literature on HIV and mental illness in developing countries performed by Collins et al. (2006) found 13 studies published between 1990 and 2005 from middle or low-income countries that reported rates of psychiatric disorder based on diagnostic interviews or psychiatric symptom scales [8]. Rates of depression ranged from 0 % to 63.3 % among HIV-positive participants. In the largest of these studies, investigators recruited every third subject seeking medical services in Bangkok, Thailand; Kinshasa, Democratic Republic of Congo; Nairobi,

Kenya; Sao Paolo, Brazil and Munich, Germany [9]. To ascertain psychiatric diagnoses, the Composite International Diagnostic Interview (CIDI), a structured diagnostic interview developed by the WHO and validated for cross-cultural use, was used and to ascertain depressive symptoms the Montgomery-Asberg Depression Rating Scale (MADRS) was used. Rates of depression among asymptomatic HIV-positive people in the four developing country sites averaged 6.0 % (range: 0 % in Kinshasa to 10.9 % in Sao Paolo). Symptomatic HIV-positive patients had rates of depression, ranging from 4.4 % in Kinshasa to 19.6 % in Sao Paolo. Depression was the only diagnosis for which a higher prevalence among symptomatic HIV-positive patients reached significance compared with HIV-negative controls.

Since 2005, the expansion of ART programs with scaling up of ART provision in rural areas in Sub-Saharan Africa has led to more research on depression of HIV positive individuals. These studies are summarized in Table 10.1. In 30 studies, HIV positive individuals using ART have been screened with various depression screeners resulting in prevalence estimates of significant depression symptoms ranging from 9.4 % [10] to 81 % [11]. Six studies report on prevalence rates of current major depression ranging from 11.8 % [12] to 34.9 % [13]. Two studies report on prevalence rates of lifetime major depression ranging from 13.3 % [14] to 18.1 % [13] among HIV positive individuals. The Ugandan studies estimate prevalence rates of significant depression symptoms to range from 30 % [15] to 54 % [16].

The studies on prevalence of depression in HIV positive populations give variable prevalence estimates of depression; from as high as 81 % in HIV positive individuals attending an HIV treatment program in Rwanda to as low as 0 % in HIV positive individuals in the Democratic Republic of Congo (DRC). If the findings of these studies are to be taken at face value, then eight of ten HIV positive patients in Rwanda has significant depression symptoms and depression is non-existent in DRC. A critical re-evaluation of these studies is required given the variability of findings.

A recent systematic review of studies documenting the prevalence of significant depressive symptoms and major depression among HIV-positive individuals enrolled in ART programs in sub-Saharan Africa, found prevalence estimates of 31 % and 18 %, respectively [17]. These estimates are much higher than prevalence estimates of depressive symptoms and major depression in community studies in Uganda and South Africa [2], suggesting an increased risk of depressive symptoms and major depression in HIV-positive individuals.

Most studies reporting on the prevalence of depression among PLWHA, have not assessed subjects for bipolar disorder [18], an important diagnosis to rule out. Many studies screened or assessed people for depressive symptoms and without further evaluation, no distinction can be made between subclinical depression and other depressive disorders besides major depression [15, 19, 20]. The few studies that have evaluated study participants with a diagnostic interview have neither reported on subclinical depression nor lifetime depressive disorders [13, 21, 22]. Knowledge of the prevalence of specific depressive disorders would allow for better resource allocation to provide required treatments (e.g., pharmacotherapy and psychotherapies) [23, 24] while management of lifetime depression would focus on relapse prevention using psychosocial interventions and maintenance medication.

**Table 10.1** Summary of studies describing prevalence estimates of depression symptoms and major depression among HIV positive individuals and their impact on adherence to ART in sub-Saharan Africa

| Author | Location<br>Study design<br>Setting<br>Sample size<br>% Females | Measures of depression symptoms<br>Validation measure<br>% depression symptoms | Measure of major depression<br>% major depression | Association between depression and ART adherence |
|---|---|---|---|---|
| Adewuya 2008†‡ | Nigeria<br>Cross-sectional<br>HIV psychosocial support center<br>N = 87<br>56.3 % females | 15.1 % depression symptoms | Mini international neuropsychiatric interview<br>NA<br>11.8 % major depression | NA |
| Adewuya 2010†§ | Nigeria<br>Cross-sectional<br>HIV psychosocial support center<br>N = 182<br>53 % females | General health questionnaire (12 items)<br>Cut-off score : ≥ 3<br>Not locally validated in study population<br>65.4 % depression symptoms | | Depressed patients were less likely to be adherent to ART compared to non-depressed patients<br>AOR = 0.23; 95% CI (0.09–0.55) |
| Amberbir 2008†§ | Ethiopia<br>Longitudinal<br>HIV treatment clinic attached to general hospital<br>Baseline<br>N = 400<br>59.8 % females | Becks depression Inventory (21 items)<br>Cut-off score: ≥10<br>Not locally validated in study population<br>55.8 % baseline depression symptoms | | Depressed patients were less likely to be adherent to ART compared to non depressed patients<br>OR = 0.47; 95% CI (0.26–0.90)<br>Association between alcohol use and adherence was not assessed |
| Byakika-Tusime 2009§ | Uganda<br>Cross-sectional<br>Mother-to-child-transmission plus program<br>N = 177<br>70.1 % females | Becks Depression Inventory (BDI) (21 items)<br>Cut-off score : not reported<br>Not locally validated in study population<br>Mean BDI score for the sample was 9.74 (SD = 4.6) | | Among those who had used ART for less than 6 months, the odds of adherence decreased by 99 % for every unit increase in depression symptom score<br>AOR = 0.01; 95% CI (0.00–0.77)<br>Among those "stable" on ART, the odds of adherence decreased by 61 % for every unit increase in depression symptom score<br>AOR = 0.39; 95% CI (0.11–1.34) |

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**Table 10.1** (continued)

| Author | Location<br>Study design<br>Setting<br>Sample size<br>% Females | Measures of depression symptoms<br>Validation measure<br>% depression symptoms | Measure of major depression<br>% major depression | Association between depression and ART adherence |
|---|---|---|---|---|
| Cohen 2009† | Rwanda<br>Cross-sectional<br>HIV psychosocial support center<br>N = 658<br>100 % females | Center for epidemiological studies depression scale (20 items)<br>Cut-off score: ≥16<br>Not locally validated in study population<br>81 % depression symptoms | | NA |
| Do 2010† | Botswana<br>Cross-sectional<br>HIV treatment clinic attached to general hospital<br>N = 300<br>76.3 % females | Becks depression inventory (21 items)<br>Cut-off score: ≥14<br>Not locally validated in study population<br>28.3 % depression symptoms | | NA |
| Etienne 2010§ | Kenya, Uganda, Zambia, Nigeria, and Rwanda<br>Cross-sectional<br>HIV treatment clinics attached to general hospitals<br>N = 921<br>65.4 % females | Factor scores of depression were constructed from three questions of depression (persistent feelings of sadness/ hopefulness in the past month, frequency of crying in the past month, and frequency of feeling confused in the past month)<br>Reliability score 0.67<br>57.2 % low depression scores, 22.0 % medium depression scores, 20.8 % high depression scores | | Those with high depression scores were less likely to adhere to ART compared to those with low scores<br>AOR = 0.57; 95% CI (0.39–0.84)<br>Those who never used alcohol were more likely to be adherent to ART than those who used alcohol<br>AOR = 2.14; 95% CI (1.36–3.37) |

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**Table 10.1** (continued)

| Author | Location<br>Study design<br>Setting<br>Sample size<br>% Females | Measures of depression symptoms<br>Validation measure<br>% depression symptoms | Measure of major depression<br>% major depression | Association between depression and ART adherence |
|---|---|---|---|---|
| Farley 2010†§ | Nigeria<br>Cross-sectional<br>HIV treatment clinic attached to a general hospital<br>N = 399<br>70 % females | Center for epidemiological studies depression scale (20 items)<br>Cut-off score: ≥21<br>The Cronbach alpha: 0.86<br>13 % depression symptoms | | Study participants with CES-D scores ≥16 were less likely to be adherent to ART compared to those with scores < 16<br>OR = 0.23; 95% CI (0.08–0.68)<br>No association between AUDIT scores and pharmacy refill rate<br>OR = 1.55; 95% CI (0.19–12.46) |
| Kagee 2010† | South Africa<br>Cross-sectional<br>HIV clinics within primary health care facilities<br>N = 85<br>75.3 % females | The Beck Depression Inventory 1(BDI-1)<br>Cut-off score : ≥18<br>Cronbach's alpha: 0.85<br>37.6 % depression symptoms | | NA |
| Kaharuza 2006† | Uganda<br>Cross-sectional<br>HIV psychosocial support center<br>N = 1,017<br>77 % females | A modified center for epidemiological studies depression scale (12 items) was computed by removing the CES-D items reflecting somatic complaints<br>Cut-off score: ≥23<br>Cronbach's alpha: 0.85<br>47 % depression symptoms | | NA |

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**Table 10.1** (continued)

| Author | Location<br>Study design<br>Setting<br>Sample size<br>% Females | Measures of depression symptoms<br>Validation measure<br>% depression symptoms | Measure of major depression<br>% major depression | Association between depression and ART adherence |
|---|---|---|---|---|
| Kekwaletswe 2011#§† | South Africa<br>Cross-sectional<br>HIV treatment center<br>N = 304<br>68 % females | Center for Epidemiological studies Depression scale (20 items)<br>Cut-off score : ≥16<br>Cronbach's alpha: 0.92<br>59.2 % depression symptoms | | Patients with CES-D score of >16 were less likely to be adherent to ART compared to those with scores < 16<br>OR = 0.43;.95 % CI (0.25–0.72)<br>Patients with AUDIT score >8 were less likely to be adherent to ART compared to those with scores <8<br>OR = 0.30; 95 % CI (0.19–0.73) |
| Lawler 2010†‡ | Botswana<br>Cross-sectional<br>HIV treatment clinic attached to a general hospital<br>N = 120<br>50 % females | Beck Depression Inventory-Fast Screen (BDI-FS)<br>Cut-off score: ≥4<br>Cronbach's alpha: 0.84<br>38 % depression symptoms | Prime-MD Mood Module (MM)<br>24 % major depression | NA |
| Martinez 2008† | Uganda<br>Cross-sectional<br>HIV treatment clinic attached to a general hospital<br>N = 421<br>63.2 % females | A modified depression section of the Hopkins Symptoms checklist with somatic measures removed.<br>Cut-off score: ≥1.75<br>Cronbach's alpha: 0.74<br>18.8 % depression symptoms | | NA |
| Marwick 2010‡ | Tanzania<br>Cross-sectional<br>HIV treatment clinic attached to a general hospital<br>N = 220<br>74 % females | Clinic interview schedule –Revised<br>Previously validated in primary health clinic attendees<br>Cronbach's alpha for this sample not reported | 15.5 % major depression | NA |

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**Table 10.1** (continued)

| Author | Location<br>Study design<br>Setting<br>Sample size<br>% Females | Measures of depression symptoms<br>Validation measure<br>% depression symptoms | Measure of major depression<br>% major depression | Association between depression and ART adherence |
|---|---|---|---|---|
| Monahan 2009† | Kenya<br>Cross-sectional<br>HIV psychosocial support center<br>N = 347<br>73 % females | Patient health questionnaire (9 items)<br>Cut-off score: ≥10<br>Cronbach's alpha 0.78<br>34 % depression symptoms | | NA |
| Myer 2008†‡ | South Africa<br>Cross-sectional<br>Primary health care facility<br>N = 465<br>75 % females | Center for Epidemiological studies Depression scale<br>Cut-off score : ≥ 6<br>45 % depression symptoms. Locally validated in study population.<br>Sensitivity: 79 %<br>Specificity: 61 % | Mini international neuropsychiatric interview<br>14 % major depression | NA |
| Nachega 2011#† | South Africa.<br>Longitudinal<br>HIV treatment center<br>Baseline<br>N = 274<br>60 % females | Brief Symptom Inventory (BSI) 51 items<br>Cut-off score: ≥9<br>Not locally validated in study population<br>25.4 % baseline depression symptoms | | Depression scores were not associated with ART adherence at 12 and 24 month follow-up.<br>OR =0.5, 95% CI (0.15–1.56) Alcohol abuse was a baseline independent predictor of ART adherence<br>OR 2.4, 95% CI (1.20–5.0) |
| Nakasujj 2010† | Uganda<br>Longitudinal<br>HIV treatment clinic attached to a general hospital<br>N = 102 (baseline)<br>72.6 % females | Center for epidemiological studies depression scale (20 items)<br>Cut-off score: ≥16<br>Not locally validated in study population<br>54 % baseline depression symptoms | | NA |

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**Table 10.1** (continued)

| Author | Location<br>Study design<br>Setting<br>Sample size<br>% Females | Measures of depression symptoms<br>Validation measure<br>% depression symptoms | Measure of major depression<br>% major depression | Association between depression and ART adherence |
|---|---|---|---|---|
| Nakimuli-Mpungu 2009†§ | Uganda<br>Cross-sectional<br>HIV treatment clinic attached to a Mental hospital<br>N = 122<br>78.% females | Self-reporting questionnaire (20 items)<br>Cut-off score: ≥6<br>Not locally validated in study population<br>30.3 % depression symptoms | | Those with significant depression symptoms were less likely to adhere to ART compared to those without significant depression symptoms<br>AOR = 0.27; 95% CI (0.10–0.72) |
| Nakimuli-Mpungu 2010† | Uganda<br>Cross-sectional<br>HIV treatment clinic attached to a general hospital<br>N = 244<br>63.9.% females | DSM-IV symptom checklist<br>Cut-off score: ≥6<br>Not locally validated in study population<br>40 % depression symptoms | | NA |
| Olley 2006‡ | South Africa<br>Longitudinal<br>HIV treatment clinic attached to a general hospital<br>N = 149 (baseline)<br>70.5.% females | | Mini international neuropsychiatric interview<br>Not locally validated in study population<br>34.9 % major depression | |
| Patel 2009 | Zimbabwe<br>Cross-sectional<br>HIV treatment clinic attached to a general hospital<br>N = 200<br>100 % females | Shona symptom questionnaire (14 items)<br>Cut-off score : not reported<br>Cronbach's alpha 0.86<br>Mean depression score 28.44 (9.28) | | NA |

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**Table 10.1** (continued)

| Author | Location<br>Study design<br>Setting<br>Sample size<br>% Females | Measures of depression symptoms<br>Validation measure<br>% depression symptoms | Measure of major depression<br>% major depression | Association between depression and ART adherence |
|---|---|---|---|---|
| Pearson 2009† | Mozambique<br>Longitudinal<br>HIV treatment clinic<br>N = 277 (baseline)<br>56.3 % female | Center for epidemiological studies depression scale (10 items)<br>Cut-off score: ≥10<br>Cronbach's alpha: 0.74<br>9.4 % baseline depression symptoms | | NA |
| Peltzer 2010§ | South Africa<br>Cross-sectional<br>District hospital<br>N = 519<br>73.4 % females | Center for epidemiological studies depression scale (10 items)<br>Cut-off score: not reported<br>Cronbach's alpha: 0.54<br>NA | | The odds of adherence decreased by 29 % for every unit increase in depression symptom score<br>OR = 0.88; 95% CI (0.80–0.96) |
| Pourpad 2007† | Senegal<br>Cross-sectional<br>HIV treatment clinic<br>N = 200<br>63.5 % females | Center for epidemiological studies depression scale (20 items)<br>Cut-off score : ≥16<br>Not locally validated in study population<br>18 % depression symptoms | | NA |
| Ramadhani 2007†§ | Tanzania<br>Cross-sectional<br>HIV treatment clinic<br>N = 150<br>63 % females | Hopkins symptom checklist (25 items)<br>Cut-off score: ≥1.75<br>Cronbach's alpha: 0.93<br>21 % depression symptoms | | Those with significant depression symptoms were less likely to adhere to ART compared to those without significant depression symptoms<br>AOR = 0.48; 95% CI (0.15–1.56) |

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**Table 10.1** (continued)

| Author | Location<br>Study design<br>Setting<br>Sample size<br>% Females | Measures of depression symptoms<br>Validation measure<br>% depression symptoms | Measure of major depression<br>% major depression | Association between depression and ART adherence |
|---|---|---|---|---|
| Simbayi 2007† | South Africa<br>Cross-sectional<br>Psychosocial support center<br>N = 1,063<br>60.5 % females | Modified center for epidemiological studies depression scale (11 items)<br>Cut-off score: ≥16<br>Cronbach's alpha: 0.93<br>30 % depression symptoms | | NA |
| Spies 2009‡ | South Africa<br>Cross-sectional<br>Primary health care HIV treatment facilities<br>N = 429<br>76 % females | Kessler-10<br>Cut-off score: ≥28<br>Cronbach's alpha: 0.87 | Mini international neuropsychiatric interview<br>13 % major depression | NA |
| Wagner 2011† | Uganda<br>Cross-sectional<br>HIV treatment clinic attached to a general hospital<br>N = 602<br>68 % females | Patient health questionnaire (9 items)<br>Cut-off score: ≥10<br>The Cronbach alpha coefficient for the sample not reported<br>13 % depression symptoms | | NA |
| Weidle 2006† | Uganda<br>Longitudinal<br>Psychosocial support center<br>N = 987<br>74 % females | Modified center for epidemiological studies depression scale (20 items)<br>Cut-off score: ≥23<br>Cronbach's alpha not reported<br>45 % baseline depression symptoms | | NA |

[#] This study was published as an abstract
[†] These studies reported prevalence rates of depression symptoms
[§] These studies reported the association between depression symptoms and adherence to ART
[‡] These studies reported prevalence rates of major depression

In Uganda, a recent cross-sectional study of HIV positive individuals in a rural ART program in the southern regions of the country found the prevalence estimates of any depressive disorder, subclinical depression, both current and lifetime major depression, and bipolar depression were 46.4 %, 17.8 %, 25 % and 3.6 % respectively [25]. In comparison to non-depressed patients, those with sub-clinical depression were less likely to have high levels of self-efficacy, more likely to be using ART for less than 1 year, had advanced HIV disease and current alcohol use disorders (AUD's). Those with both current and lifetime depressive disorders were less likely to be 85 % adherent to antiretroviral therapy (ART), have social support and high levels of self-efficacy, more likely to have tuberculosis and past manic episodes. Those with only lifetime depressive disorders were more likely to have current alcohol use disorder (AUD) and past manic episodes. The large proportion of HIV positive individuals with depressive disorders or significant depressive symptoms in ART programs in Uganda and other developing countries who remain undiagnosed and untreated is indeed a major unmet healthcare need.

## *Depression and Non-adherence to ART*

In 2005, two African studies investigated the association between current significant depression symptoms and adherence to ART. In both studies, the association did not attain statistical significance. Since then, two Ugandan studies, [15, 26]; one study from South Africa [27] Nigeria [28] and Ethiopia [29] have investigated this association. All studies report a statistically significant association between current significant depression symptoms and poor adherence to ART. Qualitative studies in sub-Saharan Africa on barriers to ART adherence echo similar findings [30–32].

Given that depression is a recurrent complex mood disorder with various DSM-5 categories, it is important to investigate the relationship between lifetime depressive disorders and adherence to ART. A recent case-control study among rural HIV positive individuals using anti-retroviral therapy revealed that HIV positive individuals with lifetime depressive disorders had an increased risk of non-adherence to ART after controlling for education status, income, self-efficacy, perceived social support, cognitive impairment and current alcohol use disorders [32]. This association was stronger in females than males. This finding indicates that it would be important to closely monitor and support individuals with a history of lifetime depressive disorders who are initiating ART.

Studies have shown that untreated depressive disorders increase HIV transmission risk behaviors [33, 34], decrease immune status [35, 36] and decrease adherence to antiretroviral therapy (ART) [37–40] which may result in decreased clinical effectiveness and potential development of drug resistance [41, 42]. Thus, depression does pose challenging barriers to effective medical care at multiple points along the continuum of HIV medical care engagement and treatment (i.e. the 'HIV treatment cascade') [43]. Untreated depression has been associated with a lower likelihood of receiving anti-retroviral drugs [44, 45], poor adherence [34, 46] and

increased morbidity [47–50] and mortality [35]. Depression is a predictor of clinical progression independently of non-adherence behaviors [49]. Depression is frequently under diagnosed and when recognized is often poorly treated, particularly in primary medical settings where most HIV/AIDS patients receive care [7, 51]. Mounting evidence suggests that effective treatment of depression in HIV patients may have benefits for their HIV-treatment retention, ART adherence, and virologic suppression, and, therefore, for community viral load [43].

## HIV-Related Secondary Mania

Mania in a patient with HIV/AIDS may occur as a phase of a coexisting bipolar disorder, or it may be secondary to the direct neuronal effects of HIV infection [4, 52], treatments for HIV infection [53–55], or HIV-related secondary infections of the brain [56]. Affected patients appear to present with severe psychopathology [57, 58]. In developed countries, prevalence studies have shown that mania secondary to HIV infection is common [59, 60], and it occurs more among individuals with AIDS than among those with HIV infection alone [57, 60]. Researchers have previously hypothesized that mania occurring in the early stages of HIV infection may represent bipolar disorder in its manic phase, whereas mania in persons with AIDS is secondary mania linked to the pathophysiology of HIV brain infection [59, 61].

The evidence for an etiological association with HIV neuropathy was bolstered by a prospective study of HIV-positive patients with and without mania that demonstrated a protective effect from an antiretroviral agent able to penetrate the central nervous system [62]. However, given the small sample sizes used in these studies, any conclusions drawn from them should be considered tentative. The epidemiology of mania secondary to HIV infection in Uganda and other African countries that have high rates of HIV infection and limited access to highly active antiretroviral therapy remains largely unknown.

A study in Uganda compared the presentation and correlates of primary mania in HIV-negative patients with those of first episode secondary mania in HIV-positive patients [63]. The majority of HIV-positive patients with mania met criteria for first-episode secondary mania. Compared with HIV-negative patients with primary mania, they were predominantly female, age 30–49 years and of low socioeconomic and educational status. A significant number were divorced or had been widowed as a result of losing spouses to AIDS. Clinically, the majority presented in late stages of HIV infection, in WHO clinical stages 3 and 4. They were irritable and had aggressive and disruptive behaviors, decreased need for sleep, over talkativeness, and high rates of cognitive impairment, paranoid delusions, visual hallucinations, and auditory hallucinations as well as high rates of HIV-related signs and symptoms [63].

These findings show that first-episode secondary mania in HIV-positive individuals and primary mania in HIV-negative individuals are clinically and immunologically distinct. The relationship between secondary mania and depressed CD4 counts suggests that in the setting of an AIDS epidemic in poor countries where the costs

of measures of immune status, such as CD4 cell counts, are prohibitive, secondary mania maybe used as an indicator to initiate highly active antiretroviral therapy [63]. Knowledge about the presentation of secondary mania in HIV infection may improve its clinical recognition and hence guide the development of early, effective interventions to control symptoms that not only interfere with a patient's ability to adhere to treatment but also predispose patients to HIV risk behaviors, which may lead to further spread of HIV infection.

### *Early Onset Versus Late Onset HIV-Related Secondary Mania*

A follow –up study compared the demographic and clinical characteristics of HIV-positive patients with early-onset and late-onset first-episode secondary mania in HIV infection, in order to determine whether baseline characteristics might provide insights into appropriate methods of assessment and management [61]. This study showed that among HIV-positive patients who met criteria for secondary mania, patients with early-onset and late-onset mania had comparable socio-demographic characteristics. Clinically, consistent with previous findings [57], patients with late-onset secondary mania had more manic symptoms on the Young Mania Rating Scale, YMRS. They were more irritable and had a more decreased need for sleep than patients with early-onset secondary mania.

## Bipolar Disorder Co-morbid with HIV/AIDS

Another study in Uganda revealed that patients with bipolar mania, regardless of HIV status, had a more-or-less similar demographic profile. They had comparable age at onset of first affective symptoms, marital and education status. Generally, these findings are in keeping with previous descriptions of demographic characteristics of patients with bipolar disorder elsewhere [64]. It is interesting to note that, at the time of assessment, HIV-positive patients with bipolar disorder were older than the HIV-negative patients. This indicates that the HIV-positive patients had a longer duration of bipolar illness than the HIV-negative patients. One possible explanation for this finding could be that the lack of routine screening for HIV infection in our psychiatric hospital may have delayed diagnosis of HIV in the majority of these patients. Previous researchers have argued that HIV-positive patients with various bipolar subtypes may have associated impulsive, risk-taking traits that may play a role in HIV risk-behavior such as unprotected sex [65].

This study also confirmed the hypothesis that the demographic profiles of HIV-positive patients with bipolar mania and those with secondary mania were different. Although, at assessment, both groups had comparable ages, those with primary bipolar mania were younger when they had their first episode of affective symptoms. Also, the bipolar-mania group had more education and was more likely to be

employed than the secondary-mania group. However, both groups of HIV-positive patients had comparable female-to-male ratios, with women being more often affected than men. In Africa, where heterosexual transmission predominates, men usually have multiple sexual partners. Therefore women are more at risk of acquiring HIV infection [66].

Clinically, as expected, the HIV-positive patients, regardless of mania status, had more immune suppression, more cognitive impairment, and more severe manic symptoms, with more irritability and more psychotic symptoms than the HIV negative patients with bipolar mania.

Interestingly, this study also shows that the HIV-positive individuals regardless of manic status had comparable severity of manic symptoms. This finding suggests that the presence of HIV infection in patients with bipolar disorder may alter subsequent manic episodes, making them similar to that of HIV-positive patients with secondary mania. Therefore, one may argue that recurrent manic episodes in patients with bipolar disorder infected with HIV may be related to the pathophysiology of HIV infection in the brain.

We also observed that the HIV-positive patients with bipolar mania had more cognitive impairment, more immune suppression, and, hence, more HIV-related illnesses than those with secondary mania. This finding is in contrast to previous findings from earlier reports, which found that HIV-positive patients with secondary mania have more cognitive impairment and more immune suppression than HIV-positive patients considered to have bipolar mania [57]. Possible explanations could be that patients with bipolar disorder are already cognitively and functionally impaired by their illness by the time they acquire HIV infection. A growing body of evidence suggests that bipolar patients exhibit neuropsychological impairment that persists even during the euthymic state, which may be a contributory factor to poor psychosocial outcome [67].

## Anxiety Disorders

Anxiety is a common symptom in HIV-infected patients. When anxiety symptoms are severe or persistent to the extent that they interfere with normal functioning, the affected patient may have an anxiety disorder. These disorders include panic disorder, generalized anxiety disorder, obsessive-compulsive disorder, and post-traumatic stress disorder. A recent study among Ugandan HIV-infected patients receiving medical care with The AIDS Support Organization (TASO) at Mulago hospital, found that among patients with psychological distress, 27 % of these had generalized anxiety disorder and 27 % had panic disorder [68]. An earlier study conducted by Petrushkin and colleagues in 2005 had estimated panic disorder at 32.6 % in HIV-positive patients [69].

The risk factors that have been associated with development of anxiety disorders include (i) HIV-positive diagnosis: unexpected positive test result especially with no or poor pre-test counseling, late diagnosis, late stage of HIV/AIDS, (ii) lack of

social support, (iii) past sexual abuse, (iv) living in a conflict/post-conflict society, (v) violence and especially partner violence, (vi) substance abuse, (vii) poor pre-infection psychological adjustment, for example, personality disorder, past affective disorder,(viii) poor access to care: absent or inconsistent HIV care, (ix) poor economic support: unemployment, poverty, (x) loss of significant others: partner, spouse, child, parent (orphan-hood, widow, etc.) and (xi) lastly, stigma and the presence of other diseases of stigma [68, 70].

Researchers have also described AIDS phobia, obsessive compulsive disorder and post-traumatic stress disorder (PTSD) as commonly found in HIV/AIDS. PTSD has particularly been associated with the sudden news of a positive HIV test (especially where there was no pre-test counseling), past sexual abuse and living in conflict/post-conflict communities in Africa in which HIV/AIDS is often co morbid with war-related PTSD [70, 71].

## Post-traumatic Stress Disorder (PTSD)

PTSD may precede an HIV diagnosis due to previously experienced traumatic events, or may emerge post-HIV diagnosis as a result of the stress of being diagnosed with a life-threatening illness [72, 73] or subsequent challenges over the course of the HIV disease trajectory. Stresses include fears and worries about physical decline and disability, access to appropriate treatment, the welfare of dependents, loss of employment, stigma, discrimination, possible isolation, and dying or traumatic events.

Available studies from Africa suggest that the lifetime prevalence of PTSD among PLWHA ranges from 30 % to 64 %. Among recently diagnosed HIV-positive South African individuals, an estimated PTSD rate of 15 % and 26 % was determined at baseline and follow-up, respectively [74] compared to the South African general population lifetime and 12 month prevalence of PTSD of 2.3 % and 0.6 %, respectively [75, 76]. Among the 15 % who met criteria at baseline for PTSD, patients reported as their index trauma in decreasing order, being informed of their HIV-positive diagnosis (36 %), being raped (23 %), being robbed or assaulted (14 %), being the victim of intimate partner violence (9 %), experiencing a serious accident (9 %) and the death of someone close to the individual (9 %) [13, 77]. Another South African study found a lifetime PTSD rate of 54 % and an incidence of HIV-related PTSD of 40 % [73].

## Psychosis

Psychotic symptoms may be part of a major depressive disorder, schizophrenia, mania, obsessive-compulsive disorder, medication side effects, or secondary to drug or alcohol abuse, CNS complications, or medications. Thus, the pathophysiology of psychosis in HIV infection is complex, and a multifactorial etiology of psychotic symptoms is likely in many cases. However, there are many reports of psychotic symptoms in

HIV-infected persons in the absence of concurrent substance abuse, iatrogenic causes, evidence of opportunistic infection or neoplasm, or detectable cognitive impairment. These usually present atypically and with paranoia, as a common symptom in clear consciousness [71]. A common clinical feature of new onset psychosis in HIV-infected patients is the acute onset of HIV symptoms. In one Ugandan study, researchers found that HIV infection worsens neuropsychological impairment among individuals with psychosis which persists even during the euthymic state. Nakasujja and her colleagues (2012) compared cognitive function in HIV positive and HIV negative individuals in a cohort of individuals with psychosis [78]. The cognitive impairment was more pronounced among the HIV positive individuals and especially so for the females. Although earlier studies indicated that cognitive impairment and psychosis were late manifestations of HIV disease [79, 80] studies from Low and Middle Income Countries, LMICs show that the two conditions can sometimes occur early as evidenced by the moderate level of CD4 count and the intermediate WHO stages of disease manifestation [61].

## Sero-prevalence of HIV in Severe Mental Illness (SMI) Populations

Again, most studies of HIV sero-prevalence in individuals living with SMI have been undertaken in HICs. A systematic review of such studies showed HIV sero-prevalence rates ranging from 3 % to 23 % among patients with SMI [70]. The higher HIV sero-prevalence rates among people with SMI in sub-Saharan African countries including Zimbabwe [81, 82], Uganda [83], and South Africa [84, 85] have underscored the importance of giving particular attention to HIV prevention among people with SMI in sub-Saharan Africa [8].

## Risk Behaviors in SMI

Individuals with SMI, particularly those with mood disorders, engage in high rates of sexual risk behaviors associated with HIV infection, including multiple sex partners, unprotected intercourse, and sex trade [86]. Research on the mechanisms underlying the association between pre-existing mental disorders and HIV infection is limited. However, it has been hypothesized that symptoms such as impulsivity, disinhibition, poor judgment and hyper sexuality may predispose affected individuals to risky behaviors such as unsafe sexual practices resulting in acquisition of HIV infection [87].

Previous epidemiological studies conducted in developed countries make clear that persons living with an SMI are more likely to be victims of sexual coercion and intimate partner violence, to live in risky environments, to have unstable partnerships in high-risk sexual networks, to use substances that impair decision making, and to lack the emotional stability, judgment, and interpersonal skills needed to avoid risk [88].

Data emerging from sub-Saharan African countries and other LMICs reports a wide range of HIV risk sexual behaviors. A recent qualitative study in Uganda showed that SMI exacerbated sexual vulnerability in the women by contributing to casual sex, to exploitative and non-monogamous sexual relationships, and to sexual assault by non-partners [89]. Studies from Brazil showed that high rates of lifetime unprotected sex, substance use and, early sexual initiation are associated with SMI [74, 90].

## Impact of SMI on Health Outcomes

In Uganda, HIV positive individuals with SMI are often denied access to ART in general hospital settings and research studies [18] because of presumed inability to adequately adhere or tolerate treatment. However, recent efforts to scale up antiretroviral therapy (ART) led to the establishment of an ART program at the Butabika National Referral Mental Hospital. A recent study found that SMI at ART initiation was associated with worse retention in HIV care, specifically over the first 6 months [91]. This finding suggests that early interventions to support and maintain these individuals in care are needed for individuals with HIV and SMI who are initiating ART.

In South Africa, a cross-sectional retrospective folder review of 100 PLWH suffering from an SMI revealed that 63 did not attend a first 6-month HIV clinic follow-up. There were no significant differences between 6-month attenders and non-attenders on demographic or clinical variables. After adjustment, respondents who had been re-admitted to a psychiatric hospital more than once were more likely not to attend their follow-up visit compared to those with no re-admissions. These findings suggest that PLWH who have a co-morbid SMI are an especially vulnerable group of patients [92].

Despite the much vulnerability among individuals with SMI, HIV prevention and treatment programs in LMICs do not consider them as one of the most at-risk populations (MARPs) and thus, remain the most understudied vulnerable group in the HIV epidemic [93]. Recent evidence in high income countries, HICs, suggests that specialized programmes and services for serious mental illness and HIV-positive individuals have resulted in HIV care that is as good, and in some ways better than other HIV patients without SMI [94, 95]. Thus, targeted culturally sensitive HIV prevention programs [96] for individuals with SMI in LMICs should be a priority in stemming the HIV epidemic.

## Conclusion

To begin the process of any HIV care, routine HIV testing coupled with pre- and post-test counseling should be offered to patients accessing outpatient and inpatient mental health services. Psychiatric assessment should always be incorporated into any assessment of patients with HIV/AIDS. Referral networks to other healthcare

facilities should be put in place so that medical assessments to rule out organic causes can be treated. Mental health care providers should be equipped with skills and tools to provide prevention interventions for persons living with mental disorder and HIV/AIDS [97]. Likewise, HIV healthcare personnel need to be equipped with skills and tools to be able to carry out routine mental health assessments/screening for the common mental health problems in HIV/AIDS.

Lastly, HIV infection causes significant brain degeneration with resultant affective (depression, mania), psychotic, anxiety and cognitive disorders, the latter commonly referred to as HIV-Associated neurocognitive disorders or HAND. These neuropsychiatric disorders occur in both children and adults. Untreated, they will compromise adherence to treatment initiatives and pose significant HIV-infection risk behavior. All this calls for integration of mental health care in any HIV-care program for their early detection and treatment for better outcomes and improved quality of life for PLWHA and for prevention strategies if we are to stem the epidemic.

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