Prevalence of Clinical features of Depression in adult patients receiving antiretroviral treatment at the Dr George Mukhari Academic Hospital Tshepang HIV Clinic in South Africa

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I Dr E.M Thekiso hereby declare that the work on which this research is based is original(except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being or is to be submitted for another degree at this or any other university

Signature_________________________________

Date:____________________________________
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ABSTRACT

BACKGROUND: Depression has been shown to negatively impact antiretroviral treatment initiation and adherence (Ramirez-Avila et al., 2012). In Sub-Saharan Africa, the consequences of poor adherence include not only poor treatment outcomes, but also the emergence of resistance to first-line treatment regimens (Bangsberg, 2008). Sub-Saharan Africa faces a triple burden of HIV, TB and chronic disease epidemics. In South Africa, the communicable and non-communicable disease burden is high (Coovadia, Jewkes, Barron, Sanders & McIntyre, 2009; Karim, Churchyard, Karim & Lawn, 2009; Mayosi, Flisher, Laloo, Sitak, Tollman & Bradshaw, 2009), as is the burden of depression (Nyirenda, Chatterji, Rochat, Mutevedzi & Newell, 2013). Research elucidating factors affecting adherence to antiretroviral treatment are of paramount importance in the ongoing struggle to improve the quality of life of HIV-positive individuals worldwide.

OBJECTIVES: To determine the prevalence of clinical features of depression (including severity) using the Patient Health Questionnaire 9 (PHQ-9) in adult patients receiving antiretroviral treatment, as well as determine socio-demographic findings that assist in defining clinical features of depression and determine the association of various antiretroviral regimens with clinical features of depression

METHODS: This was a cross-sectional descriptive study with prospective data collection in adult patients receiving antiretroviral drugs over a twelve week period. A PHQ-9 questionnaire and a socio-demographic questionnaire were administered to all 240 patients and results tabulated using SAS release 9.2 or higher, running under Microsoft Windows for a personal computer. A regression analysis was performed to determine statistically significant predictors for depression.

RESULTS: Of the 240 participants, 58% were depressed and 42% were not depressed. Of the 58% depressed, 25.8% were mildly depressed, 20.4% were moderately depressed, 7.7% were moderately severely depressed and 4.6% were severely depressed. None of the socio-demographic factors proved to be predictors for depression. There was no association between the HAART regimen and depression status.

CONCLUSION: The results of this study demonstrate that the prevalence of depression among HIV/AIDS patients is high. A partnership between mental health care providers and HIV/AIDS care providers, similar to the TB and HIV/AIDS collaboration, should be embarked upon. All HIV/AIDS patients should be screened for depression and equally, all mental health care users should be screened for HIV/AIDS.
CHAPTER 1
INTRODUCTION

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) describes major depressive disorder as a depressed mood or lack of interest in pleasurable activities for a period of two weeks which is accompanied by clinically significant distress or impairment in social, occupational or other important areas of functioning (American Psychiatric Association, 2013). Depressive spectrum disorders seem to be the most common psychiatric manifestations of human immunodeficiency virus (HIV) disease (Dubé, Benton, Cruess & Evans, 2005).

Major depressive disorder is more prevalent among HIV-infected individuals than in the general population, with estimated prevalence rates among HIV-positive patients varying widely from 2% to 30%, or even up to 50% (Atkinson, Grant, Kennedy, Richman, Spector & McCutchan, 1998; Dubé et al., 2005; Hinkin, Castellon, Atkinson & Goodkin, 2001; Judd et al., 2005; Olley et al., 2003; Owe-Larsson, Säll, Salamon & Allgulander, 2009; Treisman & Angelino, 2007). The variable prevalence rates of major depressive disorder reported could probably be explained by variations in study population and design.

Globally, it is estimated that depressive features occur in 60% of patients living with HIV/AIDS (Bongogo, Tumbo & Govender, 2013). Bing et al. (2001) report that in the United States of America, major depression occurs in a third of HIV-infected patients seeking primary medical care (Bing et al., 2001). A similar study conducted by Bongongo et al. (2013) in the Rustenburg district in South Africa concluded that 71.8% of patients on highly active antiretroviral treatment (HAART) demonstrated depressive features (Bongongo et al., 2013).

Major depressive disorder in HIV-infected patients may be a primary consequence of central nervous system effects of HIV, a reaction to the stigmatisation and emotional consequences of the diagnosis and coping with a serious medical illness, secondary from antiretroviral treatment, or a combination of these factors, thus constituting a heterogeneous group of disorders with neurovegetative confounding factors (Hinkin et al., 2001).

Depression is one of the leading causes of disease burden globally (Collins et al., 2011; Mathers & Loncar, 2006; Patel, Boyce, Collins, Saxena & Horton, 2011). Projections suggest that, by 2030, unipolar depressive disorders will contribute 6.2% to the global burden of
disease in terms of disability-adjusted life years, roughly equal to the contribution of heart disease (Nyirenda et al., 2013; World Health Organisation, 2008).

While frequently underdiagnosed, depression in HIV/AIDS patients is fairly commonplace and is debilitating (Lapid & Rummans, 2003; Reynolds, Haley & Kozlenko, 2008). It is associated with increased disability (Arnow et al., 2006; Castro-Costa et al., 2007), increased burden on public health service utilisation (García-Peña et al., 2008; Lapid & Rummans, 2003; Rowan, Davidson, Campbell, Dobrez & Maclean, 2002) and increased risk of mortality (Antelman et al., 2007; Nyirenda et al., 2013; Snowden, Steinman & Frederick, 2008).

1.1 Study problem

Depression has been shown to impact negatively on antiretroviral treatment initiation and adherence (Ramirez-Avila et al., 2012). Poor adherence leads to poor treatment outcomes as well as emergence of resistance to first-line treatment regimens (Bangsberg, 2008).

Sub-Saharan Africa faces a triple burden of HIV, TB and chronic disease epidemics. In South Africa, the communicable and non-communicable disease burden is high (Coovadia et al., 2009; Karim et al., 2009; Mayosi et al., 2009), as is the burden of depression (Nyirenda et al., 2013). Research unpacking factors affecting adherence to antiretroviral treatment are of paramount importance in the ongoing struggle to improve the quality of life of HIV-positive individuals worldwide (Arrivillaga, Ross, Useche, Alzate & Correa, 2009).

Despite the above mentioned observations by different authors, factors associated with depression amongst adult patients receiving antiretroviral treatment at Dr George Mukhari Academic Hospital have not been concluded. The purpose of this study was thus to determine the prevalence of clinical features of depression in adult patients receiving antiretroviral treatment at Dr George Mukhari Academic Hospital. The results will enable policymakers and service provision planners to make informed decisions with regards to alleviating the burden associated with HIV infection.
CHAPTER 2
LITERATURE REVIEW

2.1 Depression

Symptoms of major depression include (1) depressed mood most of the day almost every day, (2) decreased interest and pleasure in nearly all activities, (3) changes in appetite or weight without dieting, (4) disruptions in sleep patterns nearly every day, (5) psychomotor retardation or agitation, (6) feelings of worthlessness or inappropriate guilt, (7) diminished ability to concentrate, and (8) recurrent thoughts of death or suicide. At least five of these symptoms must be present for at least two consecutive weeks to fulfil the diagnostic criteria for major depression; depressed mood most of the day nearly every day or decreased interest and pleasure in nearly all activities must be included among the five. Moreover, these symptoms must also result in significant disturbances in social and occupational functioning. Lastly, exogenous causes of depression, such as drug therapy, physical illness, and substance abuse, should be ruled out before a diagnosis of major depression is made (American Psychiatric Association, 2013; Bongongo et al., 2013; Penzak, Reddy & Grimsley, 2000).

Major depressive episodes routinely respond to standard first-generation antidepressants (e.g., tricyclic antidepressants like nortriptyline or desipramine), but most clinicians prefer the newer selective serotonin reuptake inhibitors (SSRIs, such as fluoxetine—Prozac, paroxetine—Paxil, sertraline—Zoloft) or selective serotonin noradrenaline reuptake inhibitors (SNRIs, such as venlafaxine—Effexor) because of their more favourable side effect profiles (Rabkin, Wagner & Rabkin, 1999; Zisook, Peterkin, Goggin, Sledge, Atkinson & Grant, 1998). Of the newer antidepressant drugs, sertraline, citalopram—Celexa and venlafaxine are commonly chosen because of their minimal inhibitory effects on the enzyme systems metabolising antiretrovirals, with resulting low likelihood of drug-drug interactions. (Hinkin et al., 2001).

2.2 Human immunodeficiency virus

HIV is a ribonucleic acid (RNA) retrovirus that is the causative agent for acquired immunodeficiency syndrome (AIDS). HIV belongs to the Lentivirus genus in the family Retroviridae, characterised by a replication cycle in which the viral RNA is reverse transcribed into a DNA proviral form that is integrated into the host cell genome. The retrovirus is composed of two copies of single-stranded RNA that codes for the virus’s 9
genes. The RNA is non-covalently linked to the core proteins, which in turn are surrounded by a viral envelope, which enables the virus to enter cells by binding to a specific cellular receptor located on the surface of cluster of differentiation 4 (CD4) cells. Once exposed to the body, the HIV virus antibodies may be detected after an acute flu-like illness, proceeding to infect specific cells of the immune system during an asymptomatic period that may last for years. In order to enter a cell, HIV must bind to CD4, typically found on T lymphocytes, blood monocytes, macrophages and some dendrite cells, and subsequently to one or a combination of several possible chemokine co-receptors, usually CCR5 and CXCR4 (Albright, Soldan & González-Scarano, 2003; Anthony, Arango, Stephens, Simmonds & Bell, 2008; Owe-Larsson et al., 2009).

The presence and action of HIV in the central nervous system are now much better understood. HIV crosses the blood-brain barrier by a Trojan-horse type mechanism using macrophages it infects (Lawrence & Major, 2002). Once in the brain, HIV targets and infects glial cells, from which it later secretes neurotoxins that lead to neuronal damage and death (Clifford, 2002). The extent of this neuronal damage is thought to be linked to the level of clinical neurologic deficits. Postmortem neuropathologic examinations of HIV-positive patients have revealed the presence of virus in cortical and subcortical structures, namely the frontal lobes, the subcortical white matter and the basal ganglia (Aylward et al., 1993; Navia, Cho, Petito & Price, 1986). Some authors have suggested that the caudate nucleus and the basal ganglia are the primary areas of pathogenesis (Aylward et al., 1995; Van Gorp et al., 1992). Recent evidence supports a mechanism by which neurotoxins released by periventricular macrophages and microglia trigger cytokine and chemokine release (Nath, 2002), which in turn lead to modification of synaptic architecture in the cortex (Sá et al., 2000; Everall et al., 1999; Masliah et al., 1997). It is thought that apoptosis, or programmed cell death, is the most common mechanism resulting in cell loss (Kaul, Garden & Lipton, 2001; Thompson, McArthur & Wesselingh, 2001).

2.2.1 HIV OR AIDS management

In 2013, South Arica adopted new guidelines for the management of HIV/AIDS. The goals of treatment were stated to be (Department of Health, 2013):

a. Save lives and improve the quality of life of people living with HIV
b. Achieve best health outcomes in the most cost-efficient manner
c. Implement nurse-initiated treatment
d. Decentralise service delivery to PHC facilities
e. Integrate services for HIV, TB, MCH, SRH and wellness
f. Diagnose HIV earlier
g. Prevent HIV disease progression
h. Avert AIDS-related deaths
i. Retain patients on lifelong therapy
j. Prevent new infections among children, adolescents, and adults
k. Mitigate the impact of HIV and AIDS

Table 2.1: Summary of the South African antiretroviral treatment guidelines

<table>
<thead>
<tr>
<th>First line</th>
<th>All new patients needing treatment, including pregnant women</th>
<th>TDF + FTC (OR 3TC)+EFV</th>
<th>Replace EFV with NVP in patients with significant psychiatric comorbidity or intolerance to EFV and where neuropsychiatric toxicity of EFV may impair daily functioning e.g. shift workers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescents</td>
<td>ABC + 3TC + EFV</td>
<td>FDC is preferred</td>
<td>At age 18 years an adolescent if eligible must be switched to the FDC</td>
</tr>
<tr>
<td>Contraindications to EFV</td>
<td>TDF +FTC (or 3TC) + NVP</td>
<td>Use NVP based regimen in patients with significant psychiatric comorbidity or intolerance of EFV and where the neuropsychiatric toxicity of EFV may impair daily functioning e.g. shift workers</td>
<td></td>
</tr>
<tr>
<td>Contraindications to TDF</td>
<td>AZT +3TC +EFV (or NVP)</td>
<td>Renal disease or the use of other nephrotoxic drugs e.g. aminoglycosides</td>
<td>Replace TDF with AZT</td>
</tr>
<tr>
<td>Contraindication to TDF and AZT</td>
<td>d4T +3TC+EFV(or NVP)</td>
<td>Renal disease and anaemia or the use of other nephrotoxic drugs. Switch to a d4T based regimen</td>
<td></td>
</tr>
<tr>
<td>Contraindication to TDF, AZT, and d4T</td>
<td>ABC +3TC+EFV(or NVP)</td>
<td>Renal disease, anaemia, peripheral neuropathy, the use of other</td>
<td></td>
</tr>
</tbody>
</table>
Currently on a d4T based regiment

<table>
<thead>
<tr>
<th>Current Regimen</th>
<th>New Regimen</th>
<th>Notes</th>
</tr>
</thead>
</table>
| TDF + FTC (or 3TC) + EFV | FDC preferred | Mandatory if patients experience toxicity and patients who are at high risk of toxicity (high BMI or pregnant). Switch to TDF if virally suppressed and the patient has a normal creatinine clearance, even if well tolerated.

**Second line**

Management of virological failure:

If plasma HIV RNA > 1000 copies

- Check for adherence, compliance, tolerability and drug-drug interactions. Assess psychological issues.
- Repeat viral load (VL) 2 months later
- If plasma VL confirmed > 1000 copies change regimen to second line therapy

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failing on a TDF- based first line regimen</td>
<td>AZT + 3TC + LPV/r</td>
</tr>
<tr>
<td>Failing on a d4T based first line regimen</td>
<td>TDF + 3TC (or FTC) and LPV/r</td>
</tr>
<tr>
<td>Dyslipidaemia or intractable diarrhoea associated with LPV/r</td>
<td>Switch LPV/r to ATV/r</td>
</tr>
</tbody>
</table>

**Third line**

Failure on second line treatments requires specialist referral and genotype resistance testing

Most likely regimens would include:

Raltegravir (integrase inhibitor)/Darunavir (most recently developed protease inhibitor)/Etravirine (a new NNRTI)
TDF= Tenofovir, FTC= Emtricitabine, 3TC= Lamivudine, EFV= Efavirenz, ABC= Abacavir, NVP= Nevirapine, AZT= Zidovudine, d4T= Stavudine, FDC=fixed dose combination, LPV/r Liponavir/Ritonavir (combination)

(Department of Health, 2013)

2.3 Diagnosis of depression in HIV

2.3.1 Overlap of HIV/AIDS symptoms and symptoms of depression

Recognising the psychiatric manifestations of HIV disease can be complicated by the complex biologic, psychological and social circumstances associated with this illness, and psychiatric symptoms often go unrecognised and untreated. The diagnosis of depressive disorders can be even more challenging because many vegetative symptoms of depression (e.g., fatigue, pain, anorexia and insomnia) are observed in many patients throughout the course of their HIV illness, even when depression is not present. However, in both the early and late phases of HIV disease, these symptoms correlate more closely with a mood disorder (when present) than with clinical correlates of infection (Lyketsos & Treisman, 2001). The prominence of diminished mood in the morning coupled with anhedonia should alert clinicians to the presence of a major depressive disorder and should help distinguish it from demoralisation or an adjustment disorder.

2.3.2 Apathy

Apathy may complicate diagnosis of depression in HIV/AIDS patients. Apathy is the simultaneous reduction in goal-directed thoughts, behaviours and emotions due to diminished motivation and is frequently seen in CNS disorders that disrupt frontal-subcortical connections (Marin, 1991). Persistent and pronounced apathy occurs with surprising frequency among HIV-positive patients (Castellon, Hinkin, Wood & Yarema, 1998; Rabkin, Ferrando, Van Gorp, Rieppi, McElhiney & Sewell, 2000). Although apathy is often mistakenlly considered solely a symptom of a depressive disorder, research in HIV/AIDS as well as other neurological diseases has shown that apathy can reliably be discriminated from depression and can exist independent of a depressive syndrome (Hinkin et al., 2001; Levy et al., 1998; Marin, 1997).
2.3.3 Neurocognitive impairment

Diagnosis may also be further complicated by neurocognitive impairment. The deleterious effects of HIV infection on neuropsychological function have been well established (for reviews, see Heaton et al., 1995; Hinkin, Van Gorp & Satz, 1995). HIV-associated neurocognitive dysfunction can range from subtle deficits in information-processing speed and efficiency to HIV-1-associated minor cognitive-motor disorder (MCMD) to a pronounced dementia syndrome – HIV-1-associated dementia (HAD) (also referred to as “AIDS dementia complex” and as “HIV-1 encephalopathy”) (American Academy of Neurology, 1991). The prevalence and severity of HIV-1-associated cognitive-motor impairment increases as a function of disease progression. HAD has been recently reported to show a reduced cumulative prevalence of 7-10% (Grant, Marcotte, Heaton & the HNRC Group, 1999), from prior figures of 17-25% (McArthur et al., 1993) over the course of AIDS, though the incidence may yet increase. MCMD prevalence has been less well studied but may occur in as many as 25-30% of individuals with early symptomatic HIV-1 infection and in 40% or more of those with AIDS. Subclinical impairment (in which there are deficits in cognitive test performance but no functional status sequelae) occurs in as many as 22-30% of asymptomatic HIV-1 seropositive individuals (Wilkie, Eisdorfer, Morgan, Loewenstein & Szapocznik, 1990; cf. White, Heaton & Monsch, 1995). Somewhat higher percentages with subclinical impairment are seen in early symptomatic and late symptomatic than in asymptomatic subjects (Heaton et al., 1995). Memory impairment, characterised especially by forgetfulness, motor and psychomotor slowing, attentional disruption and executive systems dysfunction, have all been repeatedly observed among HIV-positive individuals. This pattern of neurocognitive deficits is suggestive of disruption to the structures and circuitry along the prefrontal-subcortical axis, and is consistent with data from brain imaging (Aylward et al., 1995; Chang, Ernst, Leonido-Yee & Speck, 2000; Hinkin, Van Gorp, Mandelkern et al., 1995) and autopsy studies (Everall, Luthert & Lantos, 1991; Navia et al., 1986), both of which implicate preferential subcortical brain involvement.

To define MCMD, at least two of the following six symptoms must be present: impaired attention or concentration, mental slowing, impaired memory, slowed movements, incoordination, or personality change, irritability or emotional lability. Neuropsychological testing should be employed to support the foregoing diagnostic criteria. For MCMD, there must also be documentable, minor functional impairment in activities of daily living.
(although not sufficient for stage 1/mild HAD), and no other known etiology for the symptoms (American Academy of Neurology, 1991). To define HAD, there must be (1) an acquired abnormality in at least two of the following six neuropsychological domains: attention, information processing speed, abstraction, visuospatial skills, memory and language; (2) dysfunction in daily activities specific to this impairment, equivalent to American Academy of Neurology criteria (American Academy of Neurology, 1991) for at least the mild disease stage. As with MCMD, motor impairment may or may not be present; however, evidence of either motor or behavioural impairment is required. Exclusion criteria for the diagnosis of HAD must also be met: no presence of clouding of consciousness (i.e., delirium) or no evidence of another etiology for the impairment. To rule out the latter, MRI of the head is normally done to prove the diagnosis. The former is necessary prior to having a lumbar puncture, a metabolic workup to rule out hypoxemia or hepatic or uremic encephalopathy, and an evaluation to rule out toxicity of prescribed medications and psychoactive substances (Hinkin et al., 2001).

2.3.4 Under-diagnosis of depression

Despite the recorded high comorbidity between HIV/AIDS infection and psychiatric disorders, most cases are usually not detected by the attending physicians managing these patients. Petrushkin, Boardman and Ovuga (2005) reported that less than a third of these patients with co-morbid conditions were detected at a HIV clinic (Sulyman, Abiodun & Yussuf, 2013). In general, detection of psychiatric disorders in patients with chronic medical conditions by their attending physicians is usually found to be low (Feldman, Rabinowitz & Yehuda, 1995; Maoz, Rabinowitz, Mark, Antonovsky, Ribak & Kotler, 1991). Different reasons have been adduced for this low detection rate, ranging from patients’ factors to physicians’ factors. Patients may not readily disclose psychological symptoms to their doctors, while the physicians on the other hand may not ask for symptoms of psychological distress or view such as integral part of the ongoing physical illness (Gallego, Barreiro & López-Ibor, 2011; Sulyman et al., 2013). This leads to an alarming trend of under-diagnosis and under-treatment of depression.
2.4 Depression and HIV

The link between depression and HIV is largely mediated through inevitable neuro-invasion by HIV, psychological and social factors, such as stigma, substance abuse and prescribed medications such as efavirenz (Hoare & Joska, 2011).

Different factors have been enumerated to be responsible for the comorbid state. Many studies reported low socio-economic status, lack of social support, and unemployment to be essential factors (Sale & Gadanya, 2008; Adewuya et al., 2008). Other factors were advanced stage of the HIV/AIDS infection and non-tolerance of HAART (Sulyman et al., 2013).

Research suggests that HIV-positive people receiving depression treatment have higher CD4 counts, lower viral loads and decreased mortality, due to better adherence to treatment (Adams, Gaynes, McGuinness, Modi, Willig & Pence, 2012). Despite evidence supporting better outcomes, a study conducted in South America by Bess et al. (2013) revealed that only 31% of healthcare providers in an outpatient clinic for HIV patients reported routinely assessing all patients for depression and over half of the providers reported not being comfortable using FDA approved dosing ranges for depression.

It’s still questionable whether HIV-related depression is clinically different from depression in HIV-negative populations, a fact that could have treatment implications. In an attempt to close the gap regarding this knowledge, a study conducted in Uganda by Akena, Musisi and Kinyanda (2010) found that there were differences in depressive symptoms compared to HIV-negative patients. Similar conclusions have been reached regarding HIV-related mood disorders (Lyketsos et al., 1996). Neuropsychiatric disorders secondary to HIV itself are usually accompanied by neurocognitive impairment and commonly, but not all times, immunosuppression. Depression due to HIV is often accompanied by psychosocial stressors and substance abuse, and is frequent in early and late stages of the disease. The severe form is more typical in the late stages of the disease (Harris, Jeste, Gleghorn & Sewell, 1991).
CHAPTER 3
METHODOLOGY

3.1 Title

The prevalence of clinical features of depression in adult patients receiving antiretroviral treatment at Dr George Mukhari Academic Hospital Tshepang HIV Clinic in South Africa.

3.2 Aims and objectives

3.2.1 Aims

To identify the prevalence of clinical features of depression in adult patients receiving antiretroviral treatment at Dr George Mukhari Academic Hospital Tshepang HIV Clinic in South Africa.

3.2.2 Objectives

1. To determine the prevalence of clinical features of depression (including severity) using the PHQ-9 in adult patients receiving antiretroviral treatment.

2. To determine socio-demographic findings that assist in defining clinical features of depression.

3. To determine the association of various antiretroviral regimens with clinical features of depression.

3.3 Research question

What is the prevalence of clinical features of depression in adult patients receiving antiretroviral treatment at Dr George Mukhari Academic Hospital Tshepang HIV Clinic in South Africa?

3.4 Methods

3.4.1 Research design

Descriptive cross-sectional study design with prospective data collection.
3.5 Sampling techniques

3.5.1 Inclusion criteria

1. Patients 18 years or older.

2. English or Setswana speaking patients.

3. Patients who had been receiving antiretroviral treatment for 3 months or longer.

4. Patients who had provided informed consent.

3.5.2 Exclusion criteria

Patients too ill to participate were excluded.

3.5.3 Sample size

Sample size estimation was based on estimation of the prevalence of clinical features of depression, that is, patients with a total PHQ-9 score of 5 or more. With a total number of 1000 patients visiting Tshepang Clinic monthly, subtracting the number of patients who would be in the exclusion criteria left a total number of 800 patients monthly who were eligible for the study. With a proposed study period of 12 weeks, the finite population was 2400 patients.

With a sample size of 232, a two-sided 95% confidence interval for the true unknown prevalence percentage of patients with clinical features of depression would be within 6% of the percentage that would be calculated from the sample, assuming a 60% depression rate and adjusting for a finite population of 2400 patients. Sample size estimation was done on nQueryAdvisor release 7.0. A rounded sample size of 240 patients was proposed for the study.

3.6 Materials, apparatus and instruments

The PHQ-9, a socio-demographic questionnaire and a consent form were used.
3.7 Data collection techniques

Data were collected over 12 weeks, i.e., 20 patients per week. Patients attending the clinic were considered to arrive in a random order. The first four evaluable cases daily were included in the study. Prospective personal interviews were conducted at Tshepang Clinic at Dr George Mukhari Academic Hospital over a 12-week period. Written informed consent was obtained from all participants. Questionnaires were administered in either English or Setswana in accordance with patient choice. The PHQ-9 administration was supported in Setswana by the principal researcher if required by the patient. This support was verbal. The socio-demographic questionnaire was available in both languages. Each PHQ-9, socio-demographic questionnaire and consent form were assigned a number and date of completion to assist with case identification and grouping of data collection for each case. To ensure anonymity, no identifying data were recorded.

3.8 Data analysis and interpretation

Scores were recorded as follows: 0-4 for no depression, 5-9 for mild depression, 10-14 for moderate depression, 15-19 for moderately severe depression and 20 or more for severe depression. The severity of depressive features was compared across age, sex, occupational status, educational level, household income, marital status, presently treated depression, presently treated mental illness other than depression, and antiretroviral regimen.

The prevalence percentage of depression was calculated as follows:

Prevalence= number of patients with depression/number of patients in the sample ×100%

A 95% confidence interval was calculated for the prevalence. All statistical procedures were performed on SAS release 9.2 or higher, running under Microsoft Windows for a personal computer. Significance testing was at the 0.05 (5%) level. Depression was considered as a dependent variable, and age, gender, marital status, occupation, level of education, antiretroviral regimen and income as predictor variables. A logistic regression analysis was performed to determine statistically significant predictors for depression.
3.9 Reliability and validity of study

The PHQ-9 was chosen as a valid tool as it has a sensitivity of 80% and specificity of 92% as a screening tool for depression or follow-up tool (Moreno et al., 2011). The principal researcher underwent training to ensure correct and consistent administration of the PHQ-9 tool. Training was furthermore undertaken to ensure the same during the administration of the socio-demographic questionnaires. Training was done by Professor Solomon Rataemane, Head of Psychiatry department at the Dr George Mukhari Academic Hospital (MBCHB, FF.PSYCH (SA), Dipl Child psych).

3.10 Bias

Bias was minimised in the following ways:

1. The principal researcher underwent training for correct and consistent administration of the PHQ-9 tool.

2. The principal researcher underwent training for correct and consistent administration of the socio-demographic questionnaire.

3. The socio-demographic questionnaire was offered in English and Setswana.

4. PHQ-9 was supported in Setswana if required by the patient. Such support was consistent across patients and aimed to simply express content of the screening tool.

5. There was an extensive recruitment period, i.e., 12 weeks, supporting improved representativeness of study population.

3.11 Ethical considerations

Approval for the study was obtained from Medunsa Research Ethics and Publications Committee. A written information pamphlet was given to all study participants prior to consenting to be part of the study. Written informed consent was obtained from each participant. All participants were informed that the information obtained was to be used solely for research purposes. Participants were also be informed of their right to withdraw from the study at any point during the study.
CHAPTER 4
RESULTS

4.1 Gender category

A total of 240 patients were interviewed, 59% of whom were female and 41% of whom were male.

Figure 4.1: Category of gender
4.2 Age group of participants

The ages of participants ranged between 18 to above 60. Regarding age groups, 68.3% were in the 35-60 age group, 22.1% were in the 25-35 age group, 5.8% were above 60 and 3.8% were aged between 18-25.

Figure 4.2: Age group of participants
4.3 Employment status of participants

Out of the 240 participants, 61.3% were unemployed whilst 32.9% were employed. Of the 32.9% employed, 22.1% were non-professional and only 10.8% were professional; 5.4% of participants were pensioners and 0.4% were students.

Figure 4.3: Employment status of participants
4.4 Monthly income of participants

Out of the 240 participants, 52.1% had a monthly income ranging between R0-R999, 19.6% had a monthly income of between R1000-R1999, 7.9% earned between R3000-R3999, 7.5% earned between R2000-R2999, whilst only 4.2% earned between R4000-R4999, 7.9% earned R5000-R9999 and only 0.8% earned more than R10 000 a month.

![Bar chart showing monthly income distribution of participants]

**Figure 4.4: Monthly income of participants**
4.5 Antidepressant treatment category

Out of the 240 participants, 97% were not on any antidepressants at the time and only 3% of the participants were on antidepressants.

Figure 4.5: Category of antidepressant treatment
4.6 Psychotropic treatment category

Out of the 240 participants, 3% were on psychotropics other than antidepressants and 97% of the participants were not on any psychotropics.

Figure 4.6: Category of psychotropic medications other than antidepressants
4.7 HAART regimen category

Out of the 240 participants, 60% were on regimen 1a (efavirenz containing regimen), 34.2% were on regimen 2b and 5.8% were on regimen 1b.

**Figure 4.7: Category of HAART regimen**

Regimen 1a: Fixed dose combination or AZT or TDF or D4T + 3TC + EFV (efavirenz containing regimen)

Regimen 1b: AZT or TDF or D4T +3TC+ NVP

Regimen 2b: AZT or ABC or TDF +3TC or DDI + Alluvia
4.8 Depression status of participants

Out of the 240 participants, 58% of the participants were depressed and 42% were not depressed.

Figure 4.8: Depression status of participants
4.9 PHQ-9 status

Of the 58% depressed, 25.8% were mildly depressed, 20.4% were moderately depressed, 7.7% were moderately severely depressed and 4.6% were severely depressed.

![Bar chart showing PHQ-9 status percentages]

Figure 4.9: PHQ-9 status
4.10 Age of participants against depression status

Of the participants aged between 18-25, 67% were depressed, whilst only 33% were not. Participants aged between 35-60 years followed with 61% who were depressed and only 39% who were not depressed. Those aged between 25-35 years followed with 53% who were depressed and 47% who were not depressed. Only 43% of those above 60 years were depressed whilst 57% were not depressed.

![Figure 4.10: Age of participants against depression status](image-url)
4.11 Gender against depression status of participants

Of the female participants, 61% were depressed and 39% were not depressed. Of the male participants, 54% were depressed and 46% were not depressed.

![Gender against depression status of participants](image)

**Figure 4.11:** Gender against depression status of participants
4.12 Marital status against depression status of participants

In the category of marital status against depression, 60% of divorced participants were depressed, 57% of married participants were depressed, 59% of single participants were depressed and 53% of widowed participants were depressed.

Figure 4.12: marital status against depression status of participants
4.13 Employment status of participants against depression status

All 100% student participants were depressed. Of the unemployed participants, 62% were depressed whilst 38% were not. Of the non-professional participants, 55% were depressed and 45% were not depressed. Of the professional participants, 54% were depressed and 46% were not depressed. Only 38% of the pensioners were depressed and 62% were not depressed.

![Bar Chart]

Figure 4.13: Employment status of participants against depression status
4.14 Highest level of education against depression status

Participants who had received no education and those whose highest level of education was grade 7 both had a depression percentage of 67%. Those whose highest level of education was grade 4 had a depression percentage of 63%. Those whose highest level of education was grade 12 then had a depression percentage of 62%. Those who furthered education beyond matric had a depression percentage of 55%, whilst those who had between grade 8 and 10 level of education had a depression percentage of 48%.

Figure 4.14: Highest level of education against depression state
4.15 Depression status against monthly income

The highest depression percentage occurred among participants whose income ranged between R0-R999, with a percentage of 62%, followed by both participants whose income was between R1000- R1999 and those who made between R4000- R4999, with a percentage of 60%. Those earning between R5000-R9999 had a depression percentage of 58%. Those earning more than R10 000 had a depression percentage of 50%. Those earning between R2000-R2999 had a depression percentage of 44% and those earning between R3000-R3999 had a depression percentage of 42%.

Figure 4.15: Depression status against monthly income
4.16 HAART regimen against depression status

The highest depression percentage was found in participants on regimen 1b with a percentage of 64%, followed by participants on regimen 2b with a percentage of 62%. The group with the least depression percentage was those who were taking regimen 1a, with a percentage of 56%.

![Figure 4.16: HAART regimen against depression status](chart)

<table>
<thead>
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<th></th>
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<tbody>
<tr>
<td>0</td>
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</tr>
<tr>
<td>1a</td>
<td>44%</td>
<td>56%</td>
</tr>
<tr>
<td>1b</td>
<td>36%</td>
<td>64%</td>
</tr>
<tr>
<td>2b</td>
<td>38%</td>
<td>62%</td>
</tr>
<tr>
<td>100%</td>
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4.17 Regression analysis

Table 4.1 Regression analysis

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<th>p value</th>
</tr>
</thead>
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<td>Age</td>
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<td>0.3147</td>
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<tr>
<td>Sex</td>
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<td>0.98</td>
<td>0.4027</td>
</tr>
<tr>
<td>Marital status</td>
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<td>0.5357</td>
</tr>
<tr>
<td>Occupation</td>
<td>5</td>
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<td>0.8069</td>
</tr>
<tr>
<td>Education</td>
<td>6</td>
<td>1.69</td>
<td>0.1258</td>
</tr>
<tr>
<td>Income</td>
<td>10</td>
<td>0.50</td>
<td>0.8901</td>
</tr>
<tr>
<td>Regimen</td>
<td>2</td>
<td>1.86</td>
<td>0.1583</td>
</tr>
</tbody>
</table>

A regression analysis of depressive symptoms, including the independent variables age, sex, marital status, occupation, highest level of education, monthly income and type of antiretroviral regimen, was tested. None of the independent variables proved to be predictors for depression.
CHAPTER 5
DISCUSSION

5.1 Depression status

The findings of this study correlate with many other studies, such as a study conducted in eastern Uganda that screened for depression in patients undergoing treatment for HIV/AIDS which concluded that 47% reported depressive symptoms (Kaharuza et al., 2006) and another study conducted in Durban, South Africa, which found that 55% participants had depressive symptoms (Ramirez-Avila et al., 2012), to name but a few. However, varying rates of depression have been reported in the literature search, varying from 2% to 30%, or even up to 50% of HIV-positive patients (Atkinson et al., 1998; Dubé et al., 2005; Hinkin et al., 2001; Judd et al., 2005; Olley et al., 2003; Owe-Larsson et al., 2009; Treisman & Angelino, 2007). The wide variability of depression estimates may be due to the use of different psychiatric rating scales, study location, and cohort composition, such as age, sex, and clinical HIV stage. The timing of the depression assessment relative to the patient’s HIV diagnosis could also affect prevalence estimates (Ramirez-Avila et al., 2012).

5.2 PHQ-9 status

This study had similarly high rates of depression to the rates of depression in participants in a study done in South Africa in the North West province, which concluded that depression was diagnosed in 71.8% of participants in that study (Bongongo et al., 2013). This is closer to the 58% found in this study (see Figure 4.8). However, the severities differed in comparison to this study; they concluded that 69.2% had mild depression, versus 25.8% in the present study, while 1.7% had moderate depression versus 7.75% and 1% versus 4.6% had severe depression, as depicted in Figure 4.9. The slight differences might be accounted for by the fact that Rustenburg is largely populated by mine workers (Bongongo et al., 2013)

5.3 Age group against depression category

As noted in Figure 4.10, in this study, the highest rate of depression was reported in participants aged between 18-25. The lowest rates were found to be in participants aged above 60. These findings were paradoxical as the data from a 1990 sample of 2 031 US adults and a 1985 sample of 809 Illinois adults showed that depression reached its lowest level in the middle aged, at about age 45. The fall of depression in early adulthood and rise in late life
mostly reflect lifecycle gains and losses in marriage, employment, and economic well-being. Depression reaches its highest level in adults 80 years old or older, because physical dysfunction and low personal control add to personal and status losses (Mirowsky & Ross, 1992).

5.4 Gender against depression category

Two studies conducted in rural areas of Pakistan found that 66% and 72% women respectively had depression in comparison to 25% and 44% of men respectively (Angold, Costello & Worthman, 1998; Niaz, Hassan, Hussain & Siddiqui, 2004). The present study also reported similar findings, with female participants being more depressed in comparison to males; 61% of the female participants were depressed whilst only 54% of the male participants were depressed (see Figure 4.11). However, contrary to many studies reporting female gender as a predictor of depression, in this study, female gender was not a predictor for depression.

5.5 Marital status against depression category

Ali’s study conducted among women of a semi-urban community of Karachi a reported married women as being less depressed than single, widowed or divorced women (Naqvi, 2007). In the present study, divorced and single participants were slightly more depressed that their married counterparts (see Figure 4.12). However, the least depressed participants in this study were the widowed participants.

5.6 Employment and monthly income against depression status category

A study of a Ugandan population in 2012 concluded that, while depression is related to work and income, its influence may only be indirect through its relationship to other factors such as work, self-efficacy and physical health functioning (Wagner et al., 2012). The present study similarly concluded that level of monthly income and employment status was not a predictor for depression (p=0.8069; see Figure 4.13 and Figure 4.17). However, the relationship between depression and impaired work activity can be explained by depressive features such as lack of motivation, poor concentration and fatigue. These findings are consistent with research by Kinyanda, Woodburn, Tugumisirize, Kagugube, Ndyanabangi and Patel (2011), who found that depression was strongly associated with lower socioeconomic status and unemployment in a general population of Ugandans, as well as Kaharuza et al. (2006) who
found higher levels of depression to be associated with lower income among PLWHIV in Uganda. Furthermore, with it being difficult to distinguish between somatic depressive symptoms (e.g., poor appetite and fatigue) and physical symptoms of HIV disease, the fact that both cognitive and somatic symptoms were associated with work status and income supports the validity of the relationship between depression and these economic outcomes.

5.7 Highest level of education against depression state

Participants who had received no education and those whose highest level of education was grade 7 both had a depression percentage of 67%. Those whose highest level of education was grade 4 had a depression percentage of 63%. Those whose highest level of education was grade 12 then had a depression percentage of 62%. Those who furthered education beyond matric had a depression percentage of 55%, whilst 48% of those who had an education level between grade 8 and 10 were depressed.

Having qualifications beyond matric carried the least association with depression, with participants having 55% rate of depression. The mean depression percentage of participants with an educational level of up to matric was 60%.

5.8 HAART regimen against depression category

There are anecdotal reports of psychiatric symptoms, including mania and depression, in patients treated with zidovudine. Several case reports document manic episodes in association with zidovudine treatment, even in patients with no previous psychiatric history (Akhtar-Danesh & Landeen, 2007; Patten et al., 2006). Psychiatric effects also have been noted with efavirenz, though they occur less frequently than neurologic effects. However, when efavirenz-associated psychiatric effects occur, they may be serious and may include anxiety, depression, and suicidal ideation (Treisman & Kaplin, 2002). A small study comparing patients who took efavirenz or PI for a mean of 45 weeks documented higher scores on psychometric scales of anxiety and hostility in the efavirenz group than in the PI group. In this study, there was no association between depression and efavirenz (see Figure 4.16 and Figure 4.17).
5.9 Antidepressant treatment category

This study demonstrated that 58% of the depressed participants were not on any antidepressants at the time and only 3% of the total participants were on antidepressants. This shows that there is under-treatment of depression in people living with AIDS.

5.10 Psychotropic treatment category

Only 3% of the participants were on psychotropics other than antidepressants and 97% of the participants were not on any psychotropics.

5.11 Regression analysis

A regression analysis with the depression score as dependent variable and all the source variables as predictor variables, revealed no statistical significance (see Figure 4.17). None of the sociodemographic factors proved to be predictors for depression. With the exception of gender, the present study did not find any association between major depression and socio-demographic variables.
CHAPTER 6

CONCLUSION

6.1 Conclusion

Out of the 240 participants, 58% were depressed and 42% were not depressed. Of the 58% who were depressed, 25.8% were mildly depressed, 20.4% were moderately depressed, 7.7% were moderately severely depressed and 4.6% were severely depressed. There was no association between the HAART regimen and depression status. None of the socio-demographic factors proved to be predictors for depression.

6.2 Limitations

The results of this study represent a sample taken from HIV/AIDS clinic; therefore, it cannot be generalised to the community. The study design was also cross-sectional study as opposed to a longitudinal study. In addition, some potential confounders such as cognitive impairment were not addressed in the survey and were therefore not measurable in the analysis.

6.3 Recommendations

A partnership between mental health care providers and HIV/AIDS care providers, similar to the TB and HIV/AIDS collaboration, should be embarked on. All HIV/AIDS patients should be screened for depression and equally all mental health care users should be screened for HIV/AIDS.

Primary health care practitioners working in the field of HIV/AIDS need to be trained in the use of screening tools for depression. More research needs to be embarked upon investigating factors leading to under-recognition and therefore under-treatment of depression by health care providers. National guidelines for management of depression and HIV/AIDS should be implemented. Interest groups should have more public awareness campaigns on the signs and symptoms of depression and should focus specific efforts on destigmatising the complex comorbidity of HIV/AIDS and mental illness.
REFERENCES


APPENDICES

APPENDIX A: SOCIO-DEMOGRAPHIC QUESTIONNAIRE

Study number:

Date of interview:

Please select appropriate box by placing a clear mark in it. Leave inappropriate boxes clear. Please request another questionnaire if incorrect selections were marked.

<table>
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<th>Age (Years)</th>
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</tr>
<tr>
<td>25-35</td>
<td>[ ]</td>
</tr>
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<td>60 and above</td>
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</table>

<table>
<thead>
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<tr>
<td>Female</td>
<td>[ ]</td>
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</table>

<table>
<thead>
<tr>
<th>Marital Status</th>
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<tbody>
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<td>Married</td>
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<tr>
<td>Single</td>
<td>[ ]</td>
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<tr>
<td>Divorced</td>
<td>[ ]</td>
</tr>
<tr>
<td>Widowed</td>
<td>[ ]</td>
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</table>

<table>
<thead>
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<tbody>
<tr>
<td>Professional</td>
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<tr>
<td>Non-professional</td>
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<tr>
<td>Pensioner</td>
<td>[ ]</td>
</tr>
<tr>
<td>Unemployed</td>
<td>[ ]</td>
</tr>
</tbody>
</table>
Socio-demographic Questionnaire

Please select appropriate box by placing a clear mark in it. Leave inappropriate boxes clear. Please request another questionnaire if incorrect selections were marked.

Level of Education

Grade 1-4

Grade 4-7

Grade 8-10

Grade 10-12

Post grade 12 formal education

Monthly household income

R0 to R999

R1000 to R1999

R2000 to R2999

R3000 to R3999

R4000 to R4999

R5000 to R9999

More than R10000
Socio-demographic Questionnaire

Please select appropriate box by placing a clear mark in it. Leave inappropriate boxes clear. Please request another questionnaire if incorrect selections were marked.

Presently on depression treatment (medication)

Yes [ ]
No [ ]

Presently on treatment (medication) for mental illness other than depression

Yes [ ]
No [ ]

Antiretroviral regimen

Regimen 1 (as per Tshepang clinic) [ ]
Regimen 2 (as per Tshepang clinic) [ ]
Other regimens (as per Tshepang clinic) [ ]
## Patient Health Questionnaire (PHQ-9)

Over the *last 2 weeks*, how often have you been bothered by any of the following problems?

<table>
<thead>
<tr>
<th>Problem</th>
<th>Nearly every day</th>
<th>More than half the days</th>
<th>Several days</th>
<th>Not at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>Little interest or pleasure in doing things</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling down, depressed, or hopeless</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouble falling or staying asleep, or sleeping too much</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Feeling tired or having little energy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor appetite or overeating</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling bad about yourself—or that you are a failure or have let yourself or your family down</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Thoughts that you would be better off dead, or of hurting yourself in some way</td>
<td></td>
<td></td>
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</tbody>
</table>