AN ANALYSIS OF THE MANAGEMENT OF HIV-MENTAL ILLNESS COMORBIDITY AT THE PSYCHIATRIC UNIT OF THE DR GEORGE MUKHARI ACADEMIC HOSPITAL, PRETORIA, SOUTH AFRICA.

By

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Submitted in partial fulfilment of requirements for the Degree of Masters of Medicine in the Department of Psychiatry at the University of Limpopo.

On the 15th December 2014

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DECLARATION

I declare that this dissertation hereby submitted to the University of Limpopo for the Degree of Masters of Medicine – Psychiatry, has not been previously submitted by me for a degree at this or any other university, that it is my work in design and in execution and that all material contained here has been truly acknowledged.

Signed at the University of Limpopo on the

Mosima Lydia Maodi

.............................
DEDICATION

I dedicate this research to my husband Kabelo and my son Kabelo Junior for their love, support and understanding throughout my journey.
ACKNOWLEDGEMENTS

I would like to express my gratitude and thanks to first and foremost GOD the almighty, without whom none of this would have been possible. A special thanks to my parents, especially my mom, for loving me and teaching me the value of education. I would also like to thank my family and my in-laws for their unwavering support and belief in me.

I am indebted to a great number of people who have contributed to this research project. I would like to express my thanks to the following people for making this research project possible:

- My supervisors – Prof. S. T. Rataemane and Dr Thanda Kyaw – for your patience, assistance, continuous guidance and encouragement throughout the whole process
- My consultants, colleagues and friends for their support and motivation
- The Dr George Mukhari psychiatry unit staff for assistance with data collection
- My Nanny Mmaletuma for her support and patience through the difficult times
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<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
</tr>
<tr>
<td>ART</td>
<td>Antiretroviral Therapy</td>
</tr>
<tr>
<td>DGMAH</td>
<td>Dr George Mukhari Academic Hospital</td>
</tr>
<tr>
<td>DSM</td>
<td>Diagnostic and statistical manual of mental disorders</td>
</tr>
<tr>
<td>EPSE</td>
<td>Extra-pyramidal side effects</td>
</tr>
<tr>
<td>HAART</td>
<td>Highly active antiretroviral therapy</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>MI</td>
<td>Mental illness</td>
</tr>
<tr>
<td>MREC</td>
<td>Medunsa Research and Ethics Committee</td>
</tr>
<tr>
<td>PTB</td>
<td>Pulmonary tuberculosis</td>
</tr>
<tr>
<td>SMI</td>
<td>Severe mental illness</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>United Nations program on HIV/AIDS</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
</tbody>
</table>
ABSTRACT

BACKGROUND: Human immunodeficiency virus (HIV) is the leading infectious killer of adults in the world today. However, the advent of highly active antiretroviral therapy (HAART) has increased the lifespan of HIV-infected patients drastically over the past few decades. As a result, a rise has been observed in the neuropsychiatric manifestations of HIV. Clinicians are now faced with the challenge of managing HIV and mental illness (MI) comorbidity. The complexity of the management of HIV and mental illness requires an integrated system of care among two overlapping, yet distinct, service systems – mental health and general medical care.

AIM: This study aimed to evaluate the inpatient management of HIV-MI comorbidity in the psychiatric unit at Dr George Mukhari Academic Hospital (DGMAH) and to describe the associated HIV-related infections in these patients.

METHOD: A retrospective cross-sectional study was conducted at the psychiatric unit of DGMAH. The records of all patients admitted to the unit with a diagnosis of HIV-MI comorbidity over a 12-month period, from June 2011 to June 2012, were reviewed. Data concerning demographic parameters of patients, associated medical conditions, management of psychiatric disorders and the management of HIV were recorded using an extraction data sheet.

RESULTS: Hospital records of 75 patients with HIV-MI comorbidity were retrieved and analysed after obtaining permission from the Medunsa Research Ethics Committee. The mean age of patients in this study was 36.75 years with an age range of 23 years to 56 years. The management of psychiatric disorders was excellent for all patients. However, challenges were observed in HIV management. Incomplete recording of ART history was identified in 38% of patients. At least 3% of patients were discharged on ART regimen 1, which is not ideal for patients with MI as it includes efavirenz. Screening for opportunistic infections was not conducted upon admission for patients and 19% of patients were subsequently diagnosed with opportunistic infections in the ward. Candidiasis was found to be the most common HIV-related opportunistic infection, present in 93% of patients. Forty three percent of patients with opportunistic infections were not referred to other disciplines for collaborative management. However, 64% of all patients diagnosed with opportunistic infections
eventually received treatment in the psychiatric ward. Generally, the coordination of care between the psychiatrists and other disciplines was insufficient.

CONCLUSION: The findings of this study indicate the fragmentation of care for patients with HIV-MI comorbidity, although psychiatric care was found to be excellent. Psychiatrists need to be empowered with broader knowledge of HIV management, which should be supported by a better referral system. Integrated management of HIV-MI comorbidity demands effective communication between psychiatrists and HIV clinicians, as well as clinicians from other disciplines.
CHAPTER 1
INTRODUCTION

1.1 Background

Individuals with both mental illness (MI) and human immunodeficiency virus (HIV) represent a large, vulnerable, and possibly growing segment of the HIV population. Mental illness includes all psychiatric disorders with or without neurological involvements. The prevalence of HIV-MI comorbidity is exceedingly high: about 50% of those in HIV care have a comorbid mental illness (Bing et al., 2001). HIV and MI have an intertwined and reciprocal relationship. Primary MI can predispose to HIV infection through risk-related behaviours. Patients with HIV infection can develop the MI as a consequence of a direct effect of HIV on the brain, or as an indirect effect of HIV, due to psychological reactions to an HIV diagnosis, secondary to opportunistic infections, or as a side effect of HIV treatment (Badkoobehi, Chana & Everall, 2006; D. Singh, Berkman & Bresnahan, 2009). Patients with HIV-MI comorbidity are at high risk for opportunistic infections due to their poor health-seeking behaviours. Neuropsychiatric and medical sequelae of HIV infection present a spectrum of diagnostic and treatment challenges to mental health clinicians.

Individuals with this comorbidity face even greater barriers to receiving health care than those with HIV alone. A review article on mental illness and physical health by Robson and Gray (2007) emphasises that factors related to increased morbidity and mortality of physical illnesses in mentally ill patients are associated with fragmentation of health care and health behaviours of these patients. MI increases the morbidity and mortality of HIV-related opportunistic infections due to a delay in initiation of HIV treatment (Angelino & Treisman, 2001; D. Singh et al., 2009). Thus, mental health clinicians need to be familiar with the diagnosis and management of HIV-related medical and neuropsychiatric complications as they may be the first health care providers to make contact with these patients.

1.2 Study problem

People with MI are considered to have a higher risk of acquiring HIV than members of the general population for various reasons, including high risk behaviours and substance abuse (Bogart et al., 2006; D. Singh et al., 2009). Several studies in the USA have confirmed higher rates of HIV among individuals with MI than among the general population (Blank, Mandell,
Aiken & Hadley, 2002; Brogan & Lux, 2009). In South Africa, a study by D. Singh et al. (2009) at a tertiary mental institution in Durban estimated that 26.5% of patients with MI also have HIV.

Given the high prevalence of HIV in this population, HIV-infected patients admitted to psychiatric wards need to have their physical health checked routinely in order to detect common opportunistic infections to avoid treatment delay. The complexity of the management of HIV and MI comorbidity requires coordinated care among two overlapping, yet distinct service systems — mental health and general medical care. Currently, the fragmentation of health care between the two systems is still a major barrier to the health care needs of these patients. The other major considerations in managing this population are precautions that must be taken when using psychotropic drugs, because of side effect vulnerability and significant drug interactions with HIV treatment.

At Dr George Mukhari Academic Hospital (DGMAH), the management of HIV-MI comorbidity is not yet integrated. Both clinics manage patients separately, but take into account referral information from the other clinic. However, patients who have never visited the antiretroviral therapy (ART) clinic or who defaulted on ART might end up at the psychiatric clinic without information regarding their ART status. Those patients may later be complicated with opportunistic infections and reactivation of latent infections. The challenges of managing HIV-MI comorbidity should be assessed to find the way to improve care for these patients.

The study on the extent of the management of those patients by the psychiatric unit highlights the challenges faced by psychiatrists with limited resources and time. Therefore, an assessment of the management of this special population at a psychiatric unit is needed as a primary study, which will guide the identification of the weaknesses and strengths of a psychiatric unit in the management of HIV-MI comorbidity. Furthermore, these study findings can contribute to the development of a management protocol for HIV-MI comorbidity in a psychiatric unit and assist in motivation for an integrated HIV psychiatry clinic which will cater for this vulnerable population with special needs.
1.3 Research goal

The aim of the study was to evaluate the implementation of HIV-MI guidelines in practice by mental health practitioners at the psychiatric unit of DGMAH, as well as to assess the challenges of managing HIV-MI comorbidity.

1.4 Study questions

This study sought to answer the following questions:

1) How are psychiatric disorders of patients with HIV-MI comorbidity managed?

2) How are the physical illnesses presented by patients with HIV-MI comorbidity detected and managed?

1.5 Objectives

1) To assess the HIV management as well as psychiatric management conducted by the DGMAH psychiatric unit for patients with HIV-MI comorbidity.

2) To describe the associated physical (medical) illnesses presented by patients with HIV-MI comorbidity.
CHAPTER 2
LITERATURE REVIEW

2.1 Introduction

For the purpose of this study, there are three major areas of literature that are of relevance. These are: HIV/AIDS (acquired immunodeficiency syndrome), MI, and the management of HIV-MI comorbidity.

2.2 Brief overview on HIV/AIDS

AIDS was first recognised by the Centre for Disease Control and Prevention (CDC) in 1981, and its cause – HIV infection – was identified in the early part of the decade (Sharp & Hahn, 2011). HIV is a retrovirus that primarily infects components of the human immune system such as CD4+ T cells and macrophages via the CD4 receptors and co-receptors such as CCR5 and CXCR4. Dendritic cells also contribute in transporting and presenting HIV to lymph nodes where the virus meet and infect the target CD4+T cells. T lymphocytes are essential to the immune response and without them the body cannot fight infections or kill cancerous cells (Cheung, Pantanowitz & Dezube, 2005; B.T. Smith, 2008).

HIV has many strategies to evade the host immune system. Upon entry into the target CD4+ T cell, the viral RNA genome is converted (reverse transcribed) into double-stranded DNA by a virally encoded reverse transcriptase that is transported along with the viral genome in the virus particle. The resulting viral DNA is then imported into the cell nucleus and integrated into the cellular DNA by a virally encoded integrase enzyme and host co-factors (J.A. Smith & Daniel, 2006). Once integrated into the host cell genome, the virus becomes a persistent pathogen in the host cells which in turn produce more free virions. Infected CD4+ T cells eventually deplete in number as well as quality, thus leading to a severe immunodeficiency state. Opportunistic pathogens such as Mycobacterium tuberculosis, Pneumocystis jiroveci, candida, and other parasites and latent viruses take advantage of the weakened immune system and lead to severe multisystem infections. These opportunistic infections are major causes of high morbidity and mortality in HIV-infected patients.
2.3 Epidemiology of HIV

HIV/AIDS is considered a pandemic – a disease outbreak which is present over a large area and is actively spreading (Kallings, 2008). As of 2012, approximately 35.3 million people worldwide have HIV, with the number of new infections that year being about 2.3 million. This is down from 3.1 million new infections in 2001. Of these, approximately 16.8 million are women and 3.4 million are less than 15 years old. It resulted in about 1.6 million deaths in 2012, down from a peak of 2.2 million in 2005. Since its discovery in 1981, AIDS has caused an estimated 36 million deaths worldwide as of 2012 (Joint United Nations Programme on HIV/AIDS, 2013).

Sub-Saharan Africa is the region most affected by HIV and AIDS. In 2010, an estimated 68% (22.9 million) of all HIV cases and 66% of all deaths (1.2 million) occurred in this region. This means that about 5% of the adult population is infected by HIV, and it is believed to be the cause of 10% of all deaths in children. In Sub-Saharan Africa, in contrast to other regions, women compose nearly 60% of cases. At 5.9 million, South Africa has the largest population of people with HIV of any country in the world (Joint United Nations Programme on HIV/AIDS, 2013).

2.4 Transmission of HIV

HIV is transmitted through body fluids. It has been isolated from a variety of body fluids including blood, semen, vaginal secretions, breast milk, urine, saliva and tears. The risk of transmission through contact with a given fluid is related both to the amount of virus present in the fluid and to the type of exposure to it. HIV is found in such small concentrations in tears, saliva and urine that transmission through casual contact with these fluids is theoretically possible but highly unlikely. Behaviours that lead to certain types of exposure to blood, semen and vaginal secretions may lead to transmission. HIV is spread primarily by unprotected sexual intercourse, sharing of needles and mother to child transmission (Kripke, 2007).

2.5 Classification of HIV infection

The WHO (World Health Organization) system uses the following categories to classify the clinical stages:
• Stage I: HIV infection is asymptomatic with a CD4+ T cell count greater than 500 per microlitre (µl or cubic mm) of blood. May include generalised lymph node enlargement.

• Stage II: Mild symptoms which may include minor muco-cutaneous manifestations and recurrent upper respiratory tract infections. A CD4+ T cell count of less than 500/µl.

• Stage III: Advanced symptoms which may include unexplained chronic diarrhoea for longer than a month, severe bacterial infections including tuberculosis of the lung, and a CD4+ T cell count of less than 350/µl.

• Stage IV or AIDS: severe symptoms which include toxoplasmosis of the brain, candidiasis of the oesophagus, trachea, bronchi or lungs and Kaposi’s sarcoma. A CD4+ T cell count of less than 200/µl.

2.6 Treatment of HIV infection

There is currently no cure or effective HIV vaccine. Treatment consists of highly active antiretroviral therapy (HAART), which slows progression of the disease and may lead to a near-normal life expectancy (WHO, 2013). Treatment also includes preventive and active treatment of opportunistic infections. Treatment is accomplished through numerous combinations of antiretroviral agents from four classes: nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, protease inhibitors and nucleoside analogues. Typical combinations include: 2 nucleoside reverse transcriptase inhibitors + protease inhibitor, or 2 nucleoside reverse transcriptase inhibitors + 1 non-nucleoside reverse transcriptase inhibitor (Quashie, Mesplède & Wainberg, 2013). In March 2013, the following antiretroviral treatment was implemented in South Africa.

Table 1: Summary of the South African antiretroviral treatment guidelines

<table>
<thead>
<tr>
<th>First line</th>
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<tbody>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td>First line</td>
<td>Treatment</td>
<td>Contraindication</td>
</tr>
<tr>
<td>------------</td>
<td>-----------</td>
<td>-----------------</td>
</tr>
<tr>
<td>All new patients needing treatment, including pregnant women</td>
<td>TDF + FTC (OR 3TC)+EFV</td>
<td>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</td>
</tr>
<tr>
<td>Adolescents</td>
<td>ABC + 3TC + EFV</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>
</tr>
<tr>
<td>Contraindications to TDF</td>
<td>AZT +3TC +EFV (or NVP)</td>
<td>Renal disease or the use of other nephrotoxic drugs. Nephrotoxic drugs e.g. aminoglycosides 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>
</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 nephrotoxic drugs Switch to ABC</td>
</tr>
<tr>
<td>Currently on a d4T based regiment</td>
<td>TDF +FTC(or 3TC) + EFV</td>
<td>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</td>
</tr>
</tbody>
</table>
**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

| Failing on a TDF-based first line regimen | AZT +3TC+LPV/r | Patients with anaemia and renal failure switch to ABC |
| Failing on a d4T based first line regimen | TDF + 3TC(or FTC) and LPV/r | |
| Dyslipidaemia or intractable diarrhoea associated with LPV/r | Switch LPV/r to ATV/r | |

**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)/Etravarine (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)

Source: Department of Health (2013)

### 2.7 The impact of HIV on mental health

HIV fundamentally affects people’s mental health in many different ways. Direct viral infection of the brain occurs soon after initial infection with the activation of microglia and astrocytes. HIV has been shown to exercise an affinity for subcortical structures; the virus replicates in the brain within microglia, while astrocytes release inflammatory mediators. In an attempt to be protective, the mediators are also neurotoxic (Badkoobehi et al., 2006; K.A.
Clinically, patients present with a variety of neuropsychiatric symptoms due to an HIV-triggered neurotoxic cascade in the central nervous system. Depression, mania, anxiety disorders, psychosis, neurocognitive deficits and substance use disorders are common disorders observed in HIV-infected patients and can appear before or after the onset of advanced neuropathology. Commonly, the occurrences of neuropsychiatric symptoms are suggestive of more advanced disease (Brogan & Lux, 2009; Dubé, Benton & Cruess, 2005). MI may also develop secondary to opportunistic infections infecting the central nervous system. MI may also be triggered by resultant psychosocial stressors related to living with HIV or may emerge from adverse effects of HAART. Recent advances in the treatment of HIV infection have increased the life expectancy of HIV-positive patients, which makes it more likely that clinicians will encounter patients with neuropsychiatric manifestations of the illness. Quality of life becomes central to the management of this chronic illness.

2.8 Mental illness

Mental illness is an umbrella term denoting any one or more of the mental disorders listed in DSM-IV or ICD-10. The hallmarks of these disorders are abnormalities in mood, cognition, and the highest integrative aspects of human behaviour, such as planning and social interactions (Sadock & Sadock, 2003).

2.9 Mental illness and HIV comorbidity

People with severe mental illness, including major depression, bipolar and psychotic disorders, are at higher risk for HIV than members of the general population (Bogart et al., 2006; D. Singh et al., 2009). Among people with severe mental illness, the seroprevalence of HIV ranges from 4% to 23%, with an average of about 7% (Cournos & McKinnon, 1997), which is much higher than the 0.3% to 0.5% rate of HIV in the general population in United States. In South Africa, it is estimated that 26.5% of patients with mental illness also have HIV (D. Singh et al., 2009). Among people in HIV care, the prevalence of MI is at least 50% (Bing et al., 2001). Several studies have confirmed higher rates of MI among individuals with HIV infection than among the general population (Blank et al., 2002; Brogan & Lux, 2009). In South Africa, 16.5% of the general population suffers from some form of mental disorder (Freeman, Nkomo, Kafaar & Kelly, 2007). When it comes to people living with HIV, the
prevalence of MI goes up to 43.7%, which confirms the strong association between HIV and MI (Freeman et al., 2007).

2.10 The impact of mental illness on HIV

A nationally representative study in the USA regarding persons receiving HIV medical care determined that those with comorbid psychiatric disorders have lower scores on health-related quality of life (Sherbourne et al., 2000). Depression in particular has an effect on the actual course of HIV. This line of enquiry stems from the field of psychoneuroimmunology. Depression may alter the function of killer lymphocytes in HIV-seropositive patients and yield an increase in activated CD8+ T lymphocytes and viral load. The latter are associated with HIV disease progression and opportunistic infections, thus increasing the morbidity and mortality in the HIV-MI population (Benton, Blume & Dubé, 2010).

2.11 Management of HIV-Mental illness comorbidity

The South African society of psychiatrists has yet to develop guidelines on management of patients with HIV-MI comorbidity specific for psychiatry. However, currently the South African national guidelines for HIV/AIDS and the American Psychiatric Association guidelines for the treatment of patients with HIV/AIDS and MI are being used in the management of these patients. On average, the duration of response to psychiatric treatment regimens is documented as two to eight weeks (Sadock & Sadock, 2003). The American Psychiatric Association guidelines for the treatment of patients with HIV/AIDS (American Psychiatric Association, 2001) suggest that psychiatrists address the following areas in managing these patients:

a) Establish and maintain a therapeutic alliance
b) Collaborate and coordinate care with other mental health and medical providers
c) Diagnose and treat all associated psychiatric disorders
d) Facilitate adherence to overall treatment plan
e) Provide education about psychological, psychiatric, and neuropsychiatric disorders
f) Provide risk reduction strategies to further minimize the spread of HIV
g) Maximize psychological and social/adaptive functioning
h) Role of religion/spirituality
i) Prepare for issues of disability, death, and dying
j) Advice to significant others/family regarding sources of care and support
According to the South African national guidelines for HIV care, the management of patients diagnosed with HIV should follow the guidelines below:

### Table 2: Standardized National Monitoring for Adults and Adolescents with HIV

<table>
<thead>
<tr>
<th>At initial Diagnosis of HIV</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Check HIV result</td>
<td>Ensure that national testing algorithm has been followed</td>
</tr>
<tr>
<td>Clinical staging if HIV positive</td>
<td>To assess eligibility for ART, to assess eligibility for fast-tracking</td>
</tr>
<tr>
<td>Ask if pregnant or planning to conceive</td>
<td>To identify women who need ART or ARV for PMTCT</td>
</tr>
<tr>
<td>Screen for TB symptoms</td>
<td>To identify TB/HIV co-infected</td>
</tr>
<tr>
<td>Do the CD4⁺T cell count</td>
<td>To identify eligibility for ART or ARVs if pregnant</td>
</tr>
<tr>
<td>Hb or FBC if available</td>
<td>To detect anaemia or neutropenia</td>
</tr>
</tbody>
</table>

**FBC= Full blood count, Hb= Haemoglobin, TB= Tuberculosis, ART= Antiretroviral therapy**

<table>
<thead>
<tr>
<th>If Eligible for ART</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Creatinine if starting on a TDF based regimen</td>
<td>Refer if estimated creatinine clearance is less than 50</td>
</tr>
<tr>
<td>ALT if starting on a NVP-based regimen</td>
<td>If ALT raised, do HepBSAg and avoid NVP</td>
</tr>
<tr>
<td>Hb or FBC if available if starting on an AZT-based regimen.</td>
<td>If less than 8g/dl refer to doctor</td>
</tr>
</tbody>
</table>

**AZT= Azadothymidine, TDF= Tenofovir, ALT= Alanine transaminase, NVP= Nevirapine, HepBSAg= Hepatitis B virus surface antigen**

<table>
<thead>
<tr>
<th>Clinical stage</th>
<th>To monitor response to ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 at month 6, 1 year on ART and then every 12 months</td>
<td>To monitor response to ART</td>
</tr>
<tr>
<td>VL at month 6, 1 year on ART and then every 12 months</td>
<td>To monitor response to ART To identify problems with adherence</td>
</tr>
<tr>
<td>ALT if on NVP and develops rash or symptoms of hepatitis</td>
<td>To identify NVP toxicity</td>
</tr>
<tr>
<td>FBC at month 1, 2, 3 and 6 if on AZT</td>
<td>To identify AZT toxicity</td>
</tr>
</tbody>
</table>
2.12 The challenges of managing HIV-MI comorbidity

The treatment of HIV-MI comorbidity is more complex than the treatment of HIV alone or MI alone. Both MI and HIV treatment require a wide array of long-term services, including medication, counselling, patient education, risk reduction strategies, and other supports and services (Reid, Orrel, Stoloff & Joska, 2012).

Patients with HIV have a compromised blood-brain barrier functioning and less lean body mass, and metabolise drugs at a slower rate due to the effects of the disease. For these reasons, these patients tend to be very sensitive to side effects of psychotropic medications, especially extra-pyramidal side effects (EPSE). In addition to that, patients with very low CD4⁺ T cell counts and high viral loads are also more likely to have exaggerated adverse reactions to psychotropic medications (Gallego, Barreiro & López-Ibor, 2012).

Although most patients will end up tolerating standard doses of treatment, the advice is to start the doses at the lower end of the dosing range and increase doses slowly over time while monitoring for side effects and response. Preferably, the psychotropic agent for patients with HIV-MI comorbidity should be the drug with the fewest side effects. For example, an atypical antipsychotic drug should be the treatment of choice for HIV patients with psychotic disorders. The drug interactions of psychotropic medication, antiretroviral drugs and medication for other common medical comorbidities should also be taken into consideration (Reid et al., 2012).

It is very important to distinguish primary from secondary psychiatric symptoms in patients with HIV-MI comorbidity, as this affects the management of the patients. Most antiretroviral drugs are known to have neuropsychiatric side effects. However, efavirenz is the agent commonly implicated in severe psychological side effects, including acute onset of depression, suicidality and psychosis (Benton et al., 2010).

<table>
<thead>
<tr>
<th>Creatinine at month 3 and 6 then every 12 months if on TDF</th>
<th>To identify TDF toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting cholesterol and triglycerides at month 3 if on LPV/r</td>
<td>To identify LPV/r toxicity</td>
</tr>
</tbody>
</table>

VL= Viral load, LPV/r= Lopinavir boosted with ritonavir
Source: Department of Health (2010)
Patients with HIV infection are often on very complex drug regimens composed of antiretroviral agents, anti-tuberculosis drugs, antibiotics and antifungals. The complexity of medication dosing and the debilitating side effects are some of the main determinants of treatment adherence in psychiatric patients. The care demands are so great that coordination of care and attention to social supports become essential factors in the success of treatment.
CHAPTER 3
METHODOLOGY

3.1 Study design

A retrospective, descriptive study was conducted using medical records of all confirmed HIV-infected patients referred to Dr George Mukhari Academic hospital psychiatry unit within the period 2011 June to 2012 June. The design was appropriate to answer the above research questions.

3.2 Description of the site of study

The study was conducted at DGMAH, psychiatric unit. DGMAH is a tertiary level hospital situated in Ga-Rankuwa, a township north of Pretoria in Gauteng Province. The psychiatry unit is situated at the eastern side of the general hospital and consists of a 20-bedded female ward, a 28-bedded male ward, an outpatient department, a psychology department and a department of occupational therapy.

3.3 Study population and sample size

The study population consisted of all HIV-infected psychiatric patients who required admission to psychiatric unit for treatment. HIV status was confirmed by the ELISA test. The psychiatric disorders were diagnosed according to DSM-IV-TR criteria. The sample consisted of medical records of all confirmed HIV-infected patients referred to the DGMAH psychiatry unit in the period from 1June 2011 to 1June 2012. An estimated 100 patients were admitted during this period. However, only 87 files could be retrieved by a qualified clerk. Out of the 87 files, only 75 were complete and contained all clinical information. Therefore, the sample size used in this study consisted of 75 files of patients admitted over a one-year period.

3.3.1 Inclusion criteria

The following criteria were used:

a) Laboratory confirmed HIV-infected patients admitted to the psychiatric unit.

b) Patients who were enrolled for psychiatric management for at least 6months.
3.3.2 Exclusion criteria

Laboratory confirmed HIV-infected psychiatric patients referred to psychiatric unit for consultation without admission.

3.4 Data collection

Using the psychiatric wards register, a list of hospital numbers of all patients who were HIV-infected and admitted to the psychiatric unit during the study period was compiled. The list was given to the medical records staff to retrieve the files. Once retrieved, the researcher thoroughly studied each file to confirm that the selected file met the inclusion criteria. The selected files which met the inclusion criteria were given study identification numbers and registered with the researcher’s database, which was kept by researcher only. Each study file was thoroughly analysed by the researcher and information was documented in a data collection sheet which used the study identification numbers only.

A data collection sheet, which consisted of four sections, was formulated by the researcher for the purpose of this study (Appendices 1, 2, 3, 4).

Section A: Socio-demographic data

This section included parameters of age, gender, marital status, level of education, and occupation.

Section B: Clinical data on psychiatric illness, HIV status as well as other physical illnesses

This section documented treatment-related data such as psychiatric disorders on admission or at the time of consultation, associated physical illnesses presented, investigational procedures conducted during the management period at the psychiatric unit, HIV treatment regimen and duration, psychiatric treatment regimen, and psychiatric history.

3.5 Data capturing and analysis

All the data collected in the study were captured in a computer database. Data capturing was verified and validity checks were conducted. For each file, the researcher counted how many of the guideline procedures were correctly followed. This was expressed as a percentage of the number of procedures listed in the questionnaire, and served as a measure of adherence to
the guidelines. Data analysis was conducted by a statistician at University of Limpopo. A 95% confidence level was calculated for the mean values. All statistical procedures were performed on SAS, Release 9.2, running under Microsoft Windows.

3.6 Validity

3.6.1 Content validity

The study was conducted at an academic institution, where treating doctors (registrars) are supervised by qualified psychiatrists (consultants). The diagnoses are made according to the DSM-IV-TR, which is internationally recognised and standardised.

3.6.2 Construct validity

Only the files of patients admitted to the acute psychiatric unit at DGMAH between 1June 2011 and 1June 2012 were examined. Relevant data were transferred to the data collection sheet (Appendices 1,2,3,4). The data collection sheet took into account all relevant information that formed the basis of the profile in question.

3.7 Reliability

Patient files are kept securely by the clerks and all information is assumed correct.

3.7.1 Intra-rater reliability: The same data collection sheet(Appendices 1,2,3,4) was used for all patients. The data collection sheet took into account all relevant information required for the purpose of this study. As the same data sheet was used for each patient file, the data collected should be consistent.

3.7.2 Inter-rater reliability: It is believed that, should the same data collection sheet (Appendices 1,2,3,4) be used at a different time or place, similar patient population findings will be produced.

3.8 Bias

3.8.1 Selection bias

All efforts were made to retrieve files correctly and not to mix patient information. The sample consisted of all confirmed HIV-infected patients admitted to the acute psychiatric unit at DGMAH from 1June 2011 to 1June 2012, so there should be no selection bias.
3.8.2 Sample bias

Only patients were included that were admitted to DGMAH. Therefore, there is an element of bias. However, there is no reason to expect that patients admitted to other institutions in Pretoria are different.

3.8.3 Detection bias

Patients admitted at the acute psychiatric unit at DGMAH are interviewed extensively and thoroughly examined. Part of the examination often includes routine HIV counselling and testing. Hence, HIV is more likely to be diagnosed in this patient population. All diagnoses are made according to the DSM-IV-TR, which is standardised and used internationally.

3.8.4 Recall bias

This is a retrospective descriptive study using information recorded in patients’ files. The information in the files was obtained from patients and their families during interviews; hence, the information documented may have an element of recall bias.

3.8.5 Information bias

This is a document review. Information may be missing or not recorded in the file, which may result information bias.

3.9 Ethical considerations

1) Ethical clearance was requested and obtained from the research ethics and publication committee of the University of Limpopo prior to conducting the study.

2) Permission to access files was obtained from the CEO/medical director as well as the head of the department of Psychiatry from DGMAH.

3) A high level of confidentiality was maintained by using project ID numbers other than patients’ file numbers and patients’ names. All study material was only available to the study team.
CHAPTER 4
RESULTS

4.1 Demographic data

Of all medical records of patients who were admitted at psychiatric unit between 1 June 2011 and 1 June 2012, only 75 patients’ files were eligible for inclusion in the study according to the inclusion criteria. The age range of study patients was 20 years to 56 years with a mean age of 36.75. Of these patients, 50.67% were female, and male patients constituted 49.33% of the study subjects.

Table 3: Demographic data of study participants

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>FREQUENCY</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean = 36.75 (range: 23–56)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>58</td>
<td>78%</td>
</tr>
<tr>
<td>Married</td>
<td>14</td>
<td>21%</td>
</tr>
<tr>
<td>Divorced</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed grade 12</td>
<td>23</td>
<td>31%</td>
</tr>
<tr>
<td>High school</td>
<td>44</td>
<td>62%</td>
</tr>
<tr>
<td>Primary school</td>
<td>6</td>
<td>7%</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disability Grant</td>
<td>29</td>
<td>39%</td>
</tr>
<tr>
<td>Employed</td>
<td>22</td>
<td>29%</td>
</tr>
<tr>
<td>Unemployed</td>
<td>24</td>
<td>32%</td>
</tr>
<tr>
<td>Religion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christian</td>
<td>75</td>
<td>100%</td>
</tr>
</tbody>
</table>

4.2 Provisional diagnosis of study participants

Thirty six out of the seventy five patients (48%) had a provisional diagnosis of MI due to HIV on admission, whereas a diagnosis of functional mental illness with a comorbidity of HIV accounted for 47% (35/75) of patients. Only 3% (2/75) of patients had a diagnosis of
mental illness due to a general medical condition other than HIV and 3% (2/75) of patients had a diagnosis of a substance-induced mental illness with a comorbidity of HIV (Figure 1).

**Figure 1: Provisional diagnosis of study participants**

MI due to HIV = Mental illness due to HIV; Functional MI and HIV = Schizophrenia, bipolar mood disorder and depression with comorbid HIV; MI due to other illness = Mental illness due to a general medical condition other than HIV; Substance-induced mental illness and comorbid HIV; Frequency = Number of patients.

4.3 Final diagnosis of study participants

A final diagnosis of functional MI and HIV accounted for 55% (41/75) of patients whereas 43% (32/75) of patients had a final diagnosis of MI due to HIV. The diagnosis for the 3% (2/75) of patients with MI due to other illness and comorbid HIV remained the same on discharge (Figure 2).
Figure 2: Final diagnosis of study participants

MI due to HIV = Mental illness due to HIV; Functional MI and HIV = Schizophrenia, bipolar mood disorder and depression with comorbid HIV; MI due to other illness = Mental illness due to a general medical condition other than HIV; Substance-induced mental illness and comorbid HIV; Frequency = Number of patients.

4.4 The correlation between provisional diagnosis and final diagnosis

Of the 36 patients with a provisional diagnosis of MI due to HIV, 89% (32/36) of patients had a final diagnosis of MI due to HIV on discharge, whereas the final diagnosis of the remaining 11% (4/36) of patients on discharge had been changed to a functional MI and HIV. The diagnosis of all 35 out of 75 (47%) patients in the category of functional MI and HIV remained stable from admission through to discharge. The diagnosis of the 3% (2/75) of patients with a diagnosis of mental illness due to a general medical condition other than HIV remained the same on discharge. None of the patients had a final diagnosis of a substance-induced mental illness with a comorbidity of HIV on discharge, as the 3% (2/75) of patients with this provisional diagnosis were revised to a functional MI and HIV. Overall, the number of patients in the category of functional MI and HIV increased from 47% (35/75) to 55% (41/75) of the total number of patients. The final diagnosis of MI due to HIV accounted for 43% (32/75) of patients. The diagnosis for the remaining 3% (2/75) of patients, who had a provisional diagnosis of MI due to other illness and comorbid HIV, remained the same on discharge (Figure 3).
Figure 3: The comparison between provisional diagnosis and final diagnosis

MI due to HIV = Mental illness due to HIV; Functional MI and HIV = Schizophrenia, bipolar mood disorder and depression with comorbid HIV; MI due to other illness = Mental illness due to a general medical condition other than HIV.

4.5 Duration of hospital stay in different categories of MI

A hundred percent of patients in the categories of MI due to HIV and MI due to other illness with comorbid HIV (32/32 and 2/2, respectively) consecutively stayed in hospital for less than four weeks. In the category of functional illness and HIV, 37% (15/41) of patients stayed for less than 4 weeks whereas 63% (26/41) of patients had a longer hospital stay of more than 4 weeks (Figure 4).
Figure 4: Duration of hospital stay in different categories of MI

MI due to HIV= Mental illness due to HIV; Functional MI and HIV= Schizophrenia, bipolar mood disorder and depression with comorbid HIV; MI due to other illness = Mental illness due to a general medical condition other than HIV.

4.6 Associated substance use in study participants

Substance use was identified in 28 out of the 75 study participants. Of these 28 patients, 15 (54%) were diagnosed with MI due to HIV. The remaining 46% (13/28) of patients were in the category of a functional MI and HIV. Patients with a diagnosis of MI due to other illness and HIV were not using substances (Figure 5).
4.7 History of genetic loading in different categories of MI

Of the 75 patients included in the study, 32 patients had a family history of MI. Fourteen out of the thirty two patients (44%) were diagnosed with MI due to HIV. Genetic loading was identified in 53% (17/32) of patients with a diagnosis of functional MI and HIV. Family history was positive in 3% (1/32) of patients with a diagnosis of MI due to other illness (Figure 6).
Figure 6: Family history in different categories of MI

MI due to HIV = Mental illness due to HIV; Functional MI and HIV = Schizophrenia, bipolar mood disorder and depression with comorbid HIV; MI due to other illness = Mental illness due to a general medical condition other than HIV.

4.8 Past psychiatric history of MI

Past psychiatric history was present in 52 of the 75 patients in the study. Twenty one out of the fifty two patients (40%) diagnosed with MI due to HIV had a past history of MI. Past psychiatric history was identified in 58% (30/52) of patients with a diagnosis of functional MI and HIV. Only 2% (1/52) of patients with a diagnosis of MI due to other illness and HIV had a past psychiatric history of mental illness (Figure 7).
Figure 7: Past psychiatric history of MI in study participants
MI due to HIV= Mental illness due to HIV; Functional MI and HIV= Schizophrenia and bipolar mood disorder with comorbid HIV; MI due to other illness = Mental illness due to a general medical condition other than HIV.

4.9 Psychiatric treatment prescribed for study participants

The most commonly prescribed psychotropic drugs in a descending order were Risperdal, Clopixol depot, Seroquel XR and Epilim CR. Only 4% (3/75)of the patients were on tegretol and haloperidol consecutively. Citalopram and Modecate were the least prescribed, at 1% (1/75) of patients (Table 4).

Table 4: Prescribed psychiatric medications

<table>
<thead>
<tr>
<th>Psychotropic agents</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antipsychotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperdal</td>
<td>37</td>
<td>49</td>
</tr>
<tr>
<td>Seroquel XR</td>
<td>17</td>
<td>23</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Clopixol depot</td>
<td>19</td>
<td>25</td>
</tr>
<tr>
<td>Modecate</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Sulpiride</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Mood stabilizers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epilim CR</td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>Tegretol</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lithium</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
4.10 The occurrence of psychotropic side effects in different categories of MI

Side effects were recorded for only 27% (20/75) of patients and all were extra-pyramidal side effects (EPSE). Of the 20 patients with EPSE, 60% (12/20) had a diagnosis of MI due to HIV and 30% (6/20) had a diagnosis of functional illness and HIV. All patients in the category of MI due to other illness and HIV had EPSE, accounting for 10% (2/20) of the total patients presenting with EPSE (Figure 8).

![Diagram showing EPSE per category of final diagnosis]

Figure 8: The occurrence side effects per category of final diagnosis
MI due to HIV= Mental illness due to HIV; Functional MI and HIV= Schizophrenia, bipolar mood disorder and depression with comorbid HIV; MI due to other illness = Mental illness due to a general medical condition other than HIV.

4.10.1 Investigations requested by psychiatrists

All patients had full laboratory investigations related to psychiatric illness, whereas investigations regarding HIV infection were found to be incomplete. Viral load was performed only for 10 patients. Screening for HIV-related opportunistic infections such as tuberculosis, parasitic infections and fungal infections was not conducted for any study subject (Table 5).
### Table 5: Investigations requested by psychiatrists

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Conducted</th>
<th>Complete</th>
<th>Not conducted</th>
<th>Incomplete</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatry-related</td>
<td>75 patients</td>
<td>75 patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV-related, HBsAg</td>
<td>75 patients</td>
<td></td>
<td>75 patients</td>
<td></td>
</tr>
<tr>
<td>Opportunistic infection screening</td>
<td></td>
<td>75 patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV viral load</td>
<td>10 patients</td>
<td>65 patients</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Psychiatry-related investigations = investigations including urine toxicology, TPHA (syphilis), thyroid function test, vitamin B12 and folic acid; HIV-related investigations and screening opportunistic infection = Viral load, HIV-related parasitic, fungal infections, HBsAg (hepatitis B surface antigen) and pulmonary tuberculosis.

### 4.10.2 CD4+ T cell counts of study participants

The majority of patients had CD4+ T cell counts of less than 200 cells/µl, which accounted for 53% (40/75) of patients. Thirty five percent (26/75) of patients had a CD4+ T cell counts above 200 cells/µl but below 350 cells/µl and only 12% (9/75) of patients had a CD4+ T cell count above 350 cells/µl (Figure 9).

![CD4+ T cell counts](image)

**Figure 9: CD4+ T cell counts of study participants**
4.11 Detection of associated medical conditions and their management

4.11.1 Associated medical conditions detected in study participants

Of the 75 patients, 20 (27%) of patients had a medical condition other than HIV. Nineteen percent (14/20) of those with medical conditions were diagnosed with HIV-related opportunistic infections and 8% (6/20) had a chronic medical condition. Seventy three percent (55/75) of the patients did not have another medical condition (Figure 10).

![Figure 10: Associated medical conditions detected in study participants](image)

Chronic illness = Diabetes mellitus, hypertension, asthma and epilepsy; Opportunistic infections = Pulmonary tuberculosis, parasitic and fungal infections, etc.

4.11.2 Distribution of different opportunistic infections in patients

Some patients had two or more opportunistic infections. Candidiasis was the most common infection, accounting for 93% (13/14) of patients presenting with opportunistic infections. Diarrhoea was diagnosed for 71% (10/14) of patients and herpes zoster was the least common presentation, which occurred in 14% (2/14) of patients with opportunistic infections. Pulmonary tuberculosis presented in 21% (3/14), and 29% (4/14) of total patients with opportunistic infections had dermatitis (Figure 11).
4.11.3 Treatment of associated medical conditions by psychiatrists

Fourteen patients with opportunistic infections were identified by psychiatrists; however, only nine patients (64%) received treatment in the psychiatric ward. The remaining five patients diagnosed as having opportunistic infections were not treated by psychiatrists. Psychiatrists also prescribed treatment for all patients (6/6) with chronic medical illnesses (Figure 12).

**Figure 11: Distribution of different opportunistic infections in patients with HIV-MI comorbidity**

PTB = Pulmonary tuberculosis; Frequency= Number of patients.

**Figure 12: Treatment prescribed by psychiatrist for associated medical conditions**

Chronic illness = Diabetes mellitus, hypertension, asthma and epilepsy; Opportunistic infections = Pulmonary tuberculosis, parasitic and fungal infections, etc.; Frequency= Number of patients.
4.11.4 Interdisciplinary referrals

Of the 14 patients diagnosed with opportunistic infections, only 57% (8/14) of patients had an interdisciplinary consultation for co-management. The remaining 43% (6/14) of patients were not referred. However, 83% (5/6) of patients with the diagnosis of chronic medical conditions were referred to other disciplines (Figure 13).

![Referral to other disciplines](image.png)

**Figure 13: Referral to other disciplines by psychiatrists**
Chronic illness = Diabetes mellitus, hypertension, asthma and epilepsy; Opportunistic infections = Pulmonary tuberculosis, parasitic and fungal infections, etc.; Frequency= Number of patients.

4.12 Management of HIV infection by psychiatrists

4.12.1 Number of patients referred to clinic for antiretroviral therapy

Ninety seven percent (73/75) of all patients were referred to clinic for ART and collaborative management. Only 3% (2/75) of patients were not referred to the clinic for ART (Figure 14).
4.12.2 Antiretroviral therapy received by patients

A total of 63% (47/75) of patients were recorded as receiving ART during admission to the psychiatric unit. However, treatment regimen was not recorded for 38% (18/47) of patients who were taking ART. Fifty eight percent (27/47) of patients were taking treatment regimen 2. Only 4% (2/47) of patients were taking regimen 1, which includes efavirenz (Figure 15).
4.12.3 Duration of antiretroviral therapy prior to admission

The duration of ART prior to admission was only recorded in 15% (11/75) of patients. Of these 11 patients, 6 (55%) of the patients had been on ART for less than 2 years before admission. Five (45%) patients diagnosed with HIV-MI comorbidity had been on ART for more than two years prior to admission (Table 6).

Table 6: Duration of antiretroviral therapy

<table>
<thead>
<tr>
<th></th>
<th>Duration of ART on record</th>
<th>Duration of ART not on record</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>11</td>
<td>64</td>
</tr>
<tr>
<td>ART &gt; 2 years</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>ART &lt; 2 years</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

ART=Antiretroviral Therapy
CHAPTER 5
DISCUSSION

5.1 Gender distribution in HIV-MI comorbidity

In this study, women constituted 50.67% of total patients selected for the study. The female gender is being recognised as the dominant gender in the HIV-infected population as well as in the population with mental illness. The difference in gender may be explained by the fact that women are at increased risk of acquiring HIV compared to their male counterparts (Shisana et al., 2014). Although HIV or mental illness does not have a selective impact on a specific gender, women are definitely at a higher risk of acquiring HIV due to their anatomical and physiological nature predisposing them to exposure to HIV. If women have mental illness, they are also at a very high risk of being abused and the risk of exposure to HIV is even higher. Although the difference between the male and female population is less than 1%, there were slightly more women than men in this study. A larger sample size may show a different representation regarding gender distribution in the population of patients with HIV-MI comorbidity.

5.2 Education status

On any level of health care, the education of patients and their relatives plays an important role in improving the standard of care. Especially in HIV endemic countries, education plays an important role in preventing the transmission of disease. It is easier for patients with a basic level of education to understand and appreciate the importance of prevention, diagnosis and adherence to treatment of HIV, even if they have underlying mental illness. Studies have shown that people with a lower level of education seem to be the most affected by the comorbidity of HIV and MI (Mutinta, Gow, George, Kunda& Ojteg, 2011; Shisana et al., 2009). These studies have identified a positive link between education and knowledge of HIV and its prevention.

In this study, 67% of the patients did not complete grade 12. This is a worrying finding regarding the risk of HIV transmission and adherence to therapy. In South Africa, the economy is already burdened by the pandemic as many young adults who are supposed to be the work force of the country are affected by HIV. The prevalence of HIV in young South African adults was approaching 20% in 2005, with those who have mental illness at a higher
risk of acquiring HIV (Joska, Kaliski & Benatar, 2008). A lower education level in the majority of patients in this study is one of the examples supporting the risk of HIV-MI comorbidity. Many factors may contribute to the reason for leaving school. This study was conducted in a small township around Pretoria; the majority of households in this area fall into the low income bracket. Economic hardship may be one of the factors which contributes to the reasons why most of the study participants have lower levels of education.

The HIV transmission risk is not the only consequences of a lower education level in HIV-MI comorbidity. The risk of not adhering to HIV treatment and psychiatric treatment is also high, as is the risk of falling into a trap of narcotics and substance use which can ultimately lead to treatment failure. The important role of education in mental health and HIV management should not be ignored. The solution, to improve the education level, needs support from all levels of authority and social organisation.

5.3 Correlation of provisional diagnosis and final diagnosis

The results in this study indicate that only patients with an initial diagnosis of organic MI were eventually diagnosed with a functional disorder. Ninety two percent of the patients retained the same diagnosis from admission to discharge. It is of note that 8% (6/75) of patients had a different diagnosis on discharge than the diagnosis with which they were admitted. This finding confirmed that the psychiatrists in DGMAH conduct a good practice according to the DSM-IV-TR diagnostic system of mental disorders, which requires psychiatrists to consider other causes for a mental illness before diagnosing a functional disorder.

The relationship between HIV and mental illness is complex. This brings about diagnostic challenges in this population, because it is sometimes difficult to confirm whether HIV is a cause, a trigger or a complication of mental illness. A study by De Ronchietal. (2006), comparing first episode psychosis in schizophrenia and HIV-infected patients, found that, in patients with no clear history of mental illness prior to HIV infection, it was rarely possible to exclude an HIV-associated aetiology based on psychopathology alone. The course of the illness and other factors such as family history may help to distinguish organic psychosis from a functional psychotic disorder (Benton et al., 2010). The multi-factorial aetiology of mental illness adds to the diagnostic challenge in this population. It is noted from the study results that the majority of patients (63% or 47/75), had a genetic predisposition to mental illness across the different categories of MI.
Other factors contributing to the diagnostic challenge in patients with MI and HIV comorbidity are related to the common co-occurrence of the two conditions. Mentally ill patients are at increased risk of acquiring HIV due to high-risk behaviours, and HIV also predisposes to the development of mental illness (Galvan, Burnam & Bing, 2003; Meade & Sikkema, 2005).

5.4 Duration of hospital stay per category of mental illness

The results showed that 100% of patients with a final diagnosis of MI due to HIV and MI due to other illness (32/32 and 2/2 respectively), had a hospital stay of less than 4 weeks. Patients with organic MI usually have a rapid response to psychotropic drugs compared to those with functional MI (Sadock & Sadock, 2003). The majority (63%, 26/41) of patients with functional MI and HIV stayed in the hospital longer than 4 weeks. The duration of hospital stay in this study may also have been affected by the multiple relapses in this population group, or what is commonly called the “revolving door” as it is noted from the study that a significant number (69%, 52/75) of patients had a previous psychiatric history and the majority (40%, 30/75) had a diagnosis of a functional illness and comorbid HIV. The presence of a general medical condition in patients with severe MI may contribute to treatment resistance, while the other factor is that, overtime, severe mental MI tends to respond poorly in patients with multiple relapses.

5.5 Substance use in patients with HIV-MI comorbidity

Data collected in the study showed that 37% (28/75) of all patients with MI and HIV comorbidity were using substances. Substance use is more common in HIV-infected patients and those diagnosed with severe MI than in the general population. Substance use is associated with poorer clinical and social outcomes compared to patients with severe mental illness and HIV who do not use substances. Co-occurring substance use disorders have emerged as one of the greatest obstacles to the effective treatment of patients with severe mental illness. A literature review by Mayston, Kinyanda, Chishinga, Prince and Patel (2012) found consistent evidence that adverse mental health and alcohol consumption were associated with reduced adherence. The need to integrate substance use treatment, HIV treatment and mental health treatment is of paramount importance in order to provide more effective care for this population. The lower level of education might also have compounded the practice of substance use.
5.6 Management of HIV-MI comorbidity

According to the South African national guidelines for HIV/AIDS and The American Psychiatric Association guidelines for the treatment of patients with HIV/AIDS and MI, there are standard investigations and management guidelines that psychiatrists have to abide by to deliver quality care to patients with MI/HIV comorbidity.

5.6.1 Management of mental illness

It is noted from the results that investigations to rule out other causes of mental illness were completed in all patients, as is required by the current diagnostic classification system (DSM 5). This finding was highly satisfactory for the practice of psychiatrists under assessment. Regarding the prescription of treatment, it was also observed that atypical antipsychotics were commonly prescribed to the study participants, at 72% (54/75), for treatment of both psychotic and mood disorders. As HIV-infected patients are prone to develop EPSE which are usually associated with typical antipsychotics, it was noted that psychiatrists carefully select atypical antipsychotics for HIV-MI patients. The attitude of careful prescription is well documented and confirmed by the statistics.

In a study of 21 patients with HIV-related psychosis, A.N. Singh, Golledge and Catalan (1997) found risperidone to be efficacious, with a more favourable side-effect profile than the traditional agents such as haloperidol and thioridazine. In this study, only 4% (3/75) of patients were on haloperidol and all of them developed EPSE, which is in agreement with the above study. However, EPSE were reported in 27% (20/75) of patients, which may also be accounted for by the use of the typical depot antipsychotics prescribed. The mood stabiliser of choice was Epilim CR, which was prescribed to 17% (13/75) of patients. Epilim has less drug interaction with ARV agents and it has been generally a preferred mood stabiliser in patients with HIV/MI comorbidity.

Tegretol is an enzyme inducer of the cytochrome P450 in the liver, and is not recommended for use in patients with HIV/MI comorbidity (Benton et.al., 2010). Only 4% (3/75) of patients were prescribed tegretol, which indicates the practice of careful prescription by psychiatrists.

Studies using diagnostic assessments to ascertain psychiatric diagnosis suggest rates of 5-20% for depression, the most common psychiatric diagnosis among HIV-infected individuals (Cruess, Evans, Repetto, Gettes, Douglas & Petitto, 2003; Evans & Charney, 2003).
detection rate of depression in study subjects was very low, shown by the glaring lack of antidepressant prescription as only 1% (1/75) of total patients was on citalopram. In view of studies showing depression to be the most prevalent MI among HIV-infected patients, the low antidepressant prescription rate is a significant finding in this study. This finding may be due to several reasons.

5.6.2 Management of HIV

One major finding regarding the management of HIV and associated infections was an incomplete record of HIV-related investigations for all patients.

5.6.2.1 CD4⁺ T Cell Counts

The results of the study showed that CD4⁺ T cell counts were requested in all patients; this is a good practice, as stipulated by the guidelines.

The majority (53%, 40/75) of patients had CD4⁺ T cell counts of below 200 cells/µl and the minority (12%, 9/75) of patients had CD4⁺ T cell counts of above 350 cells/µl. The majority of patients (70%) in the category of MI due to HIV had CD4⁺ T cell counts below 200 cells/µl. This finding is consistent with the literature, as mental illness usually occurs in the AIDS stage of the disease. Lower CD4⁺ T cell counts have also been found to correlate with increased risk of developing a mental disorder, especially HIV dementia (Arora & De Sousa, 2013). This finding is also worrying for disease progression and poor prognosis for both HIV and MI, as poor health seeking behaviours are evident in patients with mental illness, which in turn delays diagnosis and initiation of treatment. D. Singh et al. (2009) also report that MI increases the morbidity and mortality from HIV-related opportunistic infections due to delays in initiation of HIV treatment.

5.6.2.2 Viral Load

High viral load has been found to correlate with an increased risk of developing a mental disorder, especially HIV dementia (Arora & De Sousa, 2013). In this study, only 13% (10/75) of patients had a viral load recorded in their hospital file. The very low percentage of HIV viral load record is questionable. However, current HIV management guidelines only allow a viral load investigation to be requested at 6-months intervals, after initiation of ART. In addition, HIV viral load testing can only be requested by HIV clinicians who have full records of their patients’ ARV history. This status of practice and the low viral load record
clearly indicates the importance of coordination of care between psychiatrists and HIV clinicians. The monitoring of immune status and response to ARV therapy influence the progress of MI and psychiatrists also need to make an effort to assess the HIV viral load results to support the management of MI in HIV-infected patients.

5.6.2.3 Screening for opportunistic infections

According to the guidelines, all patients should be screened for co-infection with pulmonary tuberculosis (PTB). All patients with CD4+T cell counts below 200 cells/µl have an increased risk of developing opportunistic infections. Of the total number of patients admitted to DGMAH with HIV-MI comorbidity, 53% (40/75) were identified as at risk for opportunistic infections based on the lower CD4+ T cell count. However, opportunistic infections were only identified in 35% (14/40) of the at-risk group by psychiatrists.

Of 14 patients identified with opportunistic infections, 3 were diagnosed with PTB and had to be transferred to the medical ward for further management. The late diagnosis of PTB in the psychiatric ward imposes serious implications for the health care workers as well as patients. PTB is transmitted by inhalation of droplets, and having a patient with active PTB in a psychiatric ward increases the risk of transmission to other patients and health care workers. Though previous history of PTB was noted in all patients prior to admission, all patients were not screened for active PTB symptoms and none of the patients were sent for a chest x-ray. Asthemajority of HIV-MI patients also have very low CD4+ T cell counts with higher risk of developing opportunistic infections, all patients should be screened by history and laboratory investigations such as sputum for acid fast bacilli culture and microscopy as well as radiological investigation. Screening for PTB should be compulsory in psychiatric patients with HIV infection, especially when they are immunocompromised. The reason for failure to screen PTB should be investigated to implement corrective action. Collection of proper quality sputum specimens might be cumbersome for psychiatric patients and psychiatric nursing staff may need support from physiotherapist. Low detection rate of positive TB sputum may be the reason for not testing, as the majority of HIV-infected patients present with extra-pulmonary TB other than PTB. Other basic investigations that are stipulated in the guidelines, including full blood count, liver function test, urea and creatinine were conducted for all patients as part of psychiatry related investigations. This indicates that the laboratory investigations were not totally neglected.
The results of the study show that screening for possible opportunistic infections was not performed on all patients. This is an important aspect of the study as it points out that psychiatrists are not following the South African national guidelines for HIV/AIDS management, which requires that every patient diagnosed with HIV should be screened for opportunistic infections. Factors that may contribute to the poor screening and management of opportunistic infections need to be looked into so as to direct appropriate intervention in the near future.

5.6.2.4 HIV treatment

According to the guidelines, psychiatrists are expected to collaborate and coordinate care with other mental health and medical providers in the management of patients with HIV-MI comorbidity.

The treatment of HIV-MI comorbidity is more complex than the treatment of HIV alone or mental illness alone, and collaboration between all clinicians is vital. The data collected in the study showed that 97% (73/75) of patients were referred to the clinic for ART and only 3% (2/75) of patients were not referred. This finding supports that a referral system is in place for collaborative management and psychiatrists are following the guidelines in this regard.

Despite the high referral rate to clinic for ART, specific treatment received for HIV was only recorded for 63% (47/75) of patients. This finding signifies that, though psychiatrists do collaborate with other HIV practitioners, there is still a lack of coordination. The care demands of this population are so great that coordination of care and attention to holistic management are essential. Not only the history of treatment but also ART regimens were not recorded for 38% (18/47) of patients. The duration of HIV treatment prior to admission was only recorded for 15% (11/75) of patients. A review by Robson and Gray (2007) emphasises that factors related to increased morbidity and mortality of physical illnesses in mentally ill patients are related to fragmentation of health care. The results show that majority of study patients had CD4+ T cell counts below 200 cells/µl, and some already presented with opportunistic infections (morbidity), yet screening was not conducted and a lack of coordination of care was also evident. The importance of ART records was undermined in study patients.

The results show that majority of patients (54%, 27/47) were on regimen 2, which does not include efavirenz, which is known to be the drug with more neuropsychiatric side effects.
Side effects of psychiatric medications, like those for ART, can be highly debilitating and are highly prevalent. The complexity of medication dosing and the severity of side effects are some of the main determinants of treatment adherence in psychiatric patients. When choosing an ART regimen, it is important for clinicians to be aware of underlying psychiatric conditions to ensure that drugs which have psychiatric side effects and drugs which can induce drug interaction with psychotropic agents are not included. Psychiatrists also have a duty to collaborate with the HIV clinicians to ensure that mentally ill patients receive appropriate ART options with fewer psychiatric side effects and less drug interaction with psychotropic drugs.

Of all patients who were taking antiretroviral agents, 4% (2/47) were on ART regimen 1, which includes efavirenz. The psychiatrists might have failed to identify the ART regimen these patients were taking, as those patients were discharged on the same treatment regimen by psychiatrists. This is an important indication that thorough knowledge of HIV pathology, investigations as well as antiretroviral therapy are essential for psychiatrists, especially for those working in an HIV endemic region.

5.6.2.5 Management of HIV-related illnesses (opportunistic infections)

Although there is an interdisciplinary referral system in place, 57% (8/14) of patients received treatment in the psychiatric ward. The other 43% (6/14) of patients were not referred for collaborative treatment. However, 64% of all patients diagnosed with opportunistic infections eventually received treatment in the psychiatric ward. Psychiatrists did prescribe treatment to other patients with opportunistic infections that might not have warranted interdisciplinary referrals, such as oral candidiasis. Once an opportunistic infection has been diagnosed, proper management is significant, especially during hospitalisation, as that may be the only contact clinicians have with the patients. The factors related to the poor management of opportunistic infections need to be further investigated. The findings also point to the need to develop referral protocols, as it is indicated in the study that not all opportunistic infections may require interdisciplinary referral. The protocol should also guide the junior doctors with less experience in HIV management working in the unit. MI increases the morbidity and mortality from HIV-related opportunistic infections by impeding HIV treatment (Angelino & Treisman, 2001; D. Singh et al., 2009). Thus, mental health clinicians need to be familiar with the diagnosis and management of HIV-related opportunistic infections and neuropsychiatric
complications, as they may be the first health care providers to make contact with these patients.
CHAPTER 6
CONCLUSION

The results from this study have demonstrated a good success rate in the detection and management of mental illness in HIV-infected patients, as supported by the common practice of proper investigations for other possible causes of mental illness and use of the DSM-IV-TR diagnostic classification system to diagnose mental disorders. All investigations that support the diagnosis of mental illness were conducted. Good prescribing practice of psychiatric drugs was noted, as atypical antipsychotics were found to be the most commonly prescribed drugs for patients with HIV-MI comorbidity. Unwanted side effects were mainly EPSE in this study group. Overall, mental illness management was well executed by psychiatrists in DGMAH.

Regarding the management of HIV, many aspects were not satisfactory. Psychiatrists not only failed to record the history of ART, but also failed to screen for opportunistic infections in patients, despite the presence of very low CD4+ T cell counts, an important indicator for the risk of developing opportunistic infections. The basic screening effort for opportunistic infections in patients with HIV-MI comorbidity was very weak. In spite of an indication that a referral system was in place, collaborative management between psychiatrists and HIV clinicians for patients with opportunistic infections was not strongly evident and South African national guidelines for HIV management were not followed.

Although good prescribing behaviour for antipsychotics was shown, errors in ART regimens were not corrected. Failure to correct the errors in selection of ART regimens indicates that psychiatrists do not have a strong knowledge of HIV management. The fragmentation of collaborative care for patients with HIV-MI comorbidity was already evident, posing a serious challenge. The factors contributing to the disturbance of the work flow should be investigated.

6.1 Limitations of the study

The limitation of this study is that the sample size was small due to the “missing files”. Incomplete documentation, especially about HIV management, was a major problem as well. The files with incomplete information, especially those without laboratory results of HIV screening, were excluded from the study. The findings of the study merely reflect a
subsection of the in-patients treated at DGMAH. For this reason, the findings cannot be generalised to all psychiatric patient populations.

6.2 Recommendations

Our standard of care for patients with MI-HIV comorbidity must be on par with the national and international treatment guidelines, as that will ensure holistic and quality service delivery to our patients. Mental health clinicians need to be familiar with the diagnosis and management of HIV-related medical and neuropsychiatric complications, as they may be the first health care providers to make contact with these patients. In order to improve the quality of service delivered to patients with HIV-MI comorbidity, the authors recommend the following:

- Future studies to investigate factors contributing to poor detection and management of opportunistic infections to guide the corrective action to be taken to combat this weakness.

- Offering of HIV management training workshops for psychiatrists on a regular basis.

- Development of a protocol for screening of HIV-MI.
  - At least assess the CD4+ T cell count and focus the at-risk group (CD4<200) for screening for opportunistic infections.

- Development of a protocol for management of HIV-MI comorbidity, as well as referral guidelines.

- Development of national guidelines for the management of HIV/MI comorbidity will help mental health care clinicians to provide good care to patients with HIV-MI comorbidity.

- An interest group for an integrated approach to HIV-MI management should be set up to invite the input and active participation of all medical disciplines in order to improve patient management, conduct clinical studies, report the findings of studies to the scientific community, and contribute appropriate advice to the relevant health management authorities.
REFERENCES


APPENDICES

Appendix 1: Demographic data collection sheet

**Origin traceability form:**

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<td>Source of income</td>
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Appendix 2: Psychiatric illness information

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<td>Substance use</td>
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<td>Psychotropic Drug history</td>
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<tr>
<td>Treatment (Rx)</td>
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<tr>
<td>Dosage</td>
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<td>Discharge/down refer date</td>
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<tr>
<td>Duration of Rx</td>
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<tr>
<td>Side effects</td>
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### Appendix 3: Other physical illness information

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<th>Diagnosis Record</th>
<th>Treatment prescribed by psychiatrists</th>
<th>Referral to other discipline</th>
<th>Chronic medication</th>
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Appendix 4: HIV treatment and psychiatric involvement/acknowledgement of the progress status of patients

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