

# Treating depression in HIV/AIDS

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The prevalence of HIV/AIDS has reached alarming proportions in South Africa. Although it is strongly associated with depressive moods, there are very few published studies on its treatment in patients with HIV/AIDS. This article reviews the prevalence, treatment and potential effects of depressive disorders on immunity and adherence to antiretroviral therapy (ART).

The studied prevalence of depressive disorders in HIV-positive patients varies widely, ranging from 0% to 47.8%. However, these patients have nearly twice the likelihood of having had a recent episode of major depressive disorder compared with HIV-negative individuals.

Currently available antidepressant medications are equally effective in treating HIV/AIDS patients and the general population. Furthermore, intervention studies have shown that psychotherapy reduces depressive symptoms and is well tolerated. Interpersonal psychotherapy is more successful than supportive psychotherapy in lessening depression, and patients experience improved functioning physically and emotionally.

Untreated depression may be associated with reduced adherence to ART, immunosuppression, and more rapid HIV illness progression. In South Africa, HIV/AIDS patients may be at greater risk for psychiatric disorder given the potentially stressful living conditions including high rates of unemployment and poverty, poor and unstable housing, inadequate social services, and high rates of crime and domestic violence. A lack of data on depression in South Africa underscores the need for further research.

HIV/AIDS has reached pandemic proportions in South Africa. The National HIV and Syphilis Seroprevalence Survey<sup>1</sup> revealed that in 2004 there were about 5.3 million people living with HIV/AIDS in South Africa; 26.5% of all pregnant women tested positive for HIV, and there were more than 1 500 new infections daily. Worldwide, UNAIDS estimated that at the end of 2003, 1.1% of adults between the ages of 15 and 49 years were living with HIV/AIDS, 3 million adults and children had died of AIDS, and 15 million children had been orphaned.<sup>2</sup>

## Prevalence of depression

Worldwide, depression is exceedingly common in the general population, with lifetime prevalence rates ranging from 9% to 20%.<sup>3</sup> Depression is twice as common in women (20%) compared with men (10%).<sup>4</sup> In patients with chronic medical diseases the rates are higher, at 15 - 36%.<sup>5</sup> Depression also appears to occur frequently among HIV/AIDS patients, emerging soon after diagnosis or during the course of illness, with major depressive disorder being the most common disorder.<sup>6</sup>

Being diagnosed with a stigmatising disorder, experience of severe physical symptoms, and loss of relationships or work as a result of the diagnosis may all contribute to the development of HIV/AIDS-associated depression.<sup>7</sup> Depression may also be secondary to neuropathology caused by HIV/AIDS itself.<sup>8</sup> The distinction between major depressive disorder and mood disorder due to HIV disease can be difficult, since both result in similar symptoms. Fatigue, lethargy, low libido, diminished appetite and weight loss may be manifestations of either HIV-related illnesses or depressive disorder. In contrast, cognitive symptoms, feeling sad, losing interest in formerly enjoyable activities, guilt, and irritability are usually aspects of mood affliction.

The prevalence of depressive disorders in HIV-positive patients varies widely in the literature, ranging from 0% to 47.8%.<sup>9-11</sup> In clinical samples the rates range from 2% to 35%,<sup>12,13</sup> while rates vary from 30% to 60% in community samples.<sup>14,15</sup> Yet other studies that compared rates of depressive disorders in HIV-positive and negative patients (matched for gender, sexual orientation and drug use) concluded that HIV infection is not associated with a higher rate of the disorder.<sup>16,17</sup> However, a meta-analysis of some of these published studies by Ciesla *et al.*<sup>18</sup> concluded that HIV-positive individuals have nearly twice the likelihood of having had a recent episode of major depressive disorder compared with HIV-negative individuals. This is probably a better estimate, as the study considered differences between groups for a number of potentially important factors such as gender, mode of transmission, access to quality health care, socio-economic status and advances in the treatment of HIV infection.

## Treatment of depression

### Pharmacological treatments

Treatment of depression in HIV-positive patients has received little systematic study,<sup>19</sup> even though medication tolerance and

potential medication interactions in such patients may influence the effectiveness and safety of antidepressant medication.<sup>20</sup>

Double-blind, randomised, placebo-controlled trials of imipramine,<sup>21,22</sup> fluoxetine<sup>23</sup> and paroxetine<sup>24</sup> have shown response rates ranging from 45% to 80%, with a placebo response of up to 48%. Despite these significant effects of medication, attrition rates were as high as 55%. By the end of 6 months more than one-third of responders had discontinued imipramine because of troublesome anticholinergic side-effects (such as dry mouth, fatigue, and muscle aches). Although tricyclic antidepressants produced significant response rates, adverse effects limit their usefulness. Selective serotonin re-uptake inhibitors (SSRIs), although not more efficacious, are more tolerable and have greater overall effectiveness.<sup>25</sup> In addition to the absence of anticholinergic side-effects, SSRIs are safer in overdose than the tricyclic antidepressants, which is an advantage in HIV patients given their higher risk of suicidal ideation.<sup>26</sup>

### Psychotherapy treatments

Psychotherapy intervention studies using large samples with sufficient statistical power have shown that psychotherapy reduces depressive symptoms, is well tolerated by HIV-infected individuals, and resulted in significant changes in the immunity of responders.<sup>27,28</sup> Markowitz *et al.*<sup>29</sup> have shown that interpersonal psychotherapy (IPT) was successful in resolving the depression of 87% of their sample. They found that in the case of depressed HIV-positive patients who were not acutely ill, IPT was more successful than supportive psychotherapy in alleviating depression. Differences were observable by the middle of treatment (8 weeks) and prevailed to termination at 12 weeks. Patients receiving IPT experienced both increased physical functioning (activities like returning to work, socialising, etc.) and emotional improvement.

Further psychotherapy treatment trials employing specific immune measures of relevance to HIV disease progression and including follow-up assessments of mood, immunity and disease progression will be helpful in drawing conclusions on the definitive role of these treatments in HIV/AIDS-related depression.

### Untreated depression

Studies of depressed but otherwise medically healthy individuals have failed to demonstrate an overall effect on the immune system.<sup>30,31</sup> There is also a paucity of research on alterations in immunity among HIV-positive individuals who are depressed. The association between depression and immunosuppression,<sup>32</sup> as well as between depression and more rapid HIV illness progression<sup>33</sup> suggest that treating depression may have a positive

effect on measures of immune status. Conversely, in treating patients with vulnerable immune systems there is concern that medication may have an adverse negative immunosuppressive effect. Although neither effect was observed in studies on tricyclic antidepressant medications, no data are available on SSRIs.

Untreated depression is associated with reduced adherence to antiretroviral therapy (ART). Adherence is the key to the effectiveness of ART.<sup>34</sup> Non-adherence may lead to ART failure and the development of medication resistance, which may worsen prognosis and limit future treatment options.<sup>35,36</sup> To ensure that the viral load in a patient is kept at undetectable levels, an adherence rate of between 90% and 100% is required.<sup>37,38</sup> The nature of ART regimens makes adherence particularly difficult, as with complex regimens many pills are taken during a day at different times, some with food and some without. ART has unpleasant side-effects including diarrhoea, nausea, vomiting and peripheral neuropathy.

It has been shown that antidepressant treatment improves adherence to ART in depressed HIV-positive patients.<sup>9</sup> ART adherence improved in the 6 months following the prescription of antidepressant therapy regardless of the patient's preceding levels of adherence. Adherence to ART was highest in patients who were also adherent to their antidepressant medication.

### Conclusion

The importance of the assessment and treatment of depression in individuals with HIV/AIDS is underscored by the decreased adherence to medication regimens in the absence thereof, and by a potential further suppression of immunity and accelerated disease progression. Available data show that currently available treatments are effective for treating depressive disorders in patients with HIV/AIDS. However, much of the work on psychiatric morbidity in HIV/AIDS has been done in the West. In South Africa, HIV/AIDS patients may be at greater risk for psychopathology than patients in certain parts of the developed world given the potentially stressful living conditions including high rates of unemployment and poverty, poor and unstable housing, inadequate social services, and high rates of crime and domestic violence. As such screening, evaluation and treatment of these disorders is crucial and should be done routinely.

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