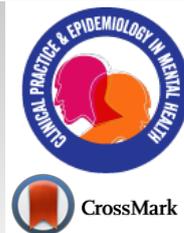


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REVIEW ARTICLE

Depression and HIV Disease Progression: A Mini-Review

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Abstract:

Background:

Depression is the most common mental disorder and a leading cause of disability, which commonly presents unexplained psychological and physical symptoms. Depression and HIV/AIDS are commonly comorbid. This review provides an insight into the effect of depression on disease progression among people living with HIV.

Methods:

A search for relevant articles was conducted using a database like MEDLINE, Scopus, PsycINFO and CINAHL. Peer-reviewed English journals published between 2015 and 2019 were included in the review.

Results:

A total of eight studies conducted in different settings were included in the review. This review has found that psychosocial, neurohormonal and virologic factors associated with depression affect HIV disease progression. Yet, the chronicity of depression, absence of the hormones that have a buffer effect on depression and lack of examination if depression is a predictor, or an outcome of disease progression, were some of the gaps that require further investigation.

Conclusion:

Considerably, more research is needed to better understand the effect of mental disorder, especially depression, on HIV disease progression to AIDS and future interventions should, therefore, concentrate on the integration of mental health screening in HIV clinical setup.

Keywords: Risk factors, Depression, Anxiety, Mental health, Disease progression, HIV, AIDS.

Article History

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1. INTRODUCTION

Depression is a common mental illness, with constant sadness and loss of interest in things that people normally enjoy, and with an incapacity to perform day-to-day work [1 - 5]. Many psychological problems can occur as a direct consequence of HIV infection and treatment disruption since both conditions are typically comorbid [6]. Individuals with chronic illnesses are at higher risk of suffering from depression [7, 8].

People living with HIV are more frequently implicated in depression than the rest of the population worldwide [9 - 11].

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Several studies around the world have found that depression occurs approximately twice as common in women than in men [3, 12, 13].

However, in HIV cases, depression remains unnoticed and it is a risky condition that may have a negative consequence not only on treatment adherence, social engagements and quality of life, but also on progression of disease and life expectancy of the HIV patients [14, 15].

Depressive symptoms of people living with HIV are associated with biological, clinical and psychosocial characteristics that affect HIV disease progression [16, 17]. Yet, there is an increasing concern in resource-limited developing countries of the world where people living with HIV do not get an early mental health screening, awareness

and assistance from mental health service to the same level in the developed countries, and the impact on daily life is still increasing [18].

In fact, evidence from certain studies conducted in high-income countries shows that adherence to highly active antiretroviral therapy decreases depression, cognitive impairment, and other mental illnesses [17, 19, 20].

A prior study in developing countries has also shown that anxiety and depression are associated with an increased risk of disease progression in HIV clinical stage III or IV, regardless of sociodemographic, psycho-social support and health condition during enrolment of the patient to HIV care [18, 21].

There is a large body of studies documenting negative stressful life events on disease progression and the existence of an association between biological vulnerability and psychosocial impacts, which are a core to the pathophysiology mechanism of depression [22, 23].

To date, most of the studies carried out around the globe that examined depression among ethnically diverse people living with HIV, have focused on socioeconomic and psychosocial factors [9, 11, 24 - 40]. However, little attention has been paid to clinical and biological aspects influencing depression, including neurological, endocrine and virologic mechanisms.

Although Anti-Retroviral treatment interventions have progressed, and the approaches that promote screening, diagnosis, and rehabilitation have advanced, depression remains largely undetected and untreated [6].

Untreated depression may lead to poor adherence and non-compliance with antiretroviral care [18, 34, 35, 41 - 43]. Therefore, this may have worse effects on people living with HIV, regardless of the cause of this situation [22].

Considering factors that can influence the impact of depression in people living with HIV, one can update psychosocial and clinical interventions that promote mental health and HIV management.

Hence, reviewing studies on the role of psychosocial, neurohormonal and virologic impacts of depression on disease progression among people living with HIV has immediate public health management implications [44].

This paper is assumed to fill the gap by providing a review of studies on psychosocial and neurohormonal factors that influence the effect of depression on HIV disease progression.

2. METHODS

The purpose of this review is to provide an insight into the effect of depression on disease progression among people living with HIV and to review the existing body of knowledge in diverse communities around the globe.

2.1. Inclusion and Exclusion Criteria

Eligibility criteria for the inclusion of the paper were; they should be peer-reviewed articles published in the English

language and articles that study people with depression and living with HIV were included in the review.

Papers on reviews, case studies, opinions and commentaries, which did not include new data, were excluded.

2.2. Search Strategies

A search for relevant articles was conducted by an electronic database like MEDLINE, Scopus, PsycINFO and CINAHL to identify articles published between 2015 to 2019 that studied HIV and depression comorbidity. To ensure the up-to-datedness of the review and avoid publication lag, only those published for the last five years were included [45].

The keywords used were HIV, AIDS, Depression, and disease progression. This mini-review adheres to and follows the PRISMA guideline [46].

The database searches retrieved a total of 766 papers that were exported to RefWorks database, while 388 duplicates and articles which did not meet the criteria were excluded. After screening the titles, abstracts and year of publication, 324 articles which were not related to depression and HIV were excluded.

On further screening of full texts, 46 papers were excluded because of ineligibility or quality criteria, resulting in 8 papers for inclusion. An outline of the search results and screening criteria are summarized in Fig. (1).

3. RESULTS

3.1. Characteristics of Studies and Participants

The selected studies were published between 2015 and 2019. Articles that examined the association of depressive symptoms on disease progression were reviewed. These studies were conducted in 8 deferent settings: Three studies in the USA, and five studies from Switzerland, South Korea, Thailand, China and East African countries (Kenya, Tanzania, Uganda).

The description of the studies is shown in Table 1.

3.2. Measurement of Depression

Among the reviewed studies, two studies used the Beck Depression Inventory (BDI) for the screening of depression. This tool has been commonly used to assess both somatic and cognitive aspects of depression in people living with HIV. Two studies also used the Center for Epidemiologic Study in Depression scale (CES-D). The remaining studies used the Hospital Anxiety and Depression Scale (HADS), The Generalized Anxiety Disorder 7-item (GAD), and one study used the clinical screening questions as shown in Table 1.

3.3. Depression and Psychosocial Factors

In this review, we emphasized the recent epidemiological findings which deal with the effect of depression on disease progression regarding psychosocial, neurohormonal and virologic factors in people living with HIV.

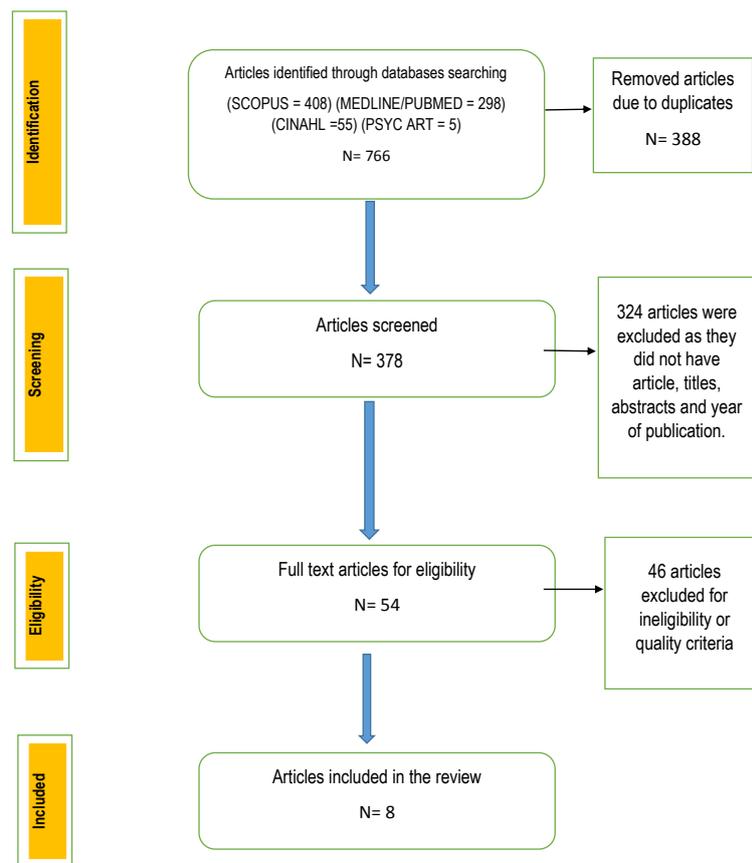


Fig. (1). Flowchart of the search process.

Table 1. Summary of study characteristics.

Author and Date	Country	Title of the Article	Study Design	Data Collection	Screening Tool	Sample
Owora (2018)	USA	Major depression disorder trajectories and HIV disease progression: results from a 6-year outpatient clinic cohort	Retrospective cohort study design	Secondary data abstracted from electronic medical records	Data extracted from EMRs	2260 HIV patients
Ironson <i>et al.</i> (2016)	USA	Psychosocial and neurohormonal predictors of HIV disease progression (CD4 cells and viral load): A 4-year prospective study.	A longitudinal prospective design	Clinical assessment interview and blood draw for CD4 and viral load assay	BDI	177 HIV positive
Taniguchi <i>et al.</i> (2015)	USA	Depression severity is associated with increased Risk behaviours and decreased CD4 cell counts	Cross sectional study design	Clinical assessment and in-depth interview	PHQ-9	624 HIV positive
Anagnostopoulos A. <i>et al.</i> (2015)	Switzerland	Frequency of and Risk Factors for Depression among Participants in the Swiss HIV Cohort Study (SHCS)	Prospective cohort study design	Clinical and laboratory assessment	DSM-Mental disorder	6756 HIV positive
M.-K. Kee <i>et al.</i> (2015)	South Korea	Anxiety and depressive symptoms among patients infected with human immunodeficiency virus in South Korea	Prospective cohort study design	Clinical assessment & Self-administered questionnaire	BDI	840 HIV patients

(Table 3) *contd....*

Author and Date	Country	Title of the Article	Study Design	Data Collection	Screening Tool	Sample
Y.-Y. WANG <i>et al.</i> (2018)	China	Prevalence of depressive syndrome and their association with demographic and clinical characteristics in Chinese HIV patients	Cross sectional study design	Clinical assessment & Standardized questionnaire sheet	CES-D & GAD-7	416 HIV patients
W. Prasithsirikul <i>et al.</i> (2016)	Thailand	Depression and anxiety were low amongst virally suppressed, long-term treated HIV- infected individuals enrolled in a public sector antiretroviral program in Thailand	Cross sectional study design	Clinical assessment & Self-administered questionnaire	HADS	2023 HIV patients
Meffert <i>et al.</i> (2019)	Kenya, Tanzania, Uganda	East African HIV care: depression and HIV outcomes	A longitudinal prospective design	Clinical assessment	CES-D	2307 HIV positives

The psychosocial effects of depression on disease progress and life expectancy were particularly noticeable among HIV seropositive people with negative psychosocial related life experience in some of the studies [17, 47, 48]. People living with HIV especially women with chronic depressive symptoms were about two times more likely to die from AIDS than those who never experienced depression [49].

Through the investigation of the number of CD4 cells and viral load, variation in HIV disease progression is mostly contributed by psychosocial factors like hopelessness, depressed mood and lack of coping; regardless of the initiation of medication [17, 50].

Psychosocial factors like social support, a coping mechanism, spirituality and good personal behaviour have a positive impact on the improvement of the lifestyle of people living with HIV and may delay disease progression to AIDS [17].

Similarly, many studies support the hypothesis that psychosocial factors and depression can affect immune suppression and disease progression in people living with HIV regardless of the occurrence of opportunistic infection [51, 52]. However, to the best of our knowledge, previous reviews did not focus on the social factors and little studies have examined the biological mechanism that is associated with disease progression and depression.

Nevertheless, the mechanism of different neuroendocrine factors and whether they are mediators of the above mentioned psychosocial factors or not, remains uncertain regarding their influence in the disease progression.

3.4. Depression and Neurohormonal Factors

Some reviewed articles have shown that regardless of the antiretroviral medication, an increased level of hormones related to anxiety, stress or depression is mostly a source for CD4 cells decline and viral load increase, which may lead to accelerated disease progression to AIDS and short life expectancy [15, 24, 27, 29].

Among the various findings obtained from these reviews, only one study has shown that hormones such as norepinephrine, cortisol, and catecholamine exacerbate the effect of depression on immune suppression through the influence of CD4 levels and viral load [17]. In contrast, another

study has presented that there is no recorded association between cortisol level and some of the disease progression markers like CD4 level [54].

Even though antiretroviral medication adherence reduces the risk of developing depression by people living with HIV [47,51, 55], some of the treatments may have an impact on the noradrenergic effect and can cause HIV disease progression, whereas beta-blocker drugs that block adrenergic mechanism may slow down disease progression [16].

In these reviewed papers, the neurohormones were non-mediators to the association between psychosocial variables and HIV disease progression. Nevertheless, some of the results have shown that both psychosocial and neurohormones predict the progression of the disease.

3.5. Depression and Virologic Factors

The association between depression and high viral load has been reported in many studies [50, 51]. Lack of adherence to antiretroviral therapy, substance abuse and other risky behaviours were mentioned as mediating factors of depression on higher viral loads resulting from poor HIV disease outcomes [56].

Some of the effects of HIV on the immune system are a significant decline of CD4 count, which makes HIV seropositive people susceptible to opportunistic infection [21].

CD4 T lymphocytes count are major cell types infected by HIV. These cells, being the producer of cytokines, play a major role in the immune defence system against opportunistic infection [56].

Higher average symptomatic depression was predictive for faster degradation in CD4 count [17, 47, 55, 48]. The hormones released by the adrenaline gland during depression and anxiety influenced CD4 count, showing the existence of an association between depression and immune suppression [17].

The severity of symptomatic depression is associated with lower CD4 cell count after adjustment for race, sex and ART adherence [17, 48]. Without controlling medication adherence, findings of measurement scales on the experience of depression and stress also significantly predicted a greater decrease in CD4 cells and an increase in viral load over the same period [17].

Recently, however, these studies have shown that effective management of depression can have a possible advantage for the decline of viral load and management of HIV disease progression.

4. DISCUSSION AND CONCLUSION

Depression, which is a common psycho-social reaction found in people living with HIV, is a stressful experience and often persistent [57]. As a consequence, depression is the world's most important source of disability [1]. As a consequence, depression is the most common primary cause of disability. To our knowledge, this is the first review examining the effect of depression on disease progression among people living with HIV across different settings.

Among the plausible similar descriptions that all these papers had in common in their findings was the significance of depression as a co-morbid disease observed in HIV patients [50, 47, 51, 55].

The studies had also consistently presented that there is a high prevalence of depression among people living with HIV/AIDS [18], and disproportionately, the number of people affected by both HIV and depression is higher than the general population. Furtherly, unlike the other reviewed findings, the study by Prasithsirikul *et al.* reported that anxiety and prevalence were low in people who are on antiretroviral treatment for long period of time [51]. The reason could be attributed to the different statistical test used for the analysis of the association between depression and treatment outcomes and not examining the positive effect of counselling on treatment adherence [58].

In addition, almost all the studies analysed also revealed a strong link between depression and the result of poor adherence to HIV treatment [17, 47, 51, 52, 55, 48, 53]. Yet, none of them has remarked the potential interactions of anti-depressants and anti-retroviral treatments and their effects on disease progression of HIV. One of the recent pieces of evidence shows that anti-depressants are a major factor for HIV disease progression and potentially, the interaction between antidepressants and ART may result in dopamine change, which may aggravate the Neuro HIV [59, 60].

Similar findings from two of the reviewed studies carried out in a different geographical setting have shown that depression and other psychological disorders are associated with lower cellular immunity [50, 49]. However, the studies did not highlight whether depression is a predictor or an outcome of disease progression. This might be related to the different methodological limitations of these studies. Hence, their findings require to be interpreted with caution.

The effects of depression on disease progress are investigated mostly from four dimensions including psychosocial, neural, hormonal and virologic factors. As stated in the findings of many studies, a broad range of factors related to psychosocial may affect the underlying viral replication including virologic increment and immune system suppression resulting in HIV disease progression [17].

This reflects the findings that found endocrine, neural and psychosocial factors as a predictor of HIV disease progression

[16, 17, 56]. However, none of these studies has highlighted the biological and behavioural mediators to the immune mechanism related with the outcome of disease progression.

People with HIV who were also depressed were more likely than people who were not depressed to advance toward AIDS. However, the identified papers for review have shown little about whether chronic or symptomatic depression was associated with disease progression to AIDS. Moreover, some studies have stated that symptomatic depression was not significantly associated with the progression of HIV.

Some of the reviewed articles [17, 50] have similarly presented that some of the neurohormones are predicting factors for HIV disease progression. They have mainly focused on the traditional neurohormonal models of stress and depression in which they examined only Sympathetic Adrenal Medullary (SAM) and Hypothalamic-Pituitary-Adrenal (HPA) axis, which is associated with the increase of cortisol, epinephrine, and norepinephrine [61].

Currently, it is found that these investigations were inadequate as some of the hormonal responses to stress or depression mechanism are not mentioned in these articles like oxytocin, which has a buffering effect on stress and depression and the immune function of people living with HIV [22].

The screening tools, study design, data collection instruments and the language used for the validated questionnaire, are one of the remarkable discrepancies in these reviewed studies. Similarly, differences in the definition regarding whether chronic or symptomatic depression are a source for the predictors for disease progression are debatable.

One of the drawbacks of this study was the limited number of studies meeting the criteria for inclusion in a systematic search.

Considerably, more research is needed to better understand the effect of mental disorder especially depression on HIV disease progression to AIDS and future interventions should, therefore, concentrate on the integration of mental health screening in HIV clinical setup.

AUTHORS' CONTRIBUTION

AY and SR performed literature search, data extraction and analysis, RM and ML contributed substantial input in the analysis, reviewed the manuscript and approved the final draft for submission.

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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AO performed literature search, data extraction and analyses, AO and OG wrote the first draft of the paper. Both authors approved the final draft for submission.

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