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# CD4 Cell Count and Depression among Patients with Human Immunodeficiency Virus Attending a General Hospital in South-South, Nigeria

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**Abstract:** *Background*: Depression is one of the commonest psychiatric disorders seen among Human immunodeficiency virus/Acquired immunodeficiency syndrome (HIV/AIDS) individuals. This study examined the potential relationship between depression and Cluster of differentiation (CD4) cell counts in patients with HIV/AIDS attending a General hospital in South-South, Nigeria. *Methods*: A descriptive cross-sectional study was conducted among 323 HIV-positive individuals attending the HIV clinic of the General hospital in South-south, Nigeria. Socio-demographic /Clinical questionnaire was designed to assess their socio-demographic/ Clinical characteristics, they had clinical interview with the Major depression episode module of Mini international neuropsychiatric interview which was used to diagnose for depression, the severity of depression was assessed using Beck's depression inventory –II. Ethical Clearance to proceed with the study was sought and obtained from the ethical committee of the Cross River State Ministry of Health. *Results*: Displayed that about 12.7% of the respondents were diagnosed to be depressed, out of which 7.7% of them had recurrent depression. Majority (83.3%) of the respondents were females and depression was significantly associated with marital status ($X^2$=7.36, df=2, p=0.03). Also, there was a significant association between monthly income and depression($X^2$=9.31, df=2, p=0.01). The presence (t=1.352, df=321, p-value=0.18) and severity (F(3, 322)=1.157, p-value=0.33) of depression were not significantly associated with CD4 cell count. *Conclusion*: The implication of this finding is that depression is one of the mental health issues that affect HIV/AIDS infected individuals in Nigeria. Furthermore, this study showed that the presence and severity of depression were not significantly associated with CD4 cells count.

**Key words:** Depression · Cluster of Differentiation 4 · Human Immunodeficiency Virus

## INTRODUCTION

The history of depression dates far back into the ancient biblical times. Depression is a mood disorder with great potentials for chronicity. It is characterized predominantly by depressed mood, low energy levels and anhedonia. Other symptoms may include sleep, appetite and weight changes, as well as a variety ofother vegetative or somatic features. It is characterized by changes in levels of the monoamines as well as receptor changes [1].

The T helper cells (Th cells), also known as CD4+ cells, are type of T cell that play an important role in the immune system, particularly in the adaptive immune system. They help the activity of other immune cells by releasing T cell cytokines. These cells help to suppress or regulate immune responses [2]. They are essential in B cell antibody class switching, in the activation and growth of cytotoxic T cells and in maximizing bactericidal activity of phagocytes such as macrophages.

Mature Th cells express the surface protein CD4 and are referred to as CD4+ T cells. Such CD4+ T cells are

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generally treated as having a pre-defined role as helper T cells within the immune system [2, 3]. For example, when an antigen-presenting cell expresses an antigen on MHC class II, a CD4+ cell will aid those cells through a combination of cell to cell interactions (e.g. CD40 (protein) and CD40L) and through cytokines.

CD154, also called CD40 ligand or CD40L, is a cell surface protein that mediates T cell helper function in a contact-dependent process [4] and is a member of the Tumor necrosis factors (TNF) superfamily of molecules. It binds to CD40 on antigen-presenting cells (APC), which leads to many effects depending on the target cell type. CD154 acts as a costimulatory molecule and is particularly important on a subset of T cells called T follicular helper cells (TFH cells) [4]. On TFH cells, CD154 promotes B cell maturation and function by engaging CD40 on the B cell surface and therefore facilitating cell-cell communication [4]. A defect in this gene results in an inability to undergo immunoglobulin class switching and is associated with hyper IgM syndrome [5]. Absence of CD154 also stops the formation of germinal centers and therefore prohibiting antibody affinity maturation, an important process in the adaptive immune system [5].

The importance of helper T cells can be seen from HIV, a virus that primarily infects CD4+ T cells. In the advanced stages of HIV infection, loss of functional CD4+ T cells leads to the symptomatic stage of infection known as the acquired immunodeficiency syndrome (AIDS). When HIV is detected early in blood or other bodily fluids, proper adherence to antiretroviral therapy will prevent the progression of HIV into AIDS and allow the body to naturally restore its own CD4 cell count. There are other rare disorders such as lymphocytopenia which result in the absence or dysfunction of CD4+ T cells [5]. These disorders produce similar symptoms, many of which are fatal.

Considering the diverse and important role helper T cells play in the immune system, it is not surprising that these cells often influence the immune response against disease. Several studies have been done to look at the potential relationship if any, between depression and CD4 cell count in patients with HIV/AIDS [6, 7].

A CD4+ count is a blood test to determine how well the immune system is working in peoplewho have been diagnosed with human immunodeficiency virus (HIV). CD4+ cell count resultsare generally available in 1 to 3 days, depending on the laboratory. In patients who are infected with HIV, the CD4 count is measured for AIDS diagnosis and for initiation of antiviral therapy. The progressive loss of CD4 T-lymphocytes in patients infected with HIV is associated with increased infections and complications. The Public Health Service has recommended that all HIV-positive patients be tested every 3 to 6 months for the level of CD4 T-lymphocytes [6, 7].

The San Francisco Men's Health Study, a 9-year longitudinal study of about 400 asymptomatic HIV-infected gay men, found that those who were depressed at study entry progressed to AIDS on average 1.4 years sooner than those who were not depressed [8]. Another study reported that depression was associated with more than twice the risk of AIDS progression, but no association with mortality [9].***

Furthermore, Several longitudinal studies have shown that there is a relationship between depression and CD4 cell count [10, 11]. Nevertheless, a 1-year study did not show any association of depression with CD4 count, CD4%, or CD4/CD8 ratio [12]. This study intends to examine the potential relationship between depression and CD4 cell counts in patients with HIV/AIDS.**

## MATERIALS AND METHODS

**Study Design and Setting:** The study was a descriptive cross-sectional study to examine the potential relationship between depression and CD4 cell counts in patients with HIV/AIDS attending General Hospital, Calabar, Cross River State, Nigeria. The hospital is located within Calabar Municipal Local Government Area. It was established in 1991 by the state government and has about one hundred beds [13].

**Study Population:** Patients who were tested and confirmed to be HIV positive that were attending the outpatient clinic of the hospital were studied.

**Inclusion Criteria:**

- Patients with confirmed diagnosis of HIV positive on follow up visit and on highly active antiretroviral therapy (HAART).
- Patients between the ages of 18-65 years.

**Exclusion Criteria:**

- Patients who were too debilitated to participate were excluded.
- Patients with previously diagnosed mental illness prior to the diagnosis of HIV B infection.
- Patients with cognitive impairment assessed by a screening form.

**Sampling Procedure:** Patients attending the HIV clinic of General Hospital, Calabar were enlightened about the purpose of the study and consecutive attendee who met the inclusion criteria were recruited into the study. A written consent was obtained from all participants after the objectives and protocol of the study had been spelt out to them. Participants were required to fill the socio-demographic/Clinical questionnaire. Furthermore, Mini International Neuropsychiatric Interview (MINI) was used by the researcher to assess for depression, those that met the criteria for depression were given Beck's Depression Inventory-II (B.D.I-II) to assess the severity of depression. Information and necessary education were given to participants who were depressed and referral to available psychiatric facility was done. Interviews were conducted strictly within clinic hours of 8:30am-4:00pm, with an average of nine patients interviewed per day. A total of 323 patients participated in the study.

**Study Instruments:** A socio-demographic questionnaire was designed for data collection and consisted of two sections (A and B)

Section A consisted of variables such as age, gender, marital status, highest level of education, monthly income, employment status, religion and ethnicity.

Section B (Clinical variables) consisted of questions assessing for family history of mental illness. Also, information about age at diagnosis, duration on HAART, duration of HIV infection and the first and last CD4 cell counts were gotten from the case note. M.I.N.I is a short structured diagnostic interview has many modules for diagnosis. Hence, the depressive episode module will be used. This category of M.I.N.I is grouped as A module which has $A_1$-$A_6$. It was used as a diagnostic instrument for depression in this study.

The most common tool used for measuring depression is the self – administered, 21-item multiple choice Beck Depression Inventory-II (BDI-II). Each of the 21 items on the BDI-II is scored from 0 to3 (0 represents symptom absent, 1 represents symptom present, 2 represents moderate symptom, 3 represents severe symptom) to indicate severity of depression. Thus, a range of 0 to 63 is possible. Typical clinical depression is usually indicated by a score of 14-28 [14]. In this study, scores of 0-13 indicates no depression, 14-19 indicates mild depression, 20-28 indicates moderate depression and a score between 29-63 indicates severe depression. It has been validated and used for assessing depression among HIV patients in Nigeria [14]. A sensitivity of 91% and specificity of 97% have been documented in Nigeria for a cut-off point of 18 and above [15]. BDI was used to determine the severity of depression in this study.

**Ethical Consideration:** Ethical Clearance to proceed with the study was sought and obtained from the ethical committee of the Cross River State Ministry of Health. Also, informed consent of each participant was obtained.

**Data Analysis:** Data was pre-coded to ensure accuracy and entered into Statistical package for social sciences 22nd version which was used for analysis. Tables were generated according to objectives and independent student t-test and Analysis of variance (ANOVA) were used to analyze parametric variables while Chi-square and Fisher's exact test were used for non-parametric variables where applicable. All analyses were done at 0.05 level of significance, two-tailed test.

## RESULTS

Table 1 gives information about the prevalence of depression among HIV-positive individuals. The results show that a total of 41 had depression. The prevalence of respondents that were diagnosed to be depressed was 12.7% (Table 1). Among those diagnosed to be depressed 25(7.7%) of them had recurrent depression (Chart 1).

Table 2 provides information about socio-demographic correlates of depression among HIV-positive individuals. The results show that depressive disorder was significantly associated with marital status ($X^2$=7.36, df=3, p=0.03) andmonthly income ($X^2$ =9.31, df=2, p=0.01) while age ($X^2$=1.26, df=3, p=0.74), gender ($X^2$=1.64, df=1, p=0.20), level of education ($X^2$=5.20, df=2, p=0.07), ethnicity ($X^2$=3.22, df =2, p=0.20), employment status ($X^2$=2.57, df=4, p=0.63) were not significantly associated with depression.

Table 3 gives information about theclinical characteristics of HIV-positive respondents. The result shows that majority (94.1%) of the respondents had no family history of depression. Almost half (48.6%) of the respondents had been on HAART ranged from 1-5 years and 46.1% of respondents had been diagnosed to be HIV positive ranged from 1-5 years. More than half (51.7%) of the respondents had $CD_4$ count greater than500 cells/$mm^3$. The age at diagnosis of respondents with HIV ranged from 10-62 years with a mean of 33 years (S.D = 10.2).

Table 1: Prevalence of depression among HIV-positive patients using M.I.N.I

| Variables | Frequency (%) N=323 |
|---|---|
| Presence of depression | 41 (12.7) |
| Absence of Depression | 282 (87.3) |

Table 2: Socio-demographic correlates of respondents with or without depression (N=323) *=significant **=Fisher's exact test

| Variables | Depressed N (%) | Non depressed N (%) | $X^2$ | df | p-value |
|---|---|---|---|---|---|
| Age | | | | | |
| 15-24 | 4(1.2) | 20(6.2) | 1.26 | 3 | 0.74 |
| 25-44 | 29(9.0) | 193(59.8) | | | |
| 45-64 | 8(2.5) | 6419.8) | | | |
| 65+ | 0(0.0) | 5(1.5) | | | |
| Gender | | | | | |
| Male | 4(1.2) | 50(15.5) | 1.64 | 1 | 0.20** |
| Female | 37(11.5) | 232(71.8) | | | |
| Educational level | | | | | |
| Primary | 20(6.2) | 93(28.8) | 5.20 | 2 | 0.07 |
| Secondary | 13(4.0) | 141(43.6) | | | |
| Tertiary | 8(2.4) | 48(14.9) | | | |
| Ethnicity | | | | | |
| Efik | 16(5.0) | 152(47.1) | 3.22 | 2 | 0.20 |
| Igbo | 2(0.6) | 9(2.8) | | | |
| Others | 23(7.1) | 121(37.5) | | | |
| Marital Status | | | | | |
| Married | 10(3.1) | 121(37.5) | 7.36 | 2 | 0.03* |
| Single | 13(4.0) | 89(27.5) | | | |
| Separated/Divorced/Widowed | 18(5.6) | 72(22.3) | | | |
| Employment status | | | | | |
| Retired | 3(0.9) | 16(4.9) | 2.57 | 4 | 0.630 |
| Self employed | 20(6.2) | 159(49.2) | | | |
| Employed by Others | 5(1.6) | 32(9.9) | | | |
| Government employ | 2(0.6) | 24(7.5) | | | |
| Unemployed | 11(3.4) | 51(15.8) | | | |
| Monthly income | | | | | |
| No income | 13(4.0) | 62(19.2) | 9.31 | 2 | 0.01* |
| ₦1-₦25000 ($82) | 26(8.1) | 146(45.2) | | | |
| >₦25000 ($82) | 2(0.6) | 74(22.9) | | | |
| Family history of depression | | | | | |
| Present | 3(0.9) | 16(5.0) | 0.139 | 1 | 0.72** |
| Absent | 38(11.8) | 266(82.3) | | | |

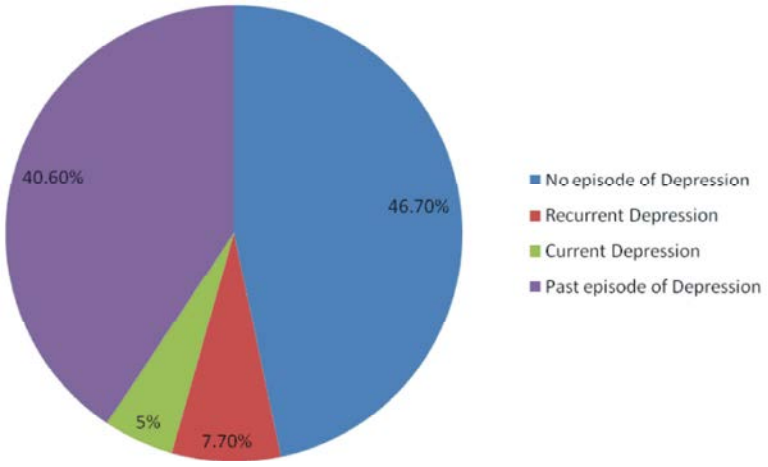


Chart 1: Pie chart showing the prevalence of depression among respondents using M.I.N.I

Table 3: Clinical characteristics of HIV-positive respondents

| Clinical characteristics | Frequency (%) (N=323) |
|---|---|
| Age at diagnosis (in years) | |
| 10-20 | 22 (6.8%) |
| 21-30 | 123 (38.1%) |
| 31-40 | 106 (32.8%) |
| 41-50 | 48 (14.9%) |
| 51-60 | 20 (6.2%) |
| 61-70 | 4 (1.2%) |
| Mean ± S.D | 33.5 ± 10.2 |
| CD4 count(cell/$mm^3$) | |
| <500 | 156 (48.3%) |
| >500 | 167 (51.7%) |
| Family history of mental illness | |
| Present | 19 (5.9%) |
| Absent | 304 (94.1%) |
| Duration on HAART (in years) | |
| <1 | 64 (19.8%) |
| 1-5 | 157 (48.6%) |
| 6-10 | 76 (23.5%) |
| 11-15 | 26 (8.1%) |
| Duration of HIV infection (in years) | |
| <1 | 52 (16.1%) |
| 1-5 | 149 (46.1%) |
| 6-10 | 107 (33.1%) |
| 11-20 | 15 (4.7%) |

Table 4: Relationship between presence and absence Depression and CD4 cellcount among respondents

| Variable | Depression Present(N=41) [Mean(SD)] | Depression Absent(N=282) [mean(SD)] | Mean difference | t-test | df | p-value |
|---|---|---|---|---|---|---|
| Mean CD4 cell count | 472.29(287.37) | 546.98(336.23) | 74.69 | 1.352 | 321 | 0.18 |

Table 5: Relationship between of severity of depression and CD4 cells count among respondents

| Variable | Sum of squares | Df | Mean Square | F-test | p-value | Eta | Eta Squared |
|---|---|---|---|---|---|---|---|
| Between groups | 379562.19 | 3 | 126520.73 | 1.157 | 0.33 | 0.104 | 0.011 |
| Within groups | 34890788.56 | 319 | 109375.513 | | | | |

Table 4 provides information about the relationship between the presence and absence of depression and CD4 cells count among the respondents. The results show that there was no significant association between the mean CD4 cell count of depressed and non-depressed patients (t = 1.352, df =321, p = 0.18).

Table 5 provides information about the relationship between the severity of depression and CD4 cells count among the respondents. The results show that there was no statistically significant difference between the severity of depression and CD4 cell counts of respondents determined by one-way Analysis of Variance (One-way ANOVA) (F(3, 322)= 1.157, df=3, p=0.33).

## DISCUSSION

In this study 12.7% of respondents met the diagnostic criteria for depressive disorder using M.I.N.I. This finding falls within the range reported in of a meta-analysis on prevalence of depression among HIV infected individuals. It was reported that the prevalence of depression ranges from 0-22.5% [16]. The finding in thisstudy is also similar to the report in a Nigeria study by Adewuya *et al.* [17] on Psychiatric disorders among HIV-Positive population in Nigeria. The prevalence rate in my study is lower than 57% reported by Shittu *et al.* in Ilorin [18], 39.1% by Aguocha et al in Owerri [19] and 63% by L'akoa *et al.* [20] in Uganda. The probable reason for this is that these latter studies used PHQ-9 for diagnosing depression though it is a screening and not a diagnostic instrument for depression [21]. In this study there was no statistically significant association between age and depression. This is similar to the reports by Bongogo *et al.* [22] in South Africa and Shittu *et al*. [18] in Ilorin. The likely reason is that individual can experience depression at different times of their lives for various reasons [22]. The finding in thisstudy differs from the outcome of the study conducted by

Getalem and Emnet [23] in Ethiopia which reported that there was significant association between age and depression. The likely reason may be fear of stigma or discrimination and fear of loss of partners in the future due to nature of the disease.

This current study showed that there was no statistically significant association between gender and depression. This is similar to the study reported by Aguocha *et al*. [19]. The finding in this study is not in keeping with the report from the study conducted by Ibrahim *et al.* [24] in North-eastern Nigeria which stated that there is a statistically significant association between gender and depression. The likely reason for this is the additional psychological stresses faced by women living with a socially stigmatizing illness both at home and work [24].

In this study there was no significant association between depression and level of education. This is similar to findings in studies conducted by Yee *et al.* [25] in Kuala Lumpur and by Aguocha *et al*. [19] in Owerri. The finding in this study differs from the report by Onyebueke *et al.* [26] in Enugu in a study on depression and suicide risk among HIV infected individuals attending outpatient HIV/AIDS clinic of a Nigerian Tertiary Health Institution. The likely reason for this difference was the smaller size of the study population compared to my study where the sample size is twice their sample size. Studies have shown that the smaller the sample size the less reliable the study [27].

In this study, there is no association between occupation and depression. This is in keeping with another study by Ibrahim *et al*. [24] in Jos. This study differs from the report by Bhatia *et al*. [28] in Delhi who looked at Prevalence of depression in people living with HIV/AIDS undergoing ART and factors associated with it. The likely reason for this difference was that significant proportion of their study population was between 14 to 20 years. It is noteworthy that this age group are less likely to be working. It is very likely that this may have accounted for the difference in the finding.

This study showed that there is significant association between income of respondents and depression. Similar finding was reported by Shittu *et al.* [18] in Ilorin. The finding in this study shows that low income predominates, thus, income has been shown to significantly affects the person overall living conditions. Shittu *et al.* [18]. Also, low-income people living in poverty, cannot afford healthy food, sufficient clothing and good housing all of which are necessary preconditions of good health [18].

In this study marital status is significantly associated with depression. This is similar to the reports by Agaba *et al*. [29] in Jos, Onyebueke *et al*. [26] in Enugu and Shittu *et al*. [18] in Ilorin. The likely reason given was that women are much likely to experience negative social stress than men because they carry the double burden of raising children and household chores [30]. The finding in my study differs from the report by Aguocha *et al*. [19] in Owerri which stated that there is no significant association between marital status and depression. The likely reason is the fact that being married with good social support system has a strong protection against depression and married people are less prone to depression. Additionally, Aguocha *et al*. [19] used PHQ-9 which is a screening instrument.

In this study there was no significant association between family history and depression among respondents. This is similar to the report by Saleh *et al*. [31]. The finding in this current study differs from the report by Kinyanda *et al*. [32] who studied Prevalence and risk factors of major depressive disorder in HIV/AIDS as seen in semi-urban Entebbe district, Uganda. The likely reason for this difference is that the study was conducted in two different clinics using cross-sectional and longitudinal study designs. Hence, the finding was consistent with family studies, which have shown that the history of depression in the first degree relations of a subject naturally increases the subjects' vulnerability to developing depression [24]. Another likely reason for the difference in findings of this present study and the Uganda study is underreporting of family history of mental illness by patients and relatives in typical African study, this is due the fear of stigmatization [24].

More than half of respondents in this study have CD4 cells count of more than 500cells count/$mm^3$, this implies that most of the respondents in this study were healthy. In this study there was no significant association between presence of depression and CD4 cell count. This is similar to studies conducted by Moosa, *et al.* [33] in South Africa. The finding in this study differs from thereport by Olisah, *et al.* [34] who looked at Depression and CD4 cell count among patients with HIV in a University Teaching Hospital in Zaria, Nigeria. The likely reason maybe because the depressive symptomatology was assessed using Center for Epidemiological Studies Depression Scale Revised (CES-DR) instrument. It should be noted that M.I.N.I was used in diagnosing depression in this study and it is more sensitive than CES-DR which is an instrument used in epidemiological studies as a screening tool for depressive symptoms [35]. This study

found no significant association between the severity of depression and CD4 cell count. Ickovics *et al.* [36] in an American study had similar findings. The finding in our study differs from the report by Taniguchi et al in Japan [37] who found that severity of depression is associated with increased risk behaviours and decreased CD4 cell counts. The likely reason for this maybe because PHQ-9 which is a screening instrument was used to diagnosed for depression.

## CONCLUSION

This study showed that majority of the respondents were females and depression was significantly associated with marital status. Also, majority of the respondents had no family history of depression. Also, this study showed that the presence and severity of depression were not significantly associated with CD4 cells count.

What is already known on this topic:

- Depression is a common mental health disorder among people who are diagnosed with HIV/AIDS
- Depression is common among female patents with HIV/AIDS

What this study adds:

- This study determined the association between severity of depression and level CD4 cell counts

**Competing Interest:** The authors have declared no competing interest existed.

**Authors Contributions:** This work was carried with the collaboration of all authors. Emmanuel Omamurhomu Olose, Cecilia Oluwafunmilayo Busari and Ekpe Esien Ekpe designed the study. Emmanuel OmamurhomuOlose wrote the protocol for the study. In addition, Cecilia Oluwafunmilayo Busari, Emmanuel Omamurhomu Olose, Ekpe Esien Ekpe, Babalola Isaiah Adubina did the literature search. Cecilia Oluwafunmilayo Busari and Emmanuel Omamurhomu Olose analyzed the data. Emmanuel Omamurhomu Olose wrote the initial draft of this publication, Oluseun Peter Ogunnubi prepared the tables and all authors made corrections for the final draft of this manuscript.

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