



## **Adherence to Anti-retroviral Therapy among HIV-Positive Individuals in Ghana: The Role of Stress and Post Traumatic Stress Symptoms**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Authors IAK, BAA and EA were involved with research concept, data analysis and interpretation of results, writing and review of manuscript. Author CES was part of the research concept, data collection, data analysis, interpretation of results and review of manuscript. Author FA's input was in relation to research concept, interpretation of results and review of manuscript. Author BM contributed to the research concept, data analysis and interpretation of results and review of manuscript. All authors reviewed and approved the final manuscript.*

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## ABSTRACT

**Aims:** To identify stress and post traumatic stress symptoms (PTSS) in HIV patients on Antiretroviral therapy (ART) and further assess the possible relationship between stress, PTSS, immune function and ART medication adherence.

**Methods:** After obtaining written informed consent, 150 HIV out-patients attending Pantang and Amasaman Hospitals in Accra, Ghana, were recruited for the study. Participants were interviewed using a questionnaire comprising of sections measuring demographic characteristics, perceived stress, post traumatic stress symptoms, and medication adherence. A measure of the immune function (CD4+) from individual's health records was noted at the time of interview.

**Results:** Ninety four (62.7%) patients exhibited higher stress levels compared to the remaining 56(37.3%). The majority of participants (74%) showed PTSS at levels that met the optimal criteria indicative of post traumatic stress disorder (PTSD) and may have required clinical attention and management. Participants with high stress levels were 84% less likely to be adherent to their antiretroviral medication compared to those with lower levels of stress [OR=0.16 (0.050–0.512),  $P < 0.0001$ ]. Patients who showed evidence of stress were approximately four times more likely to develop PTSD compared to non-stressed patients [OR=3.898 (1.428–10.635),  $P = 0.007$ ]. The experience of side effects did not influence adherence [OR = 0.536 (0.224–1.285),  $P = 0.155$ ]. On the other hand, stress significantly related with adherence when side effects were present [OR=0.648 (0.252–1.662),  $P = 0.002$ ]. The PTSD importantly associated with adherence to ART with approximately 42% less odds of attaining optimal adherence by participants with PTSD compared to non-PTSD patients [OR=0.576 (0.189–1.751),  $P = 0.017$ ].

**Conclusion:** HIV patients on ART need to be screened for stress, PTSS and PTSD in order to benefit from psychological support and therapy. This activity can significantly enhance medication adherence as well as impact positively on the general health outcomes of HIV patients on ART.

*Keywords: Stress; post traumatic stress disorder; anti-retroviral medication; adherence; HIV/AIDS; Ghana.*

## 1. INTRODUCTION

The Acquired Immune-deficiency Syndrome (AIDS), principally a sexually transmitted disease is caused by the Human Immune-deficiency Virus (HIV). In some cultures particularly sub-Saharan Africa, the transmission of HIV/AIDS is perceived to be primarily through unprotected sex and having multiple sexual partners [1]. Connoting HIV infection as a social vice becomes synonymous with stigmatization, discrimination, and the lack of emotional and psychological support. These pave the way for the development of mental health disorders such as anxiety, depression, post-traumatic stress disorders and other mental illnesses [2-4]. The relationship between socio-behavioral factors and HIV disease progression may be complex; yet, traumatic life events have been noted to complicate the course of diseases especially the disease progression from HIV to AIDS [5].

Post Traumatic Stress Disorder (PTSD) negatively affects the body's response to stress by elevating stress hormones and neuro-chemicals [6]. Whereas PTSD is approximately found in 1.3% to 37.4% of the general population, some studies have found it to be 22% to 64% among persons living with HIV and AIDS (PLWHA) [7]. The presence of PTSD may

negatively impact immune function and interfere with adherence to ART among people with HIV/AIDS. Currently, ART is commenced for persons infected with HIV when there are severe symptoms, CD4 count is 500 cells per cubic millimeter of blood or less, pregnancy, the presence of HIV related kidney disease, hepatitis B and active tuberculosis [8]. Adherence to ART is vital especially with the increasing view that HIV infection is considered as a chronic medical condition and treated as such [9]. While adherence to ART is important for improved anti-virological activity and reduced mortality, the development of drug resistant strains of the virus has been associated with poor adherence [10,11]. In optimising health outcomes, a 100% medication adherence rate to ART is vital, yet ART adherence rates in Ghana have been estimated at 60% to 80% [12-14]. To assess and improve on treatment outcomes, the mental distress determination of adherence patterns need to be considered in line with the limited information on the relationship between these variables in Ghana. Thus, this study sought to assess the possible association between stress, PTSS and ART adherence while taking note of the role of the immune marker (CD4+) and medication side effects.

## **2. METHODS**

### **2.1 Study Site**

This hospital-based cross-sectional study assessed the relationship between stress, post traumatic stress symptoms and ART medication adherence. The study was conducted in two hospitals, Pantang and Amasaman, located in districts East and West of the Greater Accra Region of Ghana respectively. Pantang Hospital manages patients with both physical and mental health conditions and in 2011, 17536 patients with physical problems were seen at the hospital while 20503 patients with varying mental health conditions received care at the facility. The hospital recorded 240 new cases of HIV in the same year in addition to the existing ones. Similarly in 2011, Amasaman Hospital managed 55697 patients with varied medical conditions and HIV (n=138). All interviews at Pantang Hospital were conducted at the ART Pharmacy division and interviews at Amasaman hospital took place in a consulting room at the HIV clinic.

### **2.2 Study Sample**

Participants were recruited from Pantang Hospital (n=93) and Amasaman Hospital (n=57). Patients who were 15 to 49 years, constituting the sexually active and HIV prevalent age group were included [15]. To establish a measurement of adherence, only patients on antiretroviral therapy at the time of data collection were recruited. Pregnant women and lactating mothers were excluded from the study because of the brief variations in ART regimen during these periods.

### **2.3 Ethical Considerations**

Ethical approval was obtained from the Institutional Review Board (IRB) of the Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, with certified protocol number (CPN) 022/10-11. The two hospitals involved also gave authorization for the study to be conducted after written permissions were sought to undertake this study. When the patients understood the study rationale and were assured of confidentiality of their information gathered, they appended their signatures, initialized their names or thumb printed to indicate their willingness to participate in the study.

## **2.4 Tools for Data Collection**

Information on the socio- demographic and clinical characteristics, perceived stress, post traumatic stress symptoms and medication adherence were obtained using a questionnaire. The demographic data sought the age, sex, educational level, marital status, religious affiliation, ethnicity, number of years diagnosed as HIV, current CD4 count, and type of ART taken.

The 4-item Perceived Stress Scale (PSS) [16] was used to measure participants' perception of stress. This version of the PSS was obtained from questions 2, 4, 5 and 10 of the 10-item PSS. This tool is a widely used psychological instrument for measuring the perception of stress. The PSS which inquires about feelings and thoughts during the past month is a measure of the degree to which individuals appraise stressful situations in their lives. The positively stated items 4 and 5 were reversely scored and then summed with the other items across the scale. The 4- item PSS has previously been validated [17] and in our study it was reliable with Cronbach's alpha of 0.73.

The 17-item PTSD Checklist- Civilian Version measured symptoms of post traumatic stress among the respondents [18]. This PTSD checklist assesses symptoms based on the post traumatic stress disorder criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) in relation to re-experiencing, avoidance/numbing, and arousal. A 5-point Likert scale was used by respondents to rate each item from 1 (not at all) to 5 (extremely). The responses indicated the extent to which they experienced and had been bothered by particular symptoms over the past month. To meet the criteria for PTSD, an individual should report being bothered quite a bit, moderately, or extremely [18]. The checklist correlates strongly with other measures of PTSD, such as the Mississippi Scale and the PK scale of the MMPI-2 (0.82) [19] The PTSD Checklist in our study showed good internal reliability (Cronbach's alpha =0.79).

In order to establish the rate of adherence to ART, a 4-item Morinsky Medication Adherence Scale (MMAS) was employed [20]. Each item elicited a 'yes' or 'no' response about patterns of past medication use. High, moderate and low adherence rates were obtained when a patient answered 'no' to all the questions, 'yes' to one question, and 'yes' to two or more questions respectively. The MMAS items demonstrated good internal reliability (Cronbach's alpha =0.75).

All data collection instruments were validated. In addition, a back and forth translation of the questionnaire was done from English to Twi (the local language) and vice versa. This was to ensure that the exact meanings of words were conveyed in both languages.

## **2.5 Data Management and Analysis**

Data was sorted, coded, and analyzed with the SPSS version 16.0. Descriptive statistics such as frequencies and percentages were used to describe and summarize the data. Analysis of contingency tables was done and Pearson's chi-square, Pearson correlation and logistic regression models were used to test for associations between the study variables and their levels of significance.

### 3. RESULTS

#### 3.1 Socio-demographic and Clinical Characteristics

The majority of study participants were women (81.3%), 82% were Christians with 49.3% between 24 – 34 years old (Table 1). Equal proportions of 63.3% were married and had attained a minimum of secondary school education. Seventy eight percent of the patients were employment. The clinical characteristics of patients are presented in Table 2. Eighty six percent of the sample had been living with HIV/AIDS for two years and less with 2% being about five years and more. Ten (6.7%) out of the 150 patients had co-morbid mental health conditions of anxiety and depression recorded in their medical record folders. The study participants were on the recommended three drug antiretroviral therapy. A high proportion of patients (32.7%) took the joint therapy of zidovudine, lamivudine and nevirapine (AZT.3TC.NVP) whereas the least number of one patient (0.7%) was on the stavudine, zidovudine and nevirapine (d4T.AZT.NVP) combination. The association between the type of medications taken and adherence was insignificant ( $\chi^2 = 11.216$ ,  $P=0.511$ ).

**Table 1. Socio-demographic characteristics of study sample**

Variable	Frequency	Percentage
<b>Sex</b>		
Male	28	18.7
Female	122	81.3
<b>Age distribution</b>		
15 – 24	9	6.0
25 – 34	74	49.3
35 - 44	48	32.0
45 - 54	16	10.7
≥ 55	3	2.0
<b>Marital status</b>		
Single	35	23.3
Married	95	63.3
Divorced	13	8.7
Widowed	7	4.7
<b>Educational level</b>		
Primary	34	22.7
Secondary	95	63.3
Tertiary	1	0.7
None	20	13.3
<b>Religion</b>		
Christian	123	82.0
Muslim	25	16.7
African Traditional Religion	2	1.3
<b>Ethnicity</b>		
Akan	54	36.0
Ewe	53	35.3
Ga	18	12.0
Northerner	25	16.7
<b>Employment status</b>		
Employed	117	78.0
Unemployed	33	22.0

The extent to which patients experienced some side effects (diarrhea, insomnia dizziness, nervousness, mental confusion, abdominal pains, flatulence, nightmares and oral ulcers) of

antiretroviral drug was recorded. Fifty five (36.7%), 93 (62%) and 2 (1.3%) of the patients reported experiencing low, moderate and severe levels of the side effects listed. Adherence to the ART varied in terms of low (32.7%), moderate (32%) and high (35.3). For 40.7%, 28% and 18% of the patients, the recorded CD4+ count at the time of data collection were in the ranges of 0–200, 201–400 and 401–600 respectively. A low proportion of patients (2%) reported with CD4+ count of 1000 and more (Fig. 1).

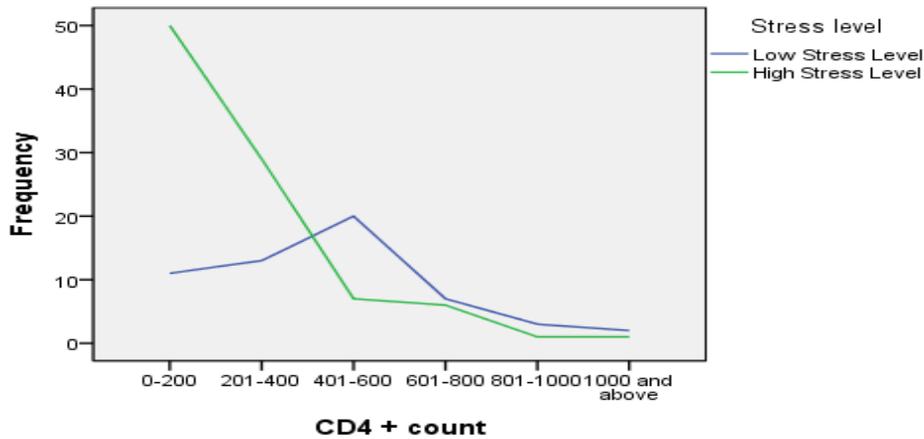


Fig. 1. Relationship between levels of stress and CD4+ counts

Table 2. Clinical characteristics of study sample

Variable	Frequency	Percentage
<b>Duration of diagnosis (years)</b>		
≤ 2	129	86.0
3 – 4	18	12.0
5 and above	3	2.0
<b>HAART taken</b>		
TNV.3TC.EFZ	17	11.3
TNV.3TC.NVP	41	27.3
AZT.3TC.EFZ	32	21.3
AZT.3TC.NVP	49	32.7
d4T.3TC.EFZ	4	2.7
d4T.3TC.NVP	6	4.0
d4T.AZT.NVP	1	0.7
<b>CD4+ count</b>		
0 - 200	61	40.7
201 - 400	42	28.0
401 - 600	27	18.0
601 - 800	13	8.7
801 - 1000	4	2.7
1001+	3	2.0
<b>Side effects</b>		
Low	55	36.7
Moderate	93	62.0
Severe	2	1.3
<b>Level of adherence</b>		
Low	49	32.7
Moderate	48	32.0
High	53	35.3

### 3.2 Stress and Adherence

Results of the PSS were analyzed utilizing descriptive statistics. The mean PSS score was determined and values above and below the mean score formed high stress (62.7%) and low stress (37.3%) levels respectively. Some stress management strategies were identified. Though few numbers of patients employed stress coping techniques of engaging in social activities (n=16), regular physical exercises (n=7), and relaxation through conscious deep breathes (n=1), many of them (n=81) used complementary and alternative therapies (CAM) (Table 3). The following were the types of CAM used; prayers (86.4%), herbs (8.6%), alcohol and alcoholic extracts of herbs (4.9%). Stress may impair immune function and a significant negative correlation between stress and CD4+ counts ( $r = -0.385$ ,  $P < 0.0001$ ) was observed. Equally, stress and adherence were negatively related ( $\chi^2 = 11.093$ ,  $P = 0.004$ ). Using a logistic regression model, the adjusted results for the association between stress and adherence are shown in Table 4. Participants with high stress levels were 84% less likely to be adherent to their antiretroviral medication compared to those with lower levels of stress [OR=0.16 (0.050–0.512),  $P < 0.0001$ ]. The chi-square analysis showed a significant relationship between the level of stress and PTSD ( $\chi^2 = 7.547$ ,  $P = 0.006$ ); and patients who showed evidence of stress were approximately four times more likely to develop PTSD compared to non-stressed patients [OR=3.898 (1.428–10.635),  $P = 0.007$ ]. The experience of side effects did not influence adherence [OR=0.536 (0.224–1.285),  $P = 0.155$ ]. On the other hand, stress significantly related with adherence when side effects were present [OR = 0.648 (0.252–1.662),  $P = 0.002$ ]. Stress did not significantly relate with the number of years a person had been living with HIV/AIDS ( $\chi^2 = 1.249$ ,  $P = 0.741$ ) or the type of ART taken ( $\chi^2 = 6.808$ ,  $P = 0.339$ ).

**Table 3. Stress coping strategies employed by patients**

<b>Stress coping strategies</b>	<b>Frequency</b>	<b>Percentage</b>
<b>Involvement in social activities</b>		
Never	110	73.3
Sometimes	24	16.0
Often	16	10.7
<b>Regular physical exercise</b>		
Never	119	79.3
Sometimes	24	16.0
Often	7	4.7
<b>Conscious deep breathing</b>		
Never	148	98.6
Sometimes	1	0.7
Often	1	0.7
<b>Use of CAM therapies</b>		
Never	69	46.0
Sometimes	0	0
Often	81	54.0
<b>Types of CAM used (n = 81)</b>		
Prayers	70	86.4
Herbs	7	8.6
Alcohol	3	3.7
Alcoholic extract of herbs	1	1.2

### 3.3 Post Traumatic Stress Symptoms

With a recommended cut-off score of 50 on the PTSD Checklist- Civilian Version, 111 (74%) patients met the optimal score criteria indicative of PTSD. The PTSD significantly inversely associated with adherence to ART ( $r=-0.219$ ,  $P=0.018$ ) with approximately 42% less odds of attaining optimal adherence by participants with PTSD compared to non-PTSD patients [OR = 0.576 (0.189–1.751),  $P=0.017$ ] (Table 4).

**Table 4. Relationship between stress, PTSD and ART adherence**

Variable	Odds ratio	95% confidence interval	p value
<b>Odds of achieving high ART adherence</b>			
Stress: high (reference: low)	0.16	0.050 – 0.512	< 0.0001
PTSD: high (reference: low)	0.576	0.189 – 1.751	0.017
<b>Odds of developing PTSD</b>			
Stress: high (reference: low)	3.898	1.428 – 10.635	0.007

*Adjusted for demographic and clinical characteristic*

## 4. DISCUSSION

### 4.1 Demographic Characteristics

Similar to the 2010 HIV Sentinel Survey Report in Ghana [15], the majority of patients fell within the age groups 24- 34(49.3%) and 35- 44 (32%) years with a male to female ratio of approximately 1: 4. Although a 1:1.4 ratio had been reported in the Ghana national survey [15], the variation observed in this study was as a result of many women reporting to the hospitals at the time of data collection and expressing willingness to be enrolled in the study compared to their male counterparts. The majority of participants were in some form of employment, yet, 33 (22%) were unemployed because they did not want to infect other people with the disease as they used sharp instruments such as knives, scissors and needles in their line of work. Others were concerned about negative perceptions from their co-workers in relation to their illness thus avoiding discrimination and stigmatization. In this study, the optimal ART adherence rate was approximately 35%. The main study variables (stress and PTSS/ PTSD) were found to be associated with the inadequate adherence to HIV pharmacotherapy.

### 4.2 Stress and Medication Adherence

A high proportion of the study participants (62.7%) reported high levels of stress which was significantly associated with considerably decreased odds (84%) of ART adherence. In the case of an HIV positive patient whose immune system is already compromised, an added effect of stress could further complicate the course of disease [21].

The PSS has been reported to predict both objective biological markers of stress and increased risk for disease among persons with chronic diseases [22]. For example, individuals with higher scores on the PSS have poor indicators on biological markers of aging, cortisol levels, immune markers, depression, infectious disease and wound healing [22]. Similarly, the study observed that the majority of the patients (40.7%) had their immune marker CD4+ counts within 0 - 200 cells per millimeter cube which was significantly related

to stress. The CD4+ cell count is used as a marker of disease progression and response to treatment of HIV infected individuals.

The antiretroviral drugs have documented side effects similar to symptoms of stress such as diarrhea (Abacavir), insomnia (Emtricitabine), dizziness (Virtigo), mental confusion (Efavirenz) and abdominal pains (Ritonavir) [23]. Although this study found a high prevalence rate (63.3%) of moderate to severe experiences with the ART side effects, this did not have any significant relationship with adherence. Yet the analysis found that co-morbid stress moderated the association between side effects and adherence, thus, the presence of stress enhanced the role of side effects with regards to ART non-adherence. Consequent to poor ART adherence is a further compounding of treatment failure leading to an increase in viral replication, HIV/AIDS disease progression and eventually high mortality rates.

Coping with stress is thus important in the life of an HIV positive patient with actual coping efforts aimed at regulating the stressor resulting in the outcomes of the coping process [24]. Though few numbers of patients employed stress coping techniques of engaging in social activities, regular physical exercises, and relaxation through conscious deep breathes, the majority of the patients used complementary and alternative therapies such as prayers, herbs, alcohol and alcoholic extracts of herbs. The high rates of the use of prayers were aimed at a spiritual intervention for healing which conforms with spiritual causal theories strongly underlining chronic conditions in Ghana [25,26]. As previously reported, some patients discontinued ART because of their belief in spiritual healing [27].

Applying a broader conceptualization of stress and coping in this study, problem- or emotion-focused coping approaches were used by the patients; although correctly dichotomizing these coping behaviours along the two dimensions may be intricate [28]. In problem-focused coping, individuals engaged in behaviors which addressed the sources of stress, whereas in emotion-focused coping, they engaged in activities to alleviate the emotional distress caused by the stressor.

### **4.3 Post Traumatic Stress Disorder and Medication Adherence**

The PTSD checklist is a good predictor of diagnosing post traumatic stress disorder [18]. Similar to related studies on PTSD [7,29] a significant proportion (74%) of the study participants would require treatment (clinical attention) for PTSD. The PTSD was significantly negatively related with adherence. Stress and PTSD diagnosis were not reported in the co-morbid conditions in this study. Yet the mental health of a patient is as important as the physical health. The HIV patient may present with other conditions which may be medical or psychological. Although negative emotions are usually not included in the co-morbidities reported by medical patients [30], anxiety and depression were the specific mental illnesses that were diagnosed in ten (6.67%) of the patients. Having a defining relationship between HIV and mental illness is usually a challenge and with multiple explanations. The HIV could affect the brain and mental health of the patient leading to the development of psychiatric illnesses or the pre-existence of a psychiatric condition could behaviorally predispose an individual to be infected with the virus.

There are reasons for which stress and PTSD go undiagnosed and untreated in people with HIV disease. Many of the symptoms of stress and PTSD such as physical reactions (heart pounding, troubled breathing and sweating), sleep disturbances, loss of interest in something one used to enjoy, and impaired concentration, are synonymous to symptomatic

HIV disease itself. As a result, these symptoms are often attributed to the HIV disease progression rather than to stress or PTSD. Another reason that PTSD goes undiagnosed and untreated is that many caregivers incorrectly assume that global demoralization, a sense of hopelessness, and loss of direction, purpose, and self-esteem—all symptoms of PTSD—are normal emotional responses to the harsh realities of living with HIV.

As a result of the negative impact on immune function, these findings emphasize the need to actively screen and manage symptoms of stress and PTSD among persons with HIV.

#### **4.4 Limitations**

The study acknowledges some limitations. First, these findings are specific to a relatively small sample of patients in two south urban communities which may not be representative of persons living with HIV/AIDS in Ghana. The relatively low participation rate among males may also affect the general reflection of the results of stress, PTSD and ART adherence.

#### **5. CONCLUSION**

From the foregoing, HIV patients do experience symptoms of stress and post traumatic stress. However, there is no service that seeks to address these problems. There is therefore the need for mental healthcare to be incorporated into routine HIV services to enable people on ART to benefit from a holistic health service delivery. By so doing, HIV patients on ART who go for their scheduled check-ups could be screened for any mental health distresses in order to benefit from psychological support and therapy. This activity can significantly enhance medication adherence as well as impact positively on the general quality of life of HIV patients on ART.

#### **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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