

## The CD4 T-cell count and the neurological manifestations among Sudanese patients with HIV/AIDS; a prospective comparative study

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**Abstract: Introduction:** The neurological manifestation of HIV/AIDS are increasing in Sudan in spite of the introduction of antiretroviral since 2006 by the WHO global fund. The present study evaluated the CD4 count and neurological manifestation in HIV-infected Sudanese patients. **Methods:** This prospective cohort hospital based study conducted at four HIV/AIDS centers in Sudan during the period from May 2011 to June 2013. Participants 18 years or above were invited to sign a written informed consent and then interviewed using a structured questionnaire. The patients then underwent a full examination by a neurologist followed by the relevant investigations including CSF analysis and CT/MRI imaging. The chi-square test was used to compare the categorical data with a  $P$ -value  $< 0.05$  considered significant. **Results:** They were 100 patients with HIV/AIDS, their ages ranged from 18-68 years, more than two-thirds were males, the commonest presenting symptoms were fever (83%), followed by diarrhea in (79%), the commonest nervous system opportunistic infection was tuberculosis (41%), followed by cerebral toxoplasmosis in 28% of the patients, while Cytomegalovirus retinitis was observed in 23%. Focal neurological signs were evident in 66% of patients. The neurological complications were higher among those with CD4 count  $< 200$ . **Conclusion:** The neurological complications were prevalent among HIV/AIDS Sudanese patients and were commoner among patients with low CD4 counts.

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**Keywords:** HIV/AIDS, Neurological manifestations, CD4 count, Sudan

### 1. Introduction:

HIV/AIDS is steadily rising since its emergence in the 1980s as one of the major health challenges of the world. It is now one of the leading causes of mortality and morbidity. There is a trend towards larger and larger share of the disease burden coming from non-communicable diseases, but HIV is a major exception. There are an increasing mortality and morbidity from HIV till the year 2004 in contrast to the declining burden from the infectious diseases [1].

The prevalence of HIV in Sudan ranged from 0.4-1.6%, but due to the fact that the country is bordered with the HIV/AIDS belt and the abundance of the risk factors for HIV transmission (poverty, illiteracy, mobility of the people due to war and instability, and refugees who flooded Sudan from near countries with high prevalence of the disease), HIV/AIDS is a major health concern [2].

The neurological manifestations of HIV/AIDS occur in more than 40% of patients (The autopsy prevalence is 80%) and could be the first sign in up to 20% of those suffering from the disease. In spite of the observed decline in the neurological complications, the mortality from these disorders remains high [3,4].

Neurological complications of HIV could be due to the virus itself or associated with immune compromise (opportunistic infections, or immune reconstitution syndrome. These complications are still present despite the introduction of antiretroviral therapy, and the CD4+Tcell nadir is a significant risk factor for neurocognitive disorder in the era of antiretroviral therapy [5].

The increasing prevalence of neurocognitive disorders and the new forms of the opportunistic infections are significant challenges to the infectious disease specialist in the daily clinical practice [6].

To our best of knowledge, this is the first study that investigated the neurological manifestation of HIV/AIDS in Sudan, in this study, we examined the relationship of CD4+ Tlymphocytes to the neurological complication in HIV patients.

### 2. Methods:

This cross-sectional prospective hospital-based study conducted at four HIV centers in Khartoum, Sudan during the period from May 2011 to June 2013. The patients with the diagnosis of HIV were selected by the simple stratified method to select one hundred patients. Since their establishment by the AIDS

control program in 2003, the Aids management centers offered VCT to more than 2500 clients and 1760 HIV/AIDS patients were enrolled in HIV care, 916 of them had got free access to ARVs and cotrimoxazole prophylaxis. The center follows the WHO guidelines for management of HIV/AIDS patients strictly. One of the crucial sequences of care in one center in Omdurman City in Khartoum, Sudan is to exclude pulmonary TB co-infection. The participants were invited to sign a written informed consent, then interviewed using a structured questionnaire, a thorough clinical examination was performed followed by the proper investigation for the diagnosis of the neurological complications. Patients below 18 years of age and those with neurological complications caused by diseases other than AIDS were excluded.

Material for HIV test and CD4 count were done by ELISA and ICT, flow cytometry and automatic heat analyzer were used to assess the CD4 counts and percentages, and brain MRI with and without contrast in addition to the CT scan and serology were applied to diagnose other infections.

The following information was collected: age, sex, occupation marital status, the level of education, mode of transmission, neurological symptoms including headache, confusion, loss of vision, weakness, photophobia, tingling, paraesthesia, and imbalance were recorded.

Tubercular meningitis was diagnosed based on the history of subacute or chronic symptoms of meningeal irritation, increased protein levels in the cerebrospinal fluid (CSF), lymphocytic pleocytosis, and presence of acid-fast tubercular bacilli (AFB). Cryptococcal meningitis was diagnosed by Indian ink staining or culture demonstrating Cryptococcus or both. Toxoplasmosis was diagnosed by multiple rings enhancing lesions on CT/MRI or raised Ig G levels and response to treatment. Progressive multifocal leukoencephalopathy was diagnosed by MRI.

The research was approved by the ethical committee of the Sudan Specialization Board. The data were coded and transferred to a master sheet from which data were entered into the computer for analysis using SPSS (Statistical Package for Social Sciences version, 20, Chicago). The chi-square test was used to compare categorical data at a *P*-value (<0.05).

### 3. Results:

Out of 100 patients with HIV/AIDS their ages ranged from 18-68 years, male dominance was apparent (68%), near two-thirds of the patients were married (59%), while 31% were single, 7% divorced, and 3% were widows. The majority (73%) were illiterate or received primary education; jobless was the most common (30%) followed by housewife 24%.

The majority (93%) acquired the infection through sexual contact. Table (1).

Table (2) depicted the neurological symptoms in which: a headache was reported in 83% of patients, followed by weakness 55%, peripheral neuropathy was present in 44%, confusion in 33%, meningeal irritation in 24%, cerebellar symptoms in 10%, while loss of vision was reported in 8%.

In the present study, hemiplegia was found in 30%, paraplegia in 24%, monoplegia in 7%, and quadriplegia in 5%. Other neurological examinations were illustrated in Table (3).

In the current data, tuberculosis was found in 36% of patients with CD4+ T-cell <200 vs. 5% in those with CD4+ > 200, toxoplasmosis in 26% vs. 2%, CMV encephalitis in 22% vs. 1%, Gillian Barrie was found in 2% of those within CD4+ T-cell <200 and not detected in those with CD4+ T-cell >200. Other neurological manifestations in correlation to CD4+ T cells were shown in Table (4).

In the present study 45% of those with CD4+ T cell <200 had anemia vs. 5% of patients with CD4+ T cell >200 with no significant statistical difference *P*-value =0.372, thrombocytopenia was reported in 7% of those with CD4+ T cell <200 and not detected in those with CD4+ T cell >200 *P*-value= 0.289, leucopenia was evident in 85% vs. 13% in patients with CD4+ T cell <200 and CD4+ T cell >200 respectively *P*-value=0.204. Table (5).

**Table (1): Basic characteristics of the study group**

Character	%
Age groups:	
18-28	20
28-38	43
38-48	30
48-58	6
58-68	1
Sex:	
Male	68
Female	32
Marital status:	
Married	59
Single	31
Divorced	7
widow	3
The level of education:	
Illiterate	33
Primary education	40
High education	27
Occupation:	
Free job	39
Housewife	24
Student	8
Soldier	8
Driver	8
Farmer	6
Employee	7
The possible mode of transmission:	
Sex	93
Blood	7

**Table (2): Neurological symptoms in 100 HIV patients with neurological complication.**

Neurological symptoms	No%
Fever	83 (83%)
Headache	81 (81%)
Convulsion	33 (33%)
Confusion	33 (33%)
Loss of vision	8 (8%)
Weakness	55 (55%)
Symptoms of meningeal irritation	24 (24%)
Tingling, paresthesia, and burning sensation	44 (44%)
Tremor and imbalance	10 (10%)

**Table (3): Neurological examination findings among 100 HIV patients with neurological complications.**

Character	No%
Higher functions involvement	86 (86%)
Hemiplegia	30 (30%)
Paraplegia	24 (24%)
Monoplegia	7 (7%)
Quadriplegia	5 (5%)

**Table 3: CD4 counts in various neurological disorders**

Diagnosis	CD4 count < 200	CD4 ≥ 200
Toxoplasmosis	26 (26%)	2 (2%)
Tuberculoma	36 (36%)	5 (5%)
CMV encephalitis	22 (22%)	2 (2%)
CMV retinitis	22 (22%)	2 (2%)
Peripheral neuropathy	31 (31%)	4 (4%)
Guillain barre syndrome	3 (3%)	0 (0%)
CIDP	2 (2%)	0 (0%)
Drug related	26 (26%)	4 (4%)
Pott's disease	7 (7%)	1 (1%)
Neuromyelitis optical	1 (1%)	0 (0%)
Psychosis	6 (6%)	2 (2%)
Dementia	5 (5%)	3 (3%)
PML	1 (1%)	0 (0%)
Mononeuritis Multiplex	17 (17%)	2 (2%)
Parkinson's disease	1 (1%)	0 (0%)
CNS Lymphoma	3 (3%)	0 (0%)

**Table 5: CD4 count among patients with anemia, leucopenia, thrombocytopenia and high ESR.**

Investigation	CD4 < 200	CD4 ≥ 200	P-value
Anemia	45 (45%)	5 (5%)	0.372
Leucopenia	85 (85%)	13 (13%)	0.204
Thrombocytopenia	7 (7%)	0 (0%)	0.289
High ESR	82 (82%)	13 (13%)	0.204

#### 4. Discussion:

Central nervous system (CNS) infections are common causes of mortality and morbidity in HIV patients, those with at least one neurological complication had a death rate more than three times higher than those without and they tend to have higher viral load and lower CD4+ T cell count at presentation [7].

In the present study, the majority of the HIV/AIDS patients were in an advanced stage with the males more affected than the females in line with a study conducted in India[8] and concluded similar results. In the present study, the majority of patients were in the age range 28-38 in accordance with the above findings.

In the current study, the majority (93%) of patients acquire the disease through sexual contact followed by blood transfusion similar to Chakravarty *et al.* [9] who observed heterosexual transmission in 80.4% of patients followed by blood transfusion in 2.5% of HIV/AIDS patients.

The commonest presenting symptoms were fever (83%), followed by diarrhea (79%) and were higher than those observed in Chakravarty *et al.* study [9].

In spite of the decreasing rates of hospitalization and death related to opportunistic infections, they are still the leading cause of mortality and morbidity in the countries in which ART is accessible and affordable, one of the leading causes of opportunistic infections is toxoplasmosis caused by *Toxoplasma Gondii* and the serology play a significant role in the diagnosis. Tuberculosis is prevalent among patients with HIV/AIDS and causing 26% of mortality of patients [10]. In the present study, the commonest nervous system opportunistic infection was tuberculosis (41%), in similarity to previous researchers [9] who observed similar results. It is interesting to note that cerebral toxoplasmosis was evident in 28% of the patients in the present study and echoes the result of Bolokadze *et al.* [11] who found cerebral toxoplasmosis in 22%. The current results were higher than the result of a study conducted in East India[9]. Previous literature [9] concluded the negative correlation of CD4+ T cells with the opportunistic infection in accordance with the present data.

Cytomegalovirus retinitis was observed in 23% of our sample in line with Balkhair *et al.* [10] who concluded the disease in 17% of patients.

In the present study loss of vision was observed in 8% of patients and was higher than similar studies which reported blurring of vision in 6% of patients, while blindness was evident in only 1% of HIV patients[12].

Progressive multifocal leukoencephalopathy (PML) was found in 1% of patients in accordance with

Patil and Patil[13] who concluded PLM in 3.7% of patients.

The commonest presentations of the current study were fever (83%), headache (81%), focal neurological signs (66%), and impaired coordination in (10%) the present data were in line with Bolokadze *et al.* [11] who concluded fever, headache, and focal neurological signs in 75%, 91%, 61%, and 29% respectively.

A headache could be the only presenting symptom of a severe neurological disease like space occupying lesion and meningitis, in the current study meningeal irritation was concluded in 24% of patients, similar researchers reported a rate of 17.8% of patients while in some studies a prevalence as high as 71.9% was reported [14]. The differences in the prevalence could be explained by the survey sample as inpatients are usually admitted in critical situation unlike the outpatient clinics.

The neurocognitive disorder is increasingly reported in the developed countries due to the early introduction of ART therapy and low viral load, in this study, dementia was reported in 8% of patients similar to Sonkar *et al.* study [14].

In the present study, convulsions were reported in 33% and were higher than the previous survey [14] in which (10%) of patients were diagnosed with seizures. CNS lymphoma was evident in 3% of the study group in accordance with Bolokadze *et al.* [11].

The peripheral sensory neuropathy could be due to the viral load, low CD4+ T cell count or due to HIV/AIDS medications, in the present study peripheral neuropathy was evident in 44% of patients in line with the previous literature [7] in which ( 57.%) of patients had at least one bilateral sign that suggest sensory neuropathy.

Previous studies showed that the low CD4+ T cell count is a continuous predictor of the neurological manifestations, in the current data the CD4 count was lower among patients with neurological complications supporting the previous observations [15].

#### Conclusion:

The neurological complications was prevalent among Sudanese patients with HIV/AIDS and are commoner among those with low CD 4+ T cell count, the adoption of early widespread testing, the promotion of early introduction and adherence to ART therapy could substantially reduce the late stage diagnosis of HIV and the burden of the opportunistic infection and the neurological of HIV disease.

**Limitations:**

The small size of the study sample, and we did not assess the cutoff of CD4+ T cell count for each pathogen.

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