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Research Article

IDIOPATHIC CD4+ T LYMPHOCYTOPAENIA AT A UNIVERSITY HOSPITAL IN NORTH-CENTRAL NIGERIA: IS IT REAL?

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ABSTRACT

The use of CD4+ T Lymphocyte counts as a sole marker to assess the rate of progression of HIV/AIDS disease in many parts of Africa continues to receive wide acceptance among health professionals. This belief is against the background that HIV/AIDS is the only disease commonly associated with CD4+ T Lymphocyte depletion. This study was set up to ascertain the patterns of CD4+ T Lymphocyte counts among HIV/AIDS patients as well as counts among those who were HIV-seronegative presenting with other forms of ailments. A total of 145 HIV-seronegative subjects were studied who presented at the hospital with either no complaint or with different clinical presentations. Venous blood was collected from superficial veins, transported to the laboratory and screened for HIV using Determine and CD4+ T Lymphocyte counts carried out using cyflow, Artec Germany. Among the male 67 subjects 2 (1.4%) and 1 (0.7%) had CD4+ T Lymphocyte counts ≤ 200 cells/µL and 201-300 cells/µL respectively while 64 (44.1) had CD4+ T Lymphocyte counts of 300 cells /µL and above. Also among the 78 female subjects, 2 (1.4%) had CD4+ T Lymphocyte counts 201-299 cells/µL while 76 (52.4%) had counts of 300 cells/µL and above. Among the clinical features associated with low CD4+ T Lymphocyte counts were: Weight loss, Fever, Pulmonary tuberculosis, Dry cough, and Generalised peripheral lymphadenopathy (1, 25.0% each). Idiopathic CD4+ T Lymphocytopaenia (ICTL) may not be as rare in our environment as hitherto believed to be and hence could mask correct interpretation and proper staging of HIV/AIDS in a newly diagnosed HIV positive patient. Interpretation of CD4+ T Lymphocyte counts in newly diagnosed HIV patient should be carried out with the understanding that ICTL may be rare but still not uncommon.

Keywords :-CD4+ T Lymphocytes, Idiopathic, Lymphocytopenia.

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INTRODUCTION

Idiopathic CD4+ T Lymphocytopaenia (ICTL) is a clinical condition characterized by a low CD4+ T Lymphocyte count in the blood of equal or less than 300/µL recorded over at least two consecutive occasions in a patient or a percentage CD4+ T Lymphocyte count of 20% or below of total T Lymphocyte count. This should be recorded in a patient with no evidence of infection with HIV-1, HIV-2, human T.cell lymphotrophic virus types 1 and 2 infection, or any other form of immunodeficiencies or immunoterapies capable of suppressing CD4+ T Lymphocytes[1,2].

ICTL is commonly associated with clinical conditions such as [3,4]:

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Viral
Human papilloma virus
Herpes meningoencephalitis, disseminated herpes, esophagitis
Hepatitis
Progressive multifocal leukoencephalopathy (JC virus)
TB or mycobacterium
Parasites— *Pneumocystis jirovecii* pneumonia
Fungal
Oral, skin, vaginal candida
Cryptococcal meningitis, osteomyelitis
Fungal toe nail
Neoplasms
Leptomeningeal lymphoma
Hodgkin lymphoma
Non-Hodgkin lymphoma
ACTH secreting adenoma
Prostate cancer

Studies from different parts of the world have also associated some rare clinical conditions such as: histoplasmosis in olecranon bursa, chronic cryptococcal meningitis, cytomegalovirus retinitis, disseminated Mycobacterium abscessus subspecies bolleti infection, and motor axonal neuropathy with ICTL. Laboratory diagnosis and treatment of these clinical conditions may pose serious challenge to physicians even in well equipped health settings, and may even be worse with poor prognostic outcomes in resource constrained health settings across the globe including sub-saharanAfrica[5-10].

At the Benue state university teaching hospital as is the case in most hospitals in the country, diagnosis of ICTL is not a common phenomenon. This may probably be because physicians do not look out for them. The fact that majority of the patients attending the facility come with one form of infection and infestation or the other, and coupled with the diverse presentations of the disease, there is therefore a pressing need to ascertain the presence or otherwise of ICTL in the hospital[11,12]. The findings will be helpful to serve as a guide in the management of patients presenting with similar and associated clinical pictures hence the need for the study.

MATERIALS AND METHODS

Experimental Setting

The study was carried out over a one year period (July 2016 to June 2017) at the Benue State University Teaching Hospital (BSUTH), a 350 bed capacity hospital located in Makurdi, the Benue state capital. The hospital offers primary, secondary and tertiary health services and also serves as a referral centre to the entire state and beyond. Subjects for the study were selected from those attending hospital for various ailments, their relations, those referred to and attendees of anti-retroviral clinic for the first time, staff and students. Subjects were recruited on a daily basis as they presented for the first time at the anti-retroviral clinic and consented to be part of the study. Structured questionnaires were either self or interviewer administered and relevant information on past medical history, socio-demographic, ingestion of drugs or otherwise, morbid and pre-morbid conditions among others were obtained. Blood samples were collected from each respondent where HIV test and CD4+ T cell counts were carried out. Results from other laboratory investigations to ascertain the scope and depth of the disease in line with the broader management of the disease by the attending physicians were also compiled and analysed to associate signs and symptoms.

Blood Sample Collection

Blood samples were collected (3-5mls) from superficial veins using sterile procedures into EDTA anticoagulant coated test tubes for CD4+ T cells and plain bottles for HIV antibody testing respectively. .

Estimation of C4+ T Lymphocytes Using Flow Cytometry

Venous blood samples (3-5 mls) were collected into ethylenediaminetetraacetic acid (EDTA) coated test tubes. T cell subset profiles were determined by flow cytometry using a Coulter Epics XL equipped with System II software (SysmexPartec GmbH Gorlitz, Germany) within 4 hours of blood collection. This flow cytometer was run, in a double platform setting where the absolute counts for both white blood cells and lymphocytes were obtained on a Celldyn 3500R haematological analyzer (Abbott, GmbH, Germany). Then from the combined results, the absolute $CD4^+$ and $CD8^+$ cell counts, CD4/CD8 ratios, as well as the % CD4 and %CD8 values among lymphocytes were automatically calculated [13,14].

HIV Testing

This was carried out using the Rapid Test Kits which are Determine (Abbott Laboratories, Berkshire, United Kingdom), Uni-gold (Trinity Biotech, Republic of Ireland) and Stat Pak (Chembio Diagnostics, New York USA). In line with the recommended algorithm for routine testing of HIV infections by the Federal republic of Nigeria, HIV testing and interpretation were carried out as follows: Initial blood sample was taken and tested using Determine and if the result was positive, the blood sample was tested using a different test principle. If the second test is also positive HIV infection is confirmed, and if the second test was found to be negative, a tie-

breaker was used and HIV status of the patient was ascertained[15].

Ethical Considerations

Ethical approval for the study was obtained from the ethics review board of the BSUTH. Informed consent was obtained from each subject before his/her voluntary enrolment into the study. Patient's confidentiality and anonymity was maintained throughout the study and in all forms of communications on the outcome of the research findings. All the religious, cultural beliefs and values of the people were taken into consideration in the course of the study.

Analysis of Results

Results obtained were collated using Microsoft Excel version 7. Data was analysed using simple descriptive methods.

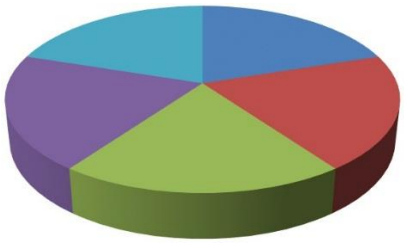
RESULTS

Of the 145 HIV sero-negative respondents studied, the CD4+ T Lymphocyte counts ranged from 200 to 1950 cells/µL, their ages ranged from 16 to 73 years and 67 (46.2%) were males while 78 (53.8%) were females. The mean age was 37 year (SD ± 5), mode 29 years and median 33 years; 5 (3.4%) of the subjects had CD4+ T Lymphocyte counts less than 300 cells/µL.

Among the male subjects 2 (1.4%) and 1 (0.7%) had CD4+ T Lymphocyte counts ≤ 200 cells/µL and 201-300 cells/µL respectively while 64 (44.1) had CD4+ T Lymphocyte counts of 300 cells /µL and above. Also among the 78 female subjects studied, 2 (1.4%) had CD4+ T Lymphocyte counts 201-299 cells/µL while 76 (52.4%) had counts of 300 cells/µL and above. There was no significant gender distribution pattern (P> 0.05) (Figure 1).

Among the clinical features associated with low CD4+ T Lymphocyte counts were: Weight loss, Fever, Pulmonary tuberculosis, Dry cough, and Generalised peripheral lymphadenopathy (1, 25.0% each) (Figure 2).

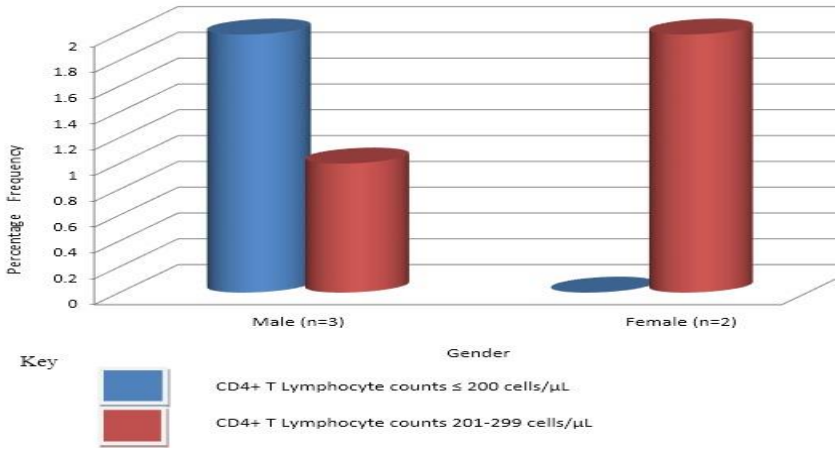
Fig 1. Signs and symptoms of HIV sero-negative patients with low CD4+ T Lymphocyte counts in Makurdi, Nigeria.



Key

01. Weight loss (01; 25.0%)
02. Fever (01; 25.0%)
03. Pulmonary Tuberculosis (01; 25.0%)
04. Dry cough (01; 25.0%)
05. Generalised Lymphadenopathy (01; 25.0%)

Fig 2. Age and Gender distribution of HIV sero-negative patients with low CD4+ T Lymphocyte counts in Makurdi, Nigeria.



CD4+ T Lymphocyte counts <300 cells/µL= 5 (3.4%), CD4+ T Lymphocyte counts <500 cells/µL = 19 (13.1%)
X^2 (Mantel-Haenszel)= 1.095; P (One Tail)= 0.1485; P (Two Tail)= 0.2970.

DISCUSSION

The most common clinical features among HIV sero-negative patients associated with low CD4+ T Lymphocyte counts observed in the present study were weight loss, fever, pulmonary tuberculosis, dry cough, and generalized peripheral lymphadenopathy (each 25.0%; n-1). These findings have further strengthened the fact that in a HIV endemic community like ours, interpretation of CD4+ T Lymphocyte counts in both diagnostic and prognostic HIV management should not be done in isolation. The fact that the community under study is still endemic to several infections and infestations involving viral, bacterial, mycotic and parasitic in nature, CD4+ T Lymphocyte depletion could manifest essentially in any of the endemic diseases prevalent in the community[16-18].

The fact that low CD4+ T Lymphocyte count among the study population could be co-incidental or incidental to HIV infection especially in those newly infected with the disease makes sole reliance on this parameter for disease progression as is the case in most parts sub-saharan Africa not completely accurate. Also interpretation of CD4+ T Lymphocyte counts among HIV-infected individuals on first day of clinic attendance should be carried out bearing in mind the existence of ICTL especially in resource-restrained settings [19-22].

In clinical settings where the clinical features of newly diagnosed HIV patients cannot easily be tied to the depth of disease progression and the CD4+ T Lymphocyte counts, additional tests such as: western blot, HIV viral load, polymerase chain reaction detecting HIV viral DNA and HIV viral RNA, HLAB*5701 and Tropism testing among others could be carried out. These along with other biochemical and haematological tests such as ALT, AST, Bilirubin, TBC+ Differential, Fasting lipid profile, Haemoglobin $A1_C$ and urinalysis could all give a more accurate picture of the HIV status and staging of the individual [23,24].

ICTL has presented with different clinical manifestations from different studies across the globe such as: dermatomyosistis in USA, chronic Hepatitis E virus infection in Germany, granulomatous invasive fungal rhinosinusitis in China, adrenal histoplasmosis in India, to post-partum disseminated cryptococcosis with marked eosinophilia in Japan. These could all pose diagnostic and also prognostic challenge to newly diagnosed HIV infected patients and hence the limitations of CD4+ T Lymphocyte counts as a single diagnostic and prognostic index [25-29].

This study is limited by the fact that confirmatory HIV tests were not carried out on patients with suspected ICTL hence their accurate HIV serostatus could not be ascertained. Also, the actual underlying causes of clinical presentations of four of those patients could not be ascertained due to infrastructural constraints. Findings should therefore be accepted with measurable levels of accuracy as they no doubt have brought up the possibility of ICTL in the community.

In conclusion, this study has shown that in newly diagnosed HIV patients with low CD4+ T lymphocyte counts, the possibility of idiopathic CD4+ T Lymphocytopenia should not be completely ruled out in the entire management process of the patients.

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CONFLICT OF INTEREST

Nil.

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