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Dr. G. Alemnji
Department of Physiological Sciences and Biochemistry, Faculty of Medicine and Biomedical Sciences, University of Yaounde 1, Cameroon

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Associations Between CD4 Cell Counts and Clinical Presentations Among HIV/AIDS Patients in Cameroon

[1]G. Alemnji, [2,3]J. Mbuagbaw, [2]G. Afetane and [1,3]M. Nkam

The present study was aimed at establishing relationships between CD4 cell counts and various clinical presentations commonly associated with HIV/AIDS patients in Cameroon. This study was made up of retrospective and prospective phases, carried out among HIV positive cases seen at the Internal Medicine Service of the University of Yaounde Teaching Hospital. After informed consent, data was collected from participants. This included information on demographic and various clinical signs and symptoms associated with HIV/AIDS as well as CD4 cell count results. The population studied consisted of 556 positive cases, 58% females (323) and 42% males (233). HIV positive status were known among 89.9% of the cases following episodes of ill health while Voluntary Counselling and Testing (VCT) diagnosed HIV only among 5% of them. Cases were grouped into clinical categories as follows: A 14.5%, B 33.2%, C 28.2% and 24.1% were not classified. Clinical signs and symptoms were dominated by anaemia 61%, pneumonia 34.5%, meningitis 9.9%, unexplained fiver 34.4%, loss of weight more than 10%, 30.4%, tiredness 21.2 %, diarrhoea 14.2% and cough 11.1%. In all, 29.6% of the subjects had CD4 cell counts less than 100 cell mm^{-3}, while 43.3% of them had counts below 200 cells mm^{-3}. Statistically significant associations were established between low CD4 cell counts and various pathologies as follows: tuberculosis $p<0.01$, oral candidosis $p<0.02$, kaposi's sarcoma $p<0.04$, herpes zoster $p<0.002$ and genital herpes $p<0.05$. The present study shows that majority of the subjects get to know their HIV status very late, already developing clinical signs and symptoms of AIDS with very low CD4 cell counts. There is need for improvement of early HIV diagnosis strategy through education and voluntary counselling among populations in Africa.

Key words: CD4 cells, Cameroon, HIV/AIDS

[1]Department of Physiological Sciences and Biochemistry, Faculty of Medicine and Biomedical Sciences, University of Yaounde 1, Cameroon
[2]Department of Internal Medicine, Faculty of Medicine and Biomedical Sciences, University of Yaounde 1, Cameroon
[3]Yaounde University Teaching Hospital

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INTRODUCTION

The Immunodeficiency virus infection touches all countries in the world particularly those of Africa, south of the Sahara. In 2005, an estimated 4.9 million (4.3-6.6 million) people in the region became newly infected, while 3.1 million (2.8-3.6 million) died of AIDS (UNAIDS, 2005). In Cameroon though the HIV prevalence has dropped from the 11.5% in 2000 (National, 2002) to present 5.5% reported in a 2004 Demographic and Health Survey (DHS) (National, 2004), the increasing number of death and hospital beds still being occupied by AIDS patients is worrying and tremendously affect the economy and health sector.

There is absolute need for early diagnosis and clinical and laboratory classification of HIV status among positive individuals in order to provide prompt medical and psychosocial support and orientation to those who need them. Past literature has shown wide and regional variations in minimum CD4 cell count levels and clinical presentations necessary to initiate ARV treatment among HIV/AIDS patients (CDC, 1993; HAART, 2002; WHO, 2002; Philips *et al.*, 2001; Anonymous, 2004; Nkengasong *et al.*, 2004). The outcome of this has been that patients initiating therapy with minimum CD4 cell counts of 200 cells mm^{-3} have poorer prognosis as compared to those with higher values (HAART, 2002, WHO, 2002; Jaffar *et al.*, 2005). Also, since abnormal clinical presentations are in most cases associated with reduced immunity due to destruction of the CD4 T cells associated with increase viremia (Jaffar *et al.*, 2005; Lawn *et al*, 2005), some studies have proposed the use of clinical presentations to suspect patients likely to be HIV positive particularly in resource poor settings where adequate diagnostic facilities are not available (Yazdanpanah *et al.*, 2001; Mbuagbaw *et al.*, 2006). This will guide clinicians in the prompt selection of patients that should be recommended for Voluntary HIV Counselling and Testing (VCT) which should reduced the problem of late diagnosis associated with low CD4 cell counts and poor clinical outcome following therapy (Philips *et al.*, 2001; Nkengasong *et al.*, 2004; Lawn *et al.*, 2005; Granade *et al.*, 2005; Jaffar *et al.*, 2005). Apart from immune deprivation, other factors such as already existing parasitic and infectious diseases in the environment may have a pronounced influence on clinical presentation among HIV/AIDS patients (Yazdanpanah *et al.*, 2001; Nacher *et al.*, 2005; Mbuagbaw *et al.*, 2006). Since existing disease patterns are not universal, there will definitely be regional variations among these parameters. This has not been well documented in Cameroon and thus greatly compromise diagnosis and classification efforts in this locality.

The present study was aimed at documenting CD4 cell count and clinical parameters among HIV/AIDS patients in Cameroon at point of first presentation as well as establishing relationships between them.

MATERIALS AND METHODS

This was a transversal descriptive study consisting of both the retrospective and prospective phases. HIV/AIDS patients were recruited from the medical clinics of the University of Yaounde Teaching Hospital at first visit. The retrospective phase consisted of collection of data from files of patients who have been followed up in this clinic for the past one year, while the prospective phase centered on the use of questionnaire for the collection of information on patients recruited in the clinic between the months of May and December 2004. Before the start of the study the protocol was submitted for review and approval to the Institutional Review Board (IRB) of the Faculty of Medicine and Biomedical Sciences as well as that of the University of Yaounde Teaching Hospital. In case of the prospective study only patients who consented to participate in the study were eventually interviewed. For both phases, information was collected on patient's sex, age, marital status and reasons for doing HIV test. All patients were examined for clinical signs and opportunistic infections associated with HIV/AIDS. Blood samples were collected for CD4 cell count estimations by FAS Count Flow Cytometry (Becton Dickinson). Data was regrouped, tabulated and analyzed using the EPI Info 2000 and Microsoft Office EXCEL 2003 packages. Chi-square test of proportion was used to compare variables with $p<0.05$ being accepted as significant.

RESULTS

A total of 556 patients (58% females (323) and 42% males) consisting of 219 in the retrospective phase and 337 in the prospective phase were involved in the study. The reasons for doing HIV testing varied: HIV testing was done in 89.9% because of ill health, only 5% were diagnosed from the voluntary counselling and testing centers. Patients who were tested because their partners were positive for HIV infection made up 3.2%, while pregnant women and parents whose children were diagnosed positive for HIV made 1.4% and 0.4% respectively (Table 1). Clinical signs and symptoms were dominated by: anaemia (61%), pneumonia (34.5%), unexplained fiver for more than one month (34.4%), loss of weight more than 10% (30.4%), tiredness more than one month (21.2%), diarrhoea more than one month (14.2%), cough more than one month (11.1%) and meningitis

Table 1: Distribution of subjects by reason for doing HIV test

Reasons for HIV test	Percentage
Ill health	89.9
Voluntary Counselling and Testing (VCT)	5.0
HIV positive partner	3.2
Pregnancy	1.4
HIV positive child	0.4

Table 2: Distribution of subjects by clinical manifestations

Clinical manifestations	No. of cases	Percentage
Anaemia	340	61.0
Pneumonia	192	34.5
Unexplained fever > 1 month	191	34.4
Loss of weight > 10%	169	30.4
Tiredness	118	21.2
Diarrhoea > 1 month	79	14.2
Cough > 1 month	68	11.1
Meningitis	55	9.9

Table 3: Pathologies associated with low CD4 cell counts

Pathology	No. of cases	Percentage	p-value	
Tuberculoses	102	18.3	0.01	(S)
Oral candidosis	101	18.2	0.02	(S)
Kaposi's sarcoma	61	11.0	0.04	(S)
Herpes zoster	54	9.7	0.002	(S)
Cerebral toxoplasmosis	30	5.4	0.50	(NS)
Genital herpes	29	5.2	0.05	(S)
Cryptococcal meningitis	17	3.1	0.40	(NS)
Cryptosporidiosis	3	0.5	0.90	(NS)
Lymphomas	3	0.5	0.15	(NS)
Pneumocysts pneumonia	2	0.4	0.80	(NS)

Table 4: Distribution of subjects by CD4 cell count ranges

CD4 Range (Cell mm^{-3})	No. of cases	Percentage
0-49	123	22.1
50-99	42	7.5
100-149	43	7.7
150-199	33	6.0
200-249	31	5.5
250-299	32	5.7
300-349	11	2.0
350-399	15	2.7
400-449	9	1.6
450-499	10	1.8
> = 500	18	3.2
No CD4 Results	189	34.0
Total	556	99.8

Table 5: Distribution of subjects following CDC, 1993 classifications

	Category (%)	Category (%)	Category (%)
CD4 cell count (Cell mm^{-3})	A 81 (14.5)	B 185 (33.2)	C 157 (28.2)
>500	A1 12 (14.8)	B1 6 (3.2)	C1 3 (2)
200-499	A2 40 (49.3)	B2 45 (24.3)	C2 33 (21)
<200	A3 29 (35.8)	B3 134 (72.4)	C3 121 (77)
Total	81	185	157

(9.9%) (Table 2). Major pathologies identified were dominated by tuberculosis (18.3%), oral Candidosis (18.2%), kaposi's sarcoma (11%), herpes zoster (9.7%), cerebral toxoplasmosis (5.4%), genital herpes (5.2%), cryptococcal meningitis (3.1%), cryptosporidiosis (0.5%), lymphomas (0.5%) and pneumocysts pneumonia (0.4%). However, after statistical analysis, the following were found to be significantly associated with low CD4 cell counts: Genital herpes ($p<0.05$), Kaposi's sarcoma ($p<0.04$), tuberculosis ($p<0.01$), herpes zoster ($p<0.002$), thrush ($p<0.02$) (Table 3). In all, 29.6% of the subjects had CD4 T cell counts less than 100 cell mm^{-3}, 13.7% between 100 and 200 cells $mm^{-3.}$ 11.2% between 200 and 300 cells mm^{-3}, 4.7% between 300 and 400 cells mm^{-3} and 3.4% between 400 and 500 cells mm^{-3} (Table 4). Following CDC 1993 classification of clinical staging, the subjects were grouped in different clinical categories as follows: category A (14.5%), category B (33.2%), category C (28.2 %) and not classified cases (24.1%) (Table 5).

DISCUSSION

The present study shows data on CD4 cell count range and clinical presentation among 556 adult (58% female and 42% male) HIV positive Cameroonians attending out patient consultation in one of the largest hospital units (University of Yaounde Teaching Hospital) in the city of Yaounde, Cameroon.

There is greater concern at the moment that HIV diagnosis among people in resource limited settings has in most cases been at the advanced stage of the infection because of several reasons. Low usage of Voluntary Counselling and Testing (VCT) services has been outstanding (Anonymous, 2004; Gaydos, 2006). Part of this is due to the fact that either most people are afraid to be tested or are at the peripheral level where subsidized and prompt diagnosis of HIV is not feasible (Alemnji, 2002; WHO, 2002; Anonymous, 2004). A reported high percentage of 89% of patients in this study who knew their HIV status as a result of referral because they were sick implies that VCT services which are currently being instituted and encouraged worldwide as best options for early identification of HIV positive cases (Anonymous, 2004; Granade *et al*., 2005), are still not yet being well utilized in Cameroon. Failure of adequate usage of VCT services has been associated with increase risk of HIV transmission, late identification and referral with resulting poor prognosis during treatment as a result of severe immune depression and presence of opportunistic infections (Granade *et al*., 2005; Nacher *et al*., 2005; Mbuagbaw *et al*., 2006).

Clinically, anaemia seen in HIV/AIDS patients has been associated with numerous inflammatory conditions, including alimentary loss from diarrhoea and malnutrition (Moyle, 2002; Behler *et al*., 2005; Jaffar *et al*., 2005). Anaemia reported in the present study may be due to similar conditions. Similarly the reported higher proportion of pneumonia and intermittent fever could be due to high prevalence of tuberculosis and other viral infection that has been reported among HIV/AIDS patients in Cameroon (Bimenyu and Kuaban, 2001, Alemnji, 2002) and confirmed by similar studies elsewhere

(Perriens, 1994; Barklett and Gallant, 2003; Lawn *et al*., 2005).

Studies on HIV pathogenesis have shown inverse correlation between cell mediated immunity with an abrupt drop of CD4 cell count and raised viral load due to binding and destruction of CD4 cells by gp120 following viral entry into the cell particularly at acute infection (McMichael and Hanke, 2003; Jaffar *et al*., 2004; Goujard *et al*., 2006). Though this stabilises at clinical latency, the relationship becomes pronounced at full blown AIDS with all clinical presentations common with low CD4 and WHO clinical stage 3 and 4 (Jaffar *et al*., 2004; Philips *et al*., 2001; WHO, 2002). The present study shows many patients already at category B and C of CDC 1993 classification and typical WHO stage 3, supporting the fact that most of them were diagnosed late, already showing clinical presentations of AIDS. The significant associations between low CD4 cell counts and certain clinical presentations reported in the present study support data from other related studies and is in line with outcome of immune deprivation that follows HIV/AIDS diseases progression (Perriens, 1994; Yazdanpanah *et al*., 2001; HAART, 2002; Barklett and Gallant, 2003; Wiwanitkit, 2004; Lawn *et al*., 2005; Mbuagbaw *et al*., 2006) In fact, postmortem studies of selected in-patient deaths in Cote D'ivoire and Botswana found that the predominant causes were tuberculosis, bacterial pneumonia and cerebral toxoplasmosis (Lucas *et al*., 1993; Ansari *et al*., 2002), similar to data from present study. This implies an already existing immune compromised state of these patients.

The proposed minimum CD4 cell count value required to start ARV treatment varies (CDC, 1993; HAART, 2002; WHO, 2002). Some studies have shown very poor correlation between clinical improvement with HIV/AIDS patients on ARV and low CD4 ranges particularly those below 200 cells mm^{-3} (HAART, 2002; Jaffar *et al*., 2005; Lawn *et al*., 2005; Van Leth *et al*., 2005; Goujard *et al*., 2006). When the CD4 cell counts are very low, the T-helper function of the CD4 cells are compromised and are unable to produce cytokines necessary for activating cellular (CD8) and humoral (B cells) functions that fights opportunistic infections (McMichael and Hanke, 2003, Jaffar *et al*., 2005; Letvin and Walker, 2003; Lawn *et al*., 2005). The fact that two hundred and forty three (43%) patients in the present study had CD4 cell three counts below 200 cells mm^{-3} are already indications of poor prognosis that may be associated with these patients once they will start antiretroviral (ARV) treatment. Apart from the fact that early diagnosis is necessary, it is advised that once HIV positive patients in this locality are diagnosed, ARV treatment should start much earlier at a higher CD4 T cell count greater than 200 cells mm^{-3} to avoid development of opportunistic infections leading to AIDS. This is supported by the fact that studies from other resource poor settings of South Africa and Uganda have shown that following development of AIDS with lower CD4 values, median survival of untreated patients is just 9-10 months (Weidle *et al*., 2002; Coetzee *et al*., 2004).

In conclusion, the present study show that majority of subjects get to know their HIV status very late, already developing clinical signs and symptoms of AIDS. There is need for improvement of early HIV diagnosis strategy as well as upward review of CD4 ranges needed to put HIV/AIDS patients on ARV treatment in Cameroon and sub-Saharan Africa

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