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Usefulness of Certain Clinical and Laboratory Parameters in Predicting Presence of HIV Infection in Adult HIV/AIDS Positive Patients in a Limited Resource Setting

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Favourable outcome in HIV/AIDS patients have been linked to early diagnosis and initiation of highly active antiretroviral therapy but studies shows that patient often presents late for care to the health care provider, hence the need for a proactive role of the care givers. The objective of this study is to look at the socio-demographic characteristics of adult people living with HIV/AIDS, as well as identify the clinical and laboratory parameters which could be useful in obtaining clues for early diagnosis in the face of non classical presentation. This is a retrospective review of computerized records of first time attendees at Special Treatment Clinic (STC) of Federal Medical Centre, Bida with HIV/AIDS between Jan 2007-Dec 2010. The centre offers free antiretroviral therapy via support from the Federal Government of Nigeria/PEPFAR through the Institute of Human Virology of Nigeria (IHVN). All patients diagnosed or referred from other hospitals, within the study period, had their blood samples taken for haemoglobin, creatinine, alanine transaminase and CD4 T-lymphocyte cell count estimation at the first visit to the centre as part of the routine work up to assess their status and need for antiretroviral therapy. A total of 1100 HIV positive adult patients presented for the first time to special treatment clinic during the period. This was made up of 724 (65.8%) females and 376 males (34.2%) with a mean age of 34.66±9.84 years. Men are marginally older than women with mean ages of 38.82 and 32.50, respectively and this is statistically significant. A greater proportion of the patients have no form of education (39.5%) they are mostly women (80.7%) who are unemployed and full time housewife. This is also statistically significant. Most of the patients are married (89.6%) but greater proportions don't know the status of their partner. The males have higher baseline mean weight, height, haemoglobin (Hb), creatinine (Cr) and alanine transaminase (ALT) than the female and this difference is statistically significant (p<0.001). However, the females had a higher mean CD4 T-lymphocyte count than the males. Of all the markers tested only the weight is positively correlated to CD4 T-lymphocyte count (r = 0.251, p<0.01). Sex, is weakly positively correlated but not statistically significant. The other markers are negatively correlated with CD4 with only age having statistically significant relationship. It can be inferred from this study that socio-demographic characteristics that could give early clue of diagnosis of HIV/AIDS, includes, females in age group (20-30), not being educated, being a full time housewife, having a partner that died from HIV/AIDS. In addition, presenting with a significant weight loss is correlated with having a lower CD4 T lymphocyte.

Key words: HIV/AIDS, early clues, socio-demographic, clinical, laboratory parameters

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INTRODUCTION

Despite the enormous attention being paid to early diagnosis and treatment of HIV/AIDS worldwide, reports still shows that most patients still present late for care (Sabin *et al.*, 2004; Sepkowitz, 2006), hence the need to identify early pointers of the disease that could enable the health workers to identify sufferers from those presenting at the hospital for other health concerns i.e., opportunistic screening. Furthermore, the impact of this on morbidity and mortality in relation to the reduced immunologic status at presentation had also been documented (Garcia *et al.*, 2004).

The HIV/AIDS is a global public health problem that has engaged the attention of the World Health Organization (WHO) due to the nature of this deadly scourge (UNAIDS., 2008). World Health Organization reported that more than 25 million people around the world (inclusive of Nigeria) have died of HIV/AIDS and AIDS related diseases. The latest available prevalence of HIV/AIDS in Nigeria was 3.1% as at 2007 with 170,000 deaths.

The HIV infection is spread primarily through heterosexual sex in Nigeria and many of those affected are youths at their prime and most productive ages with women believed to be most susceptible than men. The disease has increased among the poorest social groups and also people with less educational qualifications.

Though many clinical and laboratory markers have been used to estimate disease progression and need for antiretroviral drugs, studies have showed that evaluation of CD4 T lymphocyte cell count and HIV RNA viral load can effectively be used to monitor disease progression. However due to limitations in infrastructure, scientific technology and finances both may not be readily available at all times in all treatment centres, hence the need to evaluate the associations of this markers with disease progression.

In Nigeria, the Federal Government in collaboration with various partners runs HIV care and treatment that included the provision of free antiretroviral drugs and drugs for opportunistic infections.

The objective of this study is to look at the socio-demographic characteristics of people living with HIV/AIDS, as well as identify the clinical and laboratory parameters which could be useful in obtaining clues for early diagnosis in the face of non classical presentation.

MATERIALS AND METHODS

This is a retrospective study carried out at the Special Treatment Clinic (STC) of the Federal Medical Centre (FMC) Bida, Nigeria, one of the Institute of Human Virology, Nigeria (IHVN), supported site for HIV/AIDS referral, diagnosis and treatment in Niger state in the period January 2007 to December 2010. The hospital is 200 bedded and the centre offers free antiretroviral therapy to HIV/AIDS patients. The STC is being run by Family Medicine Department and as such the bulk of clients for the clinic come from its general outpatient department, supplemented with referrals from other departments in the hospital as well as private hospitals.

All clients coming within the study period had their blood samples taken for haemoglobin, creatinine (Cr), alanine transaminase (ALT) and CD4 T lymphocyte estimation at the first visit to the centre, as part of routine work up to assess their disease status and need for antiretroviral therapy. Samples are normally taken at the phlebotomy unit and immediately transported to the laboratory dedicated to HIV/AIDS care in our centre which is routinely subjected to internal quality control assessment using the manufacturers prepared kit/test solution as well as quarterly external quality control using a reference laboratory supervised by the IHVN.

Statistical analysis: The data generated were analyzed using SPSS version 16. The chi square test was applied for comparison of proportion and for evaluating associations of categorical variables. The CD4 was used as an independent variable in analysis of various clinical and laboratory parameters. A p value of 0.05 was taken as statistical significant.

RESULTS

One thousand one hundred adult HIV positive patients who presented for the first time to the STC clinic within the period January 2007-December 2009 were retrospectively analyzed. There were a total of 376 males and 724 females giving a male to female ratio of 1:2. The mean age of all participants at study was 34.66±9.84 years (Table 1). Men were marginally older than women, with mean ages of 38.82 and 32.50 years, respectively (Table 1 and 2). The difference was statistically significant.

Table 1 shows that the patients were predominantly in their thirties (39.4%), out of which the majority of females are made up of 20-40 year age group 560 (77.3%), while the male counterpart are in 30-50 year age group 269 (71.5%). This observed difference was statistically significant.

Overall, majority of the patient had no form of formal education 437 (39.7%) and this is accounted for mostly by the women folk 353 (80.8%). In addition, the men generally have one form of western education or the other 274 (72.8%) more than the females 329 (45.4%). The difference was statistically significant.

Most of the patients are unemployed 422 (38.4%) and this is made up of mostly full time housewife 413 (97.9%). Among those employed civil servant topped the list with 206 (30.4%), followed by traders 194 (28.6%). When disaggregated by sex there were more

Table 1: Socio-demographic characteristics of study participants disaggregated by sex

Parameters	Sex		Total		p-value
	Male	Female	No.	%	
Age					
≤20	11	15	26	2.50	0.000
20-≤30	44	272	316	28.10	
30-≤40	145	288	433	39.60	
40-≤50	124	107	231	21.10	
≥50	2	42	94	8.70	
Educational level					
None	86	353	437	39.50	0.000
Completed primary	82	120	202	18.40	
Completed secondary	116	142	258	23.50	
Completed tertiary	76	67	143	13.00	
Quaranic	16	42	58	5.30	
Occupation					
Unemployed	9	413	422	38.40	0.000
Civil servants	118	88	206	36.80	
Artisans	43	42	85	17.60	
Farmer	59	15	74	7.70	
Trader	73	121	194	18.70	
Student	20	33	53	6.70	
Driver	22	2	24	4.60	
Armed forces	21	5	26	4.80	
Others	11	5	16	2.60	
Place of residence					
Bida	164	351	515	46.20	0.374
Minna	70	133	203	18.30	
Other LG	133	221	354	32.80	
Other states	9	19	28	2.50	
Spouse/partner HIV status					
Pos	133	210	343	31.20	0.000
Neg	56	120	176	16.00	
Single	45	59	104	9.50	
Not known	120	222	342	31.10	
Dead	20	105	125	11.40	
Divorced	2	8	10	0.90	

Table 2: Mean, standard deviation and p value of markers disaggregated by sex

Parameters	Male	Female	Overall	p-value
		(Mean±SD)		
Age (years)	38.82±10.24	32.50±8.89	34.66±9.84	0.000
Weight (kg)	60.96±12.13	54.64±13.11	56.80±13.12	0.000
Height (cm)	169.61±7.58	160.14±6.83	163.41±8.40	0.000
Hb (g dL^{-1})	11.20±2.42	10.26±1.87	10.58±2.13	0.000
CD4+(cells µL^{-1})	188.86±163.83	225.95±200.05	213.27±189.20	0.376
Cr (µ mol L^{-1})	106.11±55.10	83.57±38.46	91.03±45.87	0.000
ALT (IU L^{-1})	31.77±33.54	24.70±32.76	27.08±33.17	0.000

males (57.3%) that were civil servants than females (42.7%) and more females (62.4%) that were traders than males (37.6%). This observed difference was also statistically significant. Occupations included under others are mostly clergy of both predominant religions.

The STC clients are mostly from Bida (46.2%), followed by those from Minna and then other local governments of Niger state combined. This was not statistically significant.

A good number of the clients are in a married relationship 986 (89.6%). Of these 52.6% have had HCT done and know their partner status. Out of which 343 were positive while 176 were negative. A still larger portion doesn't know their partner's status. About 125 had their partner dead some due to HIV while others are as a result of some other conditions other than HIV infection.

While a total of 10 of the client have divorced their partner. Worthy of note are those in unmarried relationship of which most of them are student at various educational levels.

Table 2 shows the mean clinical and laboratory parameters of cases. The men were older than their female counterpart. This was also seen in the case of their weight and height. The observed differences were statistically significant.

The same can be said for the laboratory parameters with statistically significant relationship, except for the CD4 count were the women folk had a higher mean CD4 than the men. However this was not statistically significant. The age ranged from 14-75 years, whilst the weight ranged from 21 to 115 kg. The height ranged from 130-191 cm. The CD4 ranged from 4 to 1391cells µL^{-1}, while the haemoglobin ranged from 4 to16 g dL^{-1}. The creatinine ranged from 41 to 616, while the ALT ranged from 1 to 553 IU L^{-1}.

Table 3 shows that 49.9% had haemoglobin less than 10 g dL^{-1} while 50.1% had their haemoglobin greater or equal to 10 g dL^{-1}. However, 59.3% have their CD4<200, 23.5% range 200-349 and 17.2% had their CD4 greater than 350 cells µL^{-1}.

Table 3: Cross tabulation of haemoglobin with CD4 T lymphocyte

Hb/CD4	≤4.9	5-7	8-9.9	≥10	Total No.	%
≤199	1	46	242	241	530	59.3
200-349	1	10	80	119	210	23.5
350-499	0	5	35	48	88	9.8
≤500	0	1	25	40	66	7.4
Total	2 (0.2)	62 (6.9)	382 (42.7)	448 (50.1)	894	100.0

$X^2 = 16.260$, $p = 0.062$

Table 4: Correlation of CD4 cell count with other socio-clinical and laboratory parameters

Markers	CD4 cell count r	p
Age	-0.080	0.049*
Sex	0.073	0.075
Weight	0.251	0.000**
Height	-0.011	0.778
Partner HIV status	-0.069	0.088
Hb	-0.064	0.117
Cr	-0.063	0.120
ALT	-0.058	0.156

**,*Correlation is significant at 0.05 and 0.01 level

When the socio-demographic, clinical and laboratory parameters was correlated with the CD4 cell count, only age and weight are significantly correlated to CD4 (Table 4). The age is negatively and weakly correlated ($r = -0.080$, $p = 0.05$), while the weight is positively correlated ($r = 0.25$, $p = <0.01$). Most of the other markers like height, partner HIV status, haemoglobin, creatinine and ALT had a weak negative and insignificant correlation with CD4 T lymphocyte.

DISCUSSION

A look at the demographic characteristics of PLWHA, that could be useful in obtaining clues for early diagnosis shows that persons in the age range 20-50 years, still constitute a population at risk. However, when the gender is taken into consideration, women are generally more at risk than the men and more so in the age range 20-30 years. The difference is statistically significant (p<0.001). This finding is in keeping with reports of HIV incidence in Nigeria (Nwokedi *et al.*, 2007; Ajayi *et al.*, 2009, 2011) and outside the country (UAC., 2003; Kilaru *et al.*, 2004). Persons in the age range 20-50 might be predisposed because they represent the reproductive and productive age group of any society and thus sexually active. However the females are more at risk because of the anatomy of the female reproductive tract that can easily be infected by HIV and other STDs (UNAIDS., 2008). Females in the age range 20-30 years age are predisposed because they are likely to become sexually active at an earlier age compared to their male counterpart. Poverty, low literacy and the subordinate status of females have been blamed for the relatively higher prevalence of HIV in females in sub-Saharan African where heterosexual transmission predominates (UNAIDS., 2008, 2010). In addition, studies done in Nigeria have also linked lack of access to education, certain social and cultural practices such as polygamous marriage practices (which also is a finding in this study) and female circumcision as promoting the spread of the infection (Kilaru *et al.*, 2004).

Other demographic parameters in our study giving clues for early diagnosis include the educational level and the occupation. Persons with no form of education are more at risk than those having a form of education and this is mostly among the women folk. The difference is statistically significant (p<0.001). Furthermore it must be acknowledged that majority of the subjects are women, with no formal education and unemployed. This high rate of unemployment is in keeping with data showing that HIV/AIDS affects mostly the poor and forces poor families deeper into poverty, while also condemning household that were relatively wealthier to similar fates (Pennington, 2006). Whereas among those employed, certain occupations have increased proportion more than the others, such as civil servants among the males, while traders among the females. This finding is in agreement with Nigerian and African studies where level of education influence type of occupation one engages in and eventually the economic power of the individual (UAC., 2003; Kilaru *et al.*, 2004; Pennington, 2006). Besides these findings, the civil servant predisposition may need to be corroborated by other studies. What may be concluded at this stage is that any occupation could pose a risk depending on the sexual behavior of the individual. Because of the absence of or low education among the women folk they could reasonably be assumed to be economically dependent on the men and unable to negotiate safer sexual practices. In addition, in this part of the country where this study is carried out, certain socio-cultural reasons may make women not eligible or permitted to work. This highlights the need for targeted intervention among women and girls to encourage education of the girl child, teaching on sex education and introduction of female condom.

Larger proportion of the subjects are married, therefore transmission between spouses is a significant finding in this study. In addition, having a dead partner is significantly associated with risk of acquisition of HIV infection. This indicates that specific strategies need be

considered for improving sexual communication and negotiating safer sex in marriage situation. This result is not surprising as majority of the patient are in their thirties, at which age they are expected to be married. This result is similar to study of Anafi *et al*. (2011) and Gwarzo (2001) who reported that there were more married people than singles among HIV/AIDS patients in Nigeria. They also suggested that the practice of polygamy in the north could contribute to this high incidence.

The high proportion of subjects who do not know their partners' status or whose partners refuse to disclose their serostatus to them is worrisome. This is against the backdrop that they could be potential source of infection to others and could even defeat the benefit of the Highly Active Antiretroviral Therapy (HAART), being administered in the centre. This indicates that our HIV/AIDS education at the clinic and the community outreaches, need to be intensified to also include use of traditional leaders, respected opinion leaders, leaders of various faiths and traditional healers. This study also highlights the need to undertake further studies of serostatus disclosure with a view of finding out the problems associated with disclosure and proffering solution.

It was expected that place of residence should not pose a risk to acquisition of HIV/AIDS infection, rather it's the individual sexual behaviour, hence this was not statistically significant.

A look at the clinical and laboratory parameters that could serve as pointer to the diagnosis of HIV/AIDS in the face of non classical presentation shows that the men generally have a higher mean age, weight, height, more than their women folk. This is similar to that observed in previous Nigerian studies where females tend to have lower values than males (Ramana *et al*., 2010; Ajayi *et al*., 2009, 2011). The reasons for this might be that the females attain sexual maturity earlier than the males and are likely to engage in sexual practices earlier than the male counterpart. Also older men may be more likely to engage in sexual acts with much younger women compared with women of their age group.

Similar differences were observed among the laboratory markers; haemoglobin, creatinine, alanine transaminase, with the exception of CD4 where this was reversed with female having a higher mean CD4 compared to the men folk. Generally the mean haemoglobin of 10.58% is low in our study. The mean Hb also reduced as the CD4 count decline. It's known that the incidence of anaemia increases with progression of HIV infection which is also the case in this study. Furthermore, other etiologic factors may play a role in development of HIV associated anaemia such as micronutrient deficiencies, immunologic myelosuppression, impaired erythropoietin production and blood loss from intestinal opportunistic infection (Ramana *et al*., 2010).

In this study, majority of the patients first presented to the centre when CD4 T lymphocyte was already in the range requiring commencement of HAART. Quite a large number have CD4 <200 (59.3%), while 269 (23.5%) had CD4 200-350, the remaining 184 (17.2%) had CD4 ≥350. This finding is similar to report from northern Nigeria (this study site is in north central) with rates between 50-54% having CD4<200 at presentation. Late presentation is not peculiar to this environment alone as between 10-30% have been reported in the western world and higher in developing countries, largely because of limited access to health care and HIV treatment and issues associated with stigmatization (Sabin *et al*., 2004; Sepkowitz, 2006; Ajayi *et al*., 2011). Thus priority must be given to identifying HIV infected individual and starting treatment earlier in the course of their illness before they develop severe opportunistic infection. This study confirms the finding in other articles that the CD4 was higher for women than men (Ojini and Coker, 2007). The reason why it is so cannot be immediately ascertained.

This study also found a significant correlation between CD4 and age and between CD4 and weight. This finding is in agreement with WHO document on clinical staging of HIV/AIDS for adults and adolescents, which ascertained both weight loss and CD4 depletion in HIV/AIDS (Peter and Jeffrey, 2005).

CONCLUSION

Majority of people with HIV/AIDS belong to the low socio-demographic and economic strata i.e., female sex, none educated, not in paid employment. The positive correlation between CD4 and weight in this study emphasizes the usefulness of these two parameters in the staging of HIV/AIDS. We suggest that individuals with severe weight loss for their age could be suspected and screened for HIV infection. This is a retrospective study with incomplete data in some laboratory data which could possibly influence some of the outcome, were it to be complete.

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