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LABORATORY PARAMETERS ABNORMALITIES IN HIV PATIENTS AND THEIR ASSOCIATION WITH PATIENTS' OUTCOME IN A TERTIARY CARE CENTRE IN SOUTH EAST NIGERIA

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***Abstract*: Laboratory parameters are used to monitor diseases and treatment processes. Abnormalities in laboratory parameters of HIV patients before commencement of anti-retroviral therapy and their association with patients' treatment outcomes were evaluated. Patients were followed up and data on laboratory investigations and WHO clinical staging of were collected from 330 patients in 2021 and 2022. One hundred and thirty-six (41.2%) were found to be anaemic. Mean baseline CD4 count was 389.9 ± 293.7. The majority had other baseline laboratory parameters within normal range, creatinine 308 (93.3%), ALAT 285 (86.4%) and ASAT 253 (76.7%). Predictor of WHO stage 1 at 6 months was CD4 ≥ 350 cells/mm^3, OR 1.474 (95% CI 0.096 – 0.545). Predictor of viral suppression at 6 months was also CD4 ≥ 350 cells/mm^3, OR 0.994 (95% CI 0.217 – 0.632).**

***Keywords*: ALAT, ASAT, CD4, creatinine, HAART, HIV, WHO staging, viral suppression.**

I. INTRODUCTION

Abnormalities in laboratory parameters in Human Immunodeficiency Virus (HIV) positive patients have been documented by many studies. Apart from the effects of antiretroviral therapy on these, there are other factors that can potentially contribute to the abnormal levels of liver enzymes which have been found to vary in different geographical locations.(1) Liver diseases are a common non-AIDS related cause of death among HIV infected patients, responsible for 14–18% of deaths.(2,3) Other studies found that liver diseases account for almost half of HIV associated deaths among hospitalized patients on HAART. The presentation range from asymptomatic, to mild elevations of liver enzymes, to cirrhosis, to end stage liver disease, and other related complications.(4,5) Many studies have linked these abnormalities in liver enzymes to hepatotoxicity caused by antiretroviral drugs without considering other factors such as viral hepatitis, HIV viral load and several other possible conditions that can potentially cause abnormalities of the liver enzymes.(6–8) A number of factors may be involved in these patients making it difficult to clearly establish the aetiology. Other studies have also shown that concurrent infections with viral hepatitis like hepatitis B and C, opportunistic infections, AIDS related malignancies, alcohol abuse, and many other health problems may be associated with abnormal levels of liver enzymes.(9–11)

World Health Organization gave guidelines for the adoption of tenofovir as a first line drug, given the advantages in terms of tolerability and availability as a once-daily formulation.(12) However, tenofovir is nephrotoxic and many HIV positive persons have been found to have chronic kidney disease.(13) Hence the need for creatinine testing before the commencement of tenofovir-based regimen. Levels of blood creatinine vary and are determined by a number of factors such as gender, age, race, and body mass. High levels of creatinine could indicate dehydration or kidney damage. People who have only one kidney could have creatinine level above normal.(14) In a multi-centre study done in Spain the commonest causes of death were cancers and liver failure.(15)

An Indian study determined that the mean baseline CD4 cell count was 112 ± 60 cells/μL. During follow-up, as many as 80.8% patients showed clinical improvement.(16) A study done among advanced AIDS patients in China showed an increase in CD4 cell count during HAART and a significant positive correlation between the change of CD4 count and plasma viral load.(12) Median CD4 cell count in a multi-centre study done in Nigeria was 323 cells/mm^3,(17) in Latin America 154 cells/mm^3,(18) and South African 248 cells/mm^3.(19)

Another multi-centre study in Nigeria found virological failure to be associated with anaemia (Hemoglobin < 10 g/dl).(20) A study in London, UK showed that mean haemoglobin levels before HAART commencement were significantly lower in women than in men (11.2 and 13.2 g/dL, respectively), and a greater proportion of women were anaemic compared to men. Haemoglobin level was significantly associated to short-term risk of AIDS and death independent of CD4 count. The study concluded that women were more likely to be anaemic before HAART commencement. Haemoglobin was a strong and independent prognostic factors for risk of AIDS and death, for both genders.(21)

A study done in the United States found that 3.7% of the HIV patients had abnormal serum creatinine values at baseline.(22) When creatinine clearance was calculated by the Cockcroft-Gault method, in a study done in Zambia, 33.5% had renal insufficiency. Risk for mortality at or before 90 days was elevated for those with reduced creatinine clearance. Renal insufficiency were also associated with increased mortality after 90 days, when compared with those with normal renal function.(23)

In Tanzania, a study found the overall proportion of HIV patients with abnormal liver enzymes to be 43.04% (95% CI: 36.6-49.3), the proportion with elevated Alanine amino transferase (ALAT) levels was 23.9%, while 26.09% had elevated Aspartate amino transferase (ASAT). Levels of ASAT were significantly high among patients with high HIV viral load (P= 0.002). The study concluded that a significant proportion of HIV positive persons who are on HAART have abnormal levels of liver enzymes, which is significantly associated with high HIV viral load.(1)

Among HAART naive HIV positive patients in Ethiopia, the prevalence of anaemia was 35%. Female patients had significantly higher prevalence of anaemia than males (62% versus 38%). A third of HAART naïve HIV positive patients were anaemic and the increase in prevalence of anaemia with decreased CD4 cell count was statistically significant.(68) Prevalence of anaemia among Ghanaian HAART-naïve patients was 46%. The proportion of female patients who had anaemia was 70% and was significantly higher in comparison to 44% of males. Haemoglobin was also a significant predictor of CD4 counts.(24)

The aim of this study was to determine the prevalence of abnormal levels of laboratory parameters (ALAT, ASAT, creatinine and haemoglobin) and their association with WHO clinical staging and viral suppression after 6 months of HAART.

II. RESEARCH METHODS

This was a cross-sectional analytical study carried out among patients on Highly Active Antiretroviral Therapy (HAART) in Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (COOUTH), Awka, Nigeria. Baseline and follow-up clinical information and laboratory investigations were collected between August 2021 and April 2022 using a proforma.

Ethical Consideration

Permission for the study was obtained from the COOUTH Ethical Review Committee.

No harm was done to study participants. All data collected were kept strictly confidential.

Data analysis

Chi square test was used to test associations between categorical variables at 5% level of significance. Multivariate analysis was done with binary logistics regression. Variables included in the enter method were those that were found to be

significant from bivariate analysis at $p \leq 0.2$, as well as factors that has been shown by other literature to be associated with WHO clinical staging and viral suppression. The enter method was used in running the logistic model. Predictors were those significant at $p = 0.05$.

III. RESULTS

Table 1: Sociodemographic characteristics

Socio-demographic characteristics	N=330 n (%)
Age group (yrs)	
≤ 24	5 (1.5)
25-34	50 (15.2)
35-44	122 (37.0)
45-54	87 (26.4)
≥ 55	66 (20.0)
Mean age (±SD)	44.7 (±10.7)
Sex	
Male	112 (33.9)
Female	218 (66.1)
Religion	
Christianity	329 (99.7)
Islam	1 (0.3)
Marital status	
Single	73 (22.1)
Married	222 (67.3)
Separated	2 (0.6)
Widowed	30 (9.1)
Divorced	3 (0.9)
Residence	
Anambra	312 (94.5)
Others	18 (5.5)

Baseline laboratory investigations

Median CD4 count was 345 cells/mm$^{3.}$ A good number of patients, 124 (37.6%) commenced HAART with a baseline CD4 of <250 cells/mm^3 which is classified as very low. Baseline mean hemoglobin for our study participants was lower in women than in men (11.5 and 12.7 g/dL respectively, P=0.009), and a higher proportion of men (68.8%) were anaemic compared with women (53.7%).

The majority of the participants had their laboratory parameters within normal range, creatinine 308 (93.3%), ALAT 285 (86.4%) and ASAT 253 (76.7%). These results are presented in Table 2.

Table 2: Baseline laboratory investigations

Baseline laboratory investigations	N=330 n (%)
CD4 baseline (cells/µL)	
Very low (<250)	124 (37.6)
Low (250 - <350)	44 (13.3)
Lower normal (350- <500)	64 (19.4)
Higher normal (≥500)	98 (29.7)
Hemoglobin level (g/dL)	
Normal (Male 13.2-16.6) (Female 11.6-15)	194 (58.8)

Low (Male <13.2) (Female <11.6)	136 (41.2)
Creatinine (mg/dl)	
Normal (Male 0.6-1.3) (Female 0.5-1.1)	308 (93.3)
High (Male >1.3) (Female >1.1)	22 (6.7)
ALAT (U/L)	
Normal (7 – 55)	285 (86.4)
High (>55)	45 (13.6)
ASAT (U/L)	
Normal (8 – 48)	253 (76.7)
High (>48)	77 (23.3)

WHO Clinical Staging

WHO clinical staging at baseline, at 6 months and at 1 year are shown in Table 3. No patient commenced treatment on stage 4. There was an improvement in staging over one-year treatment period. Despite the improvement, 8 (2.4%) of patients deteriorated clinically observed either at 6 months or at 1 year.

Table 3: WHO clinical staging of participants

WHO Clinical Staging	**N=330 n (%)**
Baseline	
Stage 1	287 (87.0)
2	32 (9.7)
3	11 (3.3)
4	0 (0.0)
6 months	
Stage 1	294 (89.1)
2	27 (8.2)
3	9 (2.7)
4	0 (0.0)
1 year	
Stage 1	309 (93.9)
2	16 (4.9)
3	4 (1.2)
4	0 (0.0)

Viral Load

This classification is used in determining treatment efficacy in the clinic. The proportion of patients that was virally suppressed at 6 months was 74.2% after 6 months of therapy, and 88.2% after 12 months. This is shown in Table 4**.**

Table 4: Classification based on viral suppression

Viral Load (VL)	**N=330 n (%)**
6 months VL (copies/ml)	
Virally suppressed (<1,000)	245 (74.2)
Not-virally suppressed (≥1,000)	85 (25.8)
1 year VL (copies/ml)	
Virally suppressed (<1,000)	291 (88.2)
Not-virally suppressed (≥1,000)	39 (11.8)

*Statistically significant

Baseline CD4 count ≥ 350 cells/µL was significantly associated with patients being on WHO stage 1 at 6 months (p <0.001). Baseline CD4 count ≥ 350 cells/µL and baseline normal haemoglobin level are significantly associated with viral suppression at 6 months (p <0.001 and 0.042, respectively). These are shown in Tables 5 & 6.

Table 5: Baseline laboratory parameters associated with WHO clinical stage 1 at 6 months

Factors	WHO clinical stage N=330 Stage 1 n (%)	Stages 2,3,4 n (%)	χ^2	p-value
CD4 (cells/µL)				
< 350	139 (82.7)	29 (17.3)		
≥ 350	155 (95.7)	7 (4.3)	14.211	<0.001*
Hemoglobin (g/dL)				
Low	170 (87.6)	24 (12.4)		
Normal	124 (91.2)	12 (8.8)	1.035	0.371
Creatinine (mg/dl)				
Normal	275 (89.3)	33 (10.7)		
High	19 (86.4)	3 (13.6)	0.180	0.720
ALAT (U/L)				
Normal	256 (89.8)	29 (10.2)		
Elevated	38 (84.4)	7 (15.6)	Fisher's exact	0.302
ASAT (U/L)				
Normal	228 (90.1)	25 (9.9)		
Elevated	66 (85.7)	11 (14.3)	1.178	0.188

*Statistically significant

Table 6: Baseline laboratory parameters associated with viral suppression at 6 months

Factors	Virally suppressed (VL <1,000 copies/ml) N=330 VL <1,000 n (%)	VL ≥ 1,000 n (%)	χ^2	p-value
CD4 (cells/µL)				
< 350	109 (64.9)	59 (35.1)		
≥ 350	136 (84.0)	26 (16.0)	15.683	0.001*
Haemoglobin (g/dL)				
Low	136 (70.1)	58 (29.9)		
Normal	109 (80.1)	27 (19.9)	4.218	0.042*
Creatinine (mg/dl)				
Normal	230 (74.7)	78 (25.3)		
High	15 (68.5)	7 (31.8)	0.453	0.614
ALAT				
Normal	212 (74.4)	73 (25.6)		
Elevated	33 (73.3)	12 (26.7)	0.023	1.000
ASAT				
Normal	189 (74.7)	64 (25.3)		
Elevated	56 (72.7)	21 (27.3)	0.121	0.767

*Statistically significant

Table 7 shows odds ratio for the laboratory predictors of WHO stage 1 at 6 months. Patients with CD4 ≥ 350 cells/mm^3 had more likelihood than those with less, with the odds of WHO stage 1, OR 1.474 (95% CI 0.096 – 0.545). This was statistically significant (p < 0.001).

Similarly, patients with CD4 ≥ 350 cells/mm^3 had more likelihood than those with less, with the odds of viral suppression at 6 months, OR 0.994 (95% CI 0.217 – 0.632). This was also statistically significant (p < 0.001). This is shown in Table 8.

Table 7: Baseline laboratory predictors of WHO stage 1 at 6 months

Model	OR	95% CI	p-value
CD4 (cells/mm^3)			
< 350	1		
≥ 350	1.474	0.096 – 0.545	<0.001*
HB			
Low	1		
Normal	0.219	0.377 – 1.712	0.571
Creatinine			
Normal	0.034	0.281 – 3.814	0.959
High	1		
ALAT			
Normal	0.142	0.394 – 3.368	0.795
Elevated	1		
ASAT			
Normal	0.235	0.510 – 3.138	0.612
Elevated	1		
Constant	-0.311		0.799

*Statistically significant

Table 8: Baseline laboratory predictors of viral suppression at 6 months

Model	OR	95% CI	p-value
CD4			
< 350	1		
≥ 350	0.994	0.217 – 0.632	<0.001*
HB			
Low	1		
Normal	0.455	0.370 – 1.087	0.098
Creatinine			
Normal	0.180	0.457 – 3.136	0.714
High	1		
ALAT			
Normal	1		
Elevated	0.211	0.349 – 1.880	0.623
ASAT			
Normal	0.095	0.557 – 2.170	0.784
Elevated	1		
Constant	0.918		0.310

*Statistically significant

IV. DISCUSSION

The mean baseline CD4 count for an Indian study was 112 ± 60 cells/μL(17) This is lower than the value obtained in our study, 389.9 ± 293.7 cells/μL. In a study in Cameroon, the mean baseline CD4 (cells/mm^3) was 510.96 (±302.09).(25) This is higher than the value in our study. These differences and similarities may be related to how early or late the patients commenced treatment.

Median baseline CD4 cell count in a multicentre study in Nigeria was 323 cells/mm^3,(17) in Latin America 154 cells/mm^3,(18) and South African 248 cells/mm^3.(19) In our study, the median CD4 at HAART initiation was 345 cells/mm^3. This is similar to that in the multi-centre study in Nigeria (17), which is higher than the values in the studies in Latin America and South Africa.

A study in London found mean baseline haemoglobin to be lower in women than in men and a higher proportion of women were anaemic compared with men.(21) Mean baseline hemoglobin for our study participants was lower in women than in men, but a higher proportion of men (68.8%) were anaemic compared with women (53.7%). A retrospective study in Ethiopia found that the prevalence of anaemia for the study population was 35%. Female HAART naive patients had significantly higher prevalence of anaemia compared to males (62% and 38%, respectively). The findings showed that a third of HAART naïve HIV positive patients were anaemic. Therefore, early diagnosis and treatment of anaemia in these

patients are essential.(26) The overall prevalence of anaemia in our study was 41.2% which is similar to the above study. On the contrary, a higher proportion of men (68.8%) were anaemic compared with women (53.7%), which was also statistically significant. Prevalence of anaemia among Ghanaian HAART-naïve patients was 46%. The proportion of female patients who had anaemia was 70% and was significantly higher in comparison to 44% of males. (24) Their finding is similar to ours as 41.2% were anaemic, but different in that a higher proportion of men were anaemic when compared with females.

A study in Tanzania showed that the overall prevalence of abnormal liver enzymes was 43.04%. A total of 26.09% had elevated ASAT while 23.9% patients had elevated ALAT levels.(35) For our study, the prevalence of elevated ASAT was 23.3% and ALAT was 13.6%. These findings are similar to those of the study in Tanzania.

A multi-centre study in Nigeria found virological failure to be associated with anaemia (Hemoglobin < 10 g/dl).(20) Haemoglobin was also a strong and independent prognostic factors for risk of AIDS and death, for both genders in the study done in London.(21) However, haemoglobin was not a predictor of virological failure in our study, but rather CD4 count. Predictor of WHO stage 1 at 6 months was CD4 $\geq$ 350 cells/mm^3, OR 1.474 (95% CI 0.096 – 0.545). Similarly, the predictor of viral suppression at 6 months was CD4 $\geq$ 350 cells/mm^3, OR 0.994 (95% CI 0.217 – 0.632).

This shows that early commencement of HAART as in the Test and Start strategy is effective. The study therefore recommends that HIV positive persons should commence treatment on HAART early so as to achieve early viral suppression and improvement in clinical staging. The majority of patients had normal levels of laboratory parameters except for haemoglobin. About 40% were anaemic. Improvement in nutrition to correct the high prevalence of anaemia can be achieved through health education and hematinics.

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