

## Plasma Biochemical Parameters as Surrogate Prognostic Markers in HIV-1 Infected Patients

<sup>1</sup>O.A. Ajose, <sup>1</sup>S.O. Banjoko, <sup>2</sup>O.A. Olasode, <sup>3</sup>V.A. Oyegunle and <sup>1</sup>J.B. Fakunle

<sup>1</sup>Department of Chemical Pathology, <sup>2</sup>Department of Dermatology,

College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria

<sup>3</sup>Department of Chemical Pathology, College of Health Sciences,

Olabisi Onabanjo University, Shagamu, Nigeria

**Abstract:** The depression of the immune system accompanied by different metabolic derangements which are worsened by secondary infections are responsible for morbidity and subsequent mortality in HIV-1 infected patients. While, the gold standard prognostic marker for the infection remains the CD4+T lymphocyte count, plasma biochemical markers are potential surrogate prognostic markers. Samples obtained from 100 consecutively diagnosed HIV-1 infected patients who were not on anti retroviral therapy and equal number of apparently healthy seronegative individuals as controls were analysed for urea, creatinine total protein, albumin, globulin and albumin: globulin ratio using kits obtained from Randox laboratories, U.K. spectrophotometrically and Na<sup>+</sup>, K<sup>+</sup> and HCO<sub>3</sub><sup>-</sup> ions concentration using the ion selective electrode analyzer obtainable from Hitachi, Japan. Compared to the controls, statistically significant differences were observed in the plasma concentrations of HCO<sub>3</sub><sup>-</sup> (p<0.001) urea (p<0.005) creatinine (p<0.001), total protein (p<0.001), albumin (p<0.0001) globulin (p<0.001) and albumin: Globulin ratio (p<0.0001). However, no significant difference were observed in the Na<sup>+</sup> and K<sup>+</sup> ion concentrations with p values of 0.10 and 0.25, respectively. Those significantly different plasma biochemical parameters can therefore be useful surrogate prognostic markers for HIV-1 infections in resource limited settings.

**Key words:** HIV-1, surrogate marker, prognosis, markers, infected patients

### INTRODUCTION

Human Immuno deficiency Virus-1 (HIV-1) infection is known to affect virtually all the organs in the body causing different metabolic derangements in addition to the depression of the immune system. Such metabolic abnormalities are also accompanied with body fat redistribution (Martinez and Gatell, 1999).

Raised plasma bicarbonate, high lactate levels, lactic acidosis and low serum albumin were observed to be strong predictors of disease progression and death in HIV-1 infected women (Feldman, 2003). Also, liver function tests had been shown to independently predict survival in HIV-1 infections.

Furthermore, different antiretroviral drugs were shown to aggravate the metabolic derangement with toxicity effects which include acidosis. For instance, increased serum bicarbonate, high lactate levels and lactic acidosis due to mitochondria toxicity had been shown to be caused by zidovudine with resultant dilated cardiomyopathy (Junko *et al.*, 2003).

And also, elevated blood lipids and glucose levels had been observed in HIV-1 patients on protease inhibitors (Junko *et al.*, 2003).

Some secondary infections like disseminated cryptococcosis had resulted in fulminant septic shock in some Auto Immune Disease (AIDS) patients (Lozano *et al.*, 1999).

In obese patients normally on low calorie diet who are on nucleoside analogues, there is a high risk of life threatening lactic acidosis (Nikolaos *et al.*, 2003).

In other studies, serum albumin was shown to be a very important marker in pretreatment assessment and therapy monitoring in HIV/AIDS patients and progressing low value was a predictor of mortality (Olawunmi and Olatunji, 2006; Elena *et al.*, 2005).

Immunoglobulin A (IgA) had also been recognized as a cheap low complexity surrogate marker for immunological and virological failure in HIV-1 infected patient (Elena *et al.*, 2005).

In developing economies where the burden of HIV infection is relatively enormous, cost effective patient

care is therefore inevitable. It is against this backdrop that alternatives to HIV-1 viral load and CD4+T lymphocyte count as prognostic markers of HIV infections and AIDS needs to be recognized (Scot, 2005).

## MATERIALS AND METHODS

Ethical approval for the study was obtained from Obafemi Awolowo University Teaching Hospital research ethical committee. One hundred consecutively diagnosed HIV-1 seropositive patients attending different clinics of the Obafemi Awolowo University Teaching Hospital Ile-Ife, Nigeria and an equal number of seronegative individuals to serve as controls were recruited for the study and their consent were obtained.

The test consisted of 59 males and 52 females. Ten milliliter of venous blood was obtained from tests and control using lithium heparinised venoject blood collection set.

Plasma samples were separated from whole blood by centrifugation at 3,000 r.p.m using bench centrifuge obtainable from Labofuge U.K.

The samples were analysed for Na<sup>+</sup>, K<sup>+</sup> and HCO<sub>3</sub><sup>-</sup> using ion selective electrode analyzer obtainable from Hitachi, Japan.

Urea, creatinine, albumin, total protein concentrations were determined using reagents kits obtained from Randox laboratories, UK and read on the uv/visible spectrophotometer obtainable from Phillips U.K

The method was controlled using commercial quality control sera obtained from Randox laboratories U.K.

## RESULTS

Plasma Na<sup>+</sup> ion concentrations in Mmol L<sup>-1</sup> for test and control subjects, respectively were 135±5.5 and 134±4.8 with a p value of 0.10 was not statistically significant.

K<sup>+</sup> ion concentrations in Mmol L<sup>-1</sup> for tests and controls, respectively were 3.6±0.7 and 3.7±0.5, p = 0.25.

Significant decrease in HCO<sub>3</sub><sup>-</sup> level was observed in test compared to controls at 21.9±2.8 and 24±2.3, respectively. p <0.0001. Plasma urea concentration was significantly increased in tests compared to controls with values of 5.1±0.7 and 4.6±1.0, respectively p<0.005.

Expectedly, mean creatinine value was also significantly increased in HIV-1 patients with values in umol L<sup>-1</sup> of 128±24. compared to controls with values of 86±15, p<0.0001. While total protein was significantly raised in tests, the contrast was true for albumin.

Total protein concentration was 76.6±5.8 g L<sup>-1</sup> in test and 73±4.6 g L<sup>-1</sup> for control, p value <0.001.

Concentrations for albumin were 33.6±6.3 and 44.2±4.9 g L<sup>-1</sup>, respectively for test and control, p<0.001.

Serum Globulin levels were 4.3.0±4.8 and 28.8±3.4 g L<sup>-1</sup>, respectively for test and control, p<0.001.

Albumin globulin ratio also showed statistically significant differences 0.9±0.04 for test and 1.6±0.06 for control, p<0.001.

## DISCUSSION

Metabolic derangements are known to accompany immune depression in HIV/AIDS patients. Severity of these metabolic derangement had been associated with disease progression and death (Feldman, 2003). Prominent plasma biochemical parameters that showed significant variations in HIV/AIDS patients and control, include bicarbonate, urea, creatinine, total protein and albumin (Table 1).

Other studies revealed variations in liver function enzymes and lipids (Mofenson *et al.*, 2003; Oguntibeju and Banjoko, 2003).

Salient pathological features of HIV infection is the depression at the CD4+ T lymphocyte population (Beddel *et al.*, 2003). Therefore, the gold standard prognostic marker remains CD4+ T lymphocyte count and viral ribonucleic acid (RNA) population (Oguntibeju and Banjoko, 2003; Rubio *et al.*, 2000).

However, organ function tests are proving useful in palliative patient care particularly in resource limited settings and also in assessing possible toxicity of anti retroviral therapy (Martinez and Gatell, 1999; Junko *et al.*, 2003; Nikolaos *et al.*, 2003).

The CD4+T lymphocyte count and viral load estimations requires expensive equipment and reagents and expertise which may not be readily available in many health facilities of developing countries.

There is therefore, the need for appropriate prognostic markers prior or during anti retroviral treatment which is becoming more available than previous.

Table 1: Plasma biochemical parameters in untreated HIV-1 patients and controls

Analyte	Test (Mean±SD) n = 100	Control (Mean±SD) n = 100	p-value
Na <sup>+</sup> ion (mMol L <sup>-1</sup> )	135.0±5.5	134.0±4.8	0.10
K <sup>+</sup> ion (mMol L <sup>-1</sup> )	3.6±0.7	3.7±0.5	0.25
HCO <sub>3</sub> <sup>-</sup> ion (mMol L <sup>-1</sup> )	21.9±2.8	2.4±2.9	<0.001
Urea (mMol L <sup>-1</sup> )	5.1±0.7	4.6±1.0	<0.005
Creatinine (uMol L <sup>-1</sup> )	128.0±28	86.0±15	<0.0001
Total protein (g L <sup>-1</sup> )	76.6±5.8	73.0±4.6	<0.001
Albumin (g L <sup>-1</sup> )	33.6±6.3	44.2±4.9	<0.0001
Globulin (g L <sup>-1</sup> )	43.0±4.8	28.8±3.4	<0.001
Albumin: globulin ratio	0.9±0.04	1.6±0.06	<0.001

Plasma albumin had persistently shown to be a very good predictor of survival in HIV infections (Feldman, 2003; Olawunmi and Olatunji, 2006). Low serum bicarbonate which is readily a source of morbidity could be the result of generalized acidosis or from septic shock caused by disseminated cryptococcus secondary infections (Lozano *et al.*, 1999).

This study revealed progressive renal function impairment in untreated HIV-1 infected patients and reduced albumin concentration which could be due to poor utilization of amino acids and reduced liver function. However, there was increased globulin turnover which could be due to ineffective circulating immunoglobulins.

**Decreased albumin:** Globulin ratio in favour of HIV-1 infected patient was also observed. The significance of which could not be readily ascertain.

## CONCLUSION

Our study showed agreement with other investigators with regards to some biochemical parameters. Therefore plasma albumin, total protein, urea, creatinine and albumin, globulin ratio could therefore be used as surrogate prognostic markers particularly in poor resort settings where there are unavailable or inadequate facilities for CD4T lymphocyte and viral load estimations and elaborate therapeutic drug monitoring programme.

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