A Comparative Study of Serum Electrolytes, Total Protein, Calcium and Phosphate Among Diabetic and HIV/AIDS Patients in Abakaliki, Southeastern, Nigeria

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Citation

Abstract

Background: Diabetic and HIV/AIDS patients often suffer electrolyte disturbances but the difference in the degree of derangement in the two conditions is not known.

Methods: Serum electrolytes, calcium, Phosphate and total protein were estimated in 60 Diabetics (45 with good glycaemic control, 15 with poor glucose control), 60 HIV/AIDS patients (24 HAART users, 36 non-HAART users) and 60 apparently healthy volunteers who were HIV-seronegative without history of D/M.

Results: Mean serum levels of some electrolytes were significantly lower in diabetics and HIV/AIDS patients than in controls, but were much lower in diabetics than in HIV/AIDS patients (p < 0.05). The greater disturbances in serum electrolytes in diabetics improved with glycaemic control. In addition to restoring electrolyte status, HAART use in HIV/AIDS patients significantly improved serum total protein.

Conclusion: This study shows that diabetic patients exhibit greater electrolyte disturbances than people living with HIV/AIDS. These preliminary findings warrant future re-examination. Strict monitoring of serum electrolytes in the two conditions is recommended as early detection and treatment of these abnormalities will enhance the quality of life of patients.

INTRODUCTION

With high morbidity and mortality worldwide, diabetes mellitus and HIV/AIDS remain two clinical conditions of public health importance especially in developing countries. However, while HIV/AIDS is caused by human immunodeficiency virus (transmitted through sexual contact, contact with HIV-contaminated sharp objects, body fluids or from mother-to-child), diabetes mellitus may be of viral or genetic and/or environmental aetiology.

Studies have shown that the incidence of diabetes has been on the increase in recent times with the introduction of highly active antiretroviral therapy (HAART) for the treatment of HIV/AIDS. It has been shown that HAART-use, especially the protease inhibitors (PI) among HIV/AIDS patients are associated with multiple complex metabolic alterations. Treatment of HIV/AIDS with PIs has been found to induce hyperlipidaemia and insulin resistance. Michael has shown that new-onset diabetes mellitus, clinically similar to type 2 diabetes will affect about (1-6%) of patients infected with HIV and are receiving protease inhibitors. Additionally, treatments with protease inhibitors have been associated with high incidence of osteopenia and osteoporosis with mean serum calcium levels declining with HIV progression.

Patients with diabetes mellitus and HIV/AIDS show some similar clinical manifestations such as excessive sweat, diarrhoea, dysuria, tiredness and weight loss. Excessive sweat, diarrhoea and dysuria have been implicated in the abnormalities of electrolyte balance. Furthermore, HIV infection has been associated with renal disease (HIV-associated nephropathy), which is characterized, by nephritic-stage proteinuria (>3.5g/dl), azotaemia, hypoalbuminaemia and occasionally hypocalcaemia. Electrolyte abnormalities and altered mineral metabolism...
which occur in patients with HIV/AIDS [13] have been found to contribute to bone diseases, cardiovascular diseases and other clinical problems [14].

With increase in life expectancy and alterations in lipid and mineral metabolism due to PI therapy, it is expected that diabetes mellitus and hypertension, which may consequently lead to secondary diabetic and hypertensive renal damage, will increase. This study which aims to provide baseline data for the differential diagnosis and effective management of HIV-infected patients who are at the risk of developing diabetes mellitus due to HAART-use will compare the plasma electrolytes, total protein, calcium and phosphate in diabetic and HIV infected Nigerians.

**METHODOLOGY**

Site and study population. This study was conducted at the Departments of Chemical Pathology, Ebonyi State University Teaching Hospital (EBSUTH), Abakaliki. The study area is defined by longitude 8° E and latitude 6° N, elevated at 380ft above sea level. The vegetation characteristic is that of the tropical rain forest with an average annual rainfall of about 1,600mm and an average atmospheric temperature of 30 ° C. There are two distinct seasons, the wet and the dry seasons; the former takes place between April and October, while the latter occurs from November to March. The main occupation of the people is subsistence farming (mainly yam and cassava) with some animal husbandry. Other professions and/ or activities such as civil service, trading, artisans, and stone quarrying are practiced also. HIV prevalence in the State is about 6.2% [15].

HIV/AIDS patients: Sixty (60) HIV/AIDS patients (38 males and 22 females) aged 30-53 years drawn from patients attending Medical Out-patient Department of Ebonyi State University Teaching Hospital (EBSUTH), Abakaliki were recruited for participation in the study. Patients included were those whose HIV/AIDS status have been confirmed (Western blot), whether symptomatic or asymptomatic and whether receiving HAART or not. Excluded from the study were patients that were not sure of their HIV/AIDS status or that were diabetic, hypertensive or have any other conditions that may interfere with the result. The patients at the entry into the study were assigned into any of the two groups: (1) HIV/AIDS patients (without AIDS) not on HAART (n=36) and (2) HIV/AIDS patients (with AIDS) on HAART (n=24).

Diabetic patients: They comprised 60 established diabetic patients (40 males and 20 females) aged 44-63 years who were regular attendees at the diabetic clinic of the Medical Out-patient Department of EBSUTH, Abakaliki. Eligibility was based on having either type I or type II D/M, controlled or uncontrolled D/M and if complication is present or not. Patients were excluded if they were HIV seropositive or have other condition that may interfere with results. They were grouped into (i) Diabetics with good glycaemic control [Fasting plasma glucose ≤ 6.7mmol/L (mean = 5.5 ± 0.1mmol/l) on three consecutive visits prior to enrolment, n = 45] and (ii) D/M with poor glucose control [Fasting plasma glucose > 6.7mmol/L (mean = 8.7 ± 0.5mmol/l) on three consecutive visits before enrolment, n = 15].

Controls: Sixty (60) apparently healthy volunteers, matched for age, sex and height comprising staff and medical students of EBSUTH, Abakaliki, (36 males and 24 females) who were non-obese, non-hypertensive and without family history of diabetes mellitus and who were sure of their HIV sero-negativity served as the controls.

The purpose of the study was explained to both the patients and the volunteers after which informed consent were obtained.

The Ethical Committee of Ebonyi State University Teaching Hospital (EBSUTH), Abakaliki. approved the study protocol. The approval was on the agreement that patient anonymity must be maintained, good laboratory practice/quality control ensured, and that every finding would be treated with utmost confidentiality and for the purpose of this research only in compliance with the Helsinki declaration.

Sociodemographic data like age, sex, weight and height as well as duration of illness/infection and treatment details were obtained from case notes of the patients, while the controls were interviewed orally to obtain their age and sex. Weight (in Kg using a standard hospital balance) and height (in m using a metal rule) were measured (in light clothing, without shoes).

**MATERIALS AND METHODS**

Five millilitres (5ml) venous blood was collected at 09.00hr every morning after overnight fast. The blood was dispensed into plane dry glass test tubes. Serums were isolated by centrifuging in a laboratory centrifuge at 2000g for three (3) minutes immediately after blood clotting and retraction at room temperature. The serums were refrigerated at 4 °C.
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SAMPLE ANALYSES
1. Serum potassium (K⁺), Sodium (Na⁺) and Calcium (Ca++) were analysed by Flame Atomic Absorption Spectrophotometer at the Department of Chemical Pathology, University of Nigeria Teaching Hospital (UNTH), Enugu.

2. Serum bicarbonate (HCO₃⁻) was determined by titration in accordance with the method described by Van Slyke [16].

3. Serum chloride (Cl⁻) was estimated by the mercuric nitrate colorimetric method described by Skeggs and Hochstrasser [17].

4. Serum Phosphate was determined spectrometrically as described by Garber and Miller [18].

5. Serum total protein was determined using method described by Reinhold [19]. This is based on the ability of alkaline cupric solution to react with at least two peptide bonds to form a violet colour, which is estimated at 540nm. This colour development takes about fifteen (15) minutes.

Body mass index (BMI) was calculated using the formula:

$$\text{BMI} = \text{weight (kg)} / \text{height (m)}^2$$

STATISTICAL ANALYSES
Student’s t-tests were used to compare the groups for continuous data. Statistical significant was achieved if P < 0.05.

RESULTS
Table 1 shows that diabetic patients were older and had longer duration of illness and higher BMI than either the controls or HIV/AIDS patients (p < 0.05).

Table 1: Characteristics Of Controls, HIV/AIDS And Diabetic Patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HIV/AIDS</th>
<th>Diabetics</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>38</td>
<td>40</td>
<td>36</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>20</td>
<td>24</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>41.4 ± 5.6†</td>
<td>54.1 ± 7.7&quot;</td>
<td>38.8 ± 7.8</td>
</tr>
<tr>
<td>Mean BMI (kg/m²)</td>
<td>22.2 ± 0.7†</td>
<td>29.3 ± 0.3&quot;</td>
<td>24.5 ± 0.7</td>
</tr>
<tr>
<td>Mean duration of illness (days)</td>
<td>3.4 ± 0.2</td>
<td>62 ± 0.3&quot;</td>
<td>NA</td>
</tr>
<tr>
<td>Mean duration of treatment (days)</td>
<td>2.0 ± 0.1</td>
<td>34 ± 0.2</td>
<td>NA</td>
</tr>
</tbody>
</table>

*p < 0.05 between diabetics and controls

Forty (40%) percent of the HIV/AIDS patients had AIDS. While HIV/AIDS patients had comparable weight as the controls, the diabetics were overweight. Diabetic patients (mean glucose concentration = 8.7±0.5mmol/l) with poor glucose control (n=15) have various complications such as retinopathy (n=3), angiopathy (n=5), nephropathy (=4) and three (3) retinopathy and nephropathy (data not shown).

Table 2 compares serum electrolytes, total protein, calcium and phosphate in diabetes mellitus, HIV/AIDS and controls. Mean serum K⁺, Cl⁻, HCO₃⁻ and PO₄³⁻ were lower in diabetic and HIV/AIDS patients than in the controls and much lower in diabetics than in the HIV/AIDS (p < 0.05). Serum total protein was significantly lower in HIV/AIDS patients than in D/M and controls (62.90 ± 6.36g/l vs 66.19 ± 6.20 and 62.90 ± 6.3g/l vs 67.5 ± 6.4 respectively). However, serum calcium was not affected by either HIV/AIDS or diabetes mellitus. With the exception of K⁺, Ca⁺⁺ and PO₄³⁻ all other parameters were significantly lower in HIV/AIDS patients not receiving HAART than in those on HAART treatment (table 3).
Expectedly D/M patients with poor glycaemic control had significantly higher fasting serum glucose than those with good glucose control. However, diabetic patients with poor glucose control had significantly lower levels of K⁺, Cl⁻ and PO₄³⁻, which were lower than the reference range for K⁺ but not for Cl⁻ and PO₄³⁻ than the diabetics with good glucose control. Serum Na⁺, Ca²⁺ and HCO₃⁻ were not significantly affected by serum glucose levels (table 4).

Table 5 shows the reference ranges of parameters analysed.

**DISCUSSION**

The significantly lower levels of some electrolytes (Na⁺, K⁺, HCO₃⁻, Cl⁻, PO₄³⁻) as well as phosphate (PO₄³⁻) observed in both diabetic and HIV/AIDS patients than in the controls in this study corroborate earlier study [3], though K⁺ was within the reference range in HIV/AIDS patients and HCO₃⁻ and PO₄³⁻ in both HIV/AIDS and diabetics. Abnormalities in fluid and electrolytes balance are common biochemical findings in both HIV/AIDS and diabetes mellitus [21] and have been attributed to increased losses, reduced intake/absorption or alterations in metabolism [22, 23]. Malabsorption in HIV/AIDS patients accompanies frequent bout of diarrhoea due to gardia, cryptosporidium and other
pathogens that affect persons with compromised immune systems. In addition to damage done to the intestinal epithelial cells, HIV-infected individuals have been found to have increased intestinal permeability and other intestinal defects even when asymptomatic [24]. In diabetes mellitus, increased urinary loss due to osmotic diuresis may be the common and most important cause of reduced electrolytes, although intracellular shift (translocation) may also be a factor [25]. More reduction in serum electrolytes in diabetic patients than people living with HIV/AIDS in this study is very curious and should be interpreted cautiously as study has shown that diarrhoea, which is common in people living with HIV/AIDS, is a common route for fluid and electrolyte loss [26]. Significantly lower serum potassium in diabetics than in the controls is consistent with the role of blood glucose in potassium metabolism (high serum glucose enhances the movement of potassium from extracellular fluid into the cells). This role of glucose in K⁺ metabolism was evidenced by significantly lower serum K⁺ in diabetics with poor glucose control. Both elevated and depressed serum K⁺ have been found to have profound effect on neurotransmission as well as cardiac functions [27-29]. The significantly lower mean value of chloride gave the same pattern as the level of Na⁺ in diabetics because Na⁺ is always (in most cases) in association with chloride. While calcium metabolism was affected by neither diabetes nor HIV/AIDS, HAART use in HIV/AIDS patients was associated with slightly higher mean serum calcium, which was statistically significant (2.1± 0.2 vs 2.3± 0.3, p < 0.05), though still within the reference range (2.15-2.55mMol/l). This finding is in contrast with earlier finding by Kuehn and his co-workers [30] who reported lower mean serum calcium in HIV/AIDS patients than in controls.

In this study mean serum calcium was elevated within the reference range and may not be of any clinical relevance. Similarly, the significantly higher phosphate levels within the reference range in HIV/AIDS than in diabetics and in diabetics with poor glucose control than in diabetes with good glycaemic control (1.3 ± 0.4 vs 1.1 ± 0.2 and 1.1 ± 0.2 vs 1.0 ± 0.2 respectively) is in accord with the role of insulin in phosphate metabolism (insulin increases proximal phosphate reabsorption), and may not be of any clinical relevance. Curiously, mean serum HCO³⁻ and PO₄³⁻ in the controls were close to the upper limit of the reference ranges (22-28mmol/l and 0.81-1.45mmol/l respectively) suggesting that significant number of them were hyperphosphataemic or alkalotic. However non of the participants showed any sign of alkalosis or hyperphosphataemia suggesting that the observed high levels of PO₄³⁻ and HCO³⁻ were characteristics of the study population and may be partly attributable to increased intake.

Significantly lower serum total protein in patients with HIV/AIDS than in diabetics and controls corroborates earlier finding [31]. Although serum total protein estimation has limited diagnostic importance when compared to albumin because of the compensatory increases in other serum proteins (the globulins) during infections, its relevance in the evaluation of patients with some clinical conditions such as malnutrition, malignancy, renal and liver diseases and immune disorders cannot be ignored [32]. Decrease in serum total protein in HIV infection has been associated with either increased losses and/or catabolism or as a result of reduction in intake and/or absorption due to sores in the mouth, pharynx and/or oesophagus, fatigue, depression and side effects of medications [33]. However, HAART users were found to have significantly higher serum total protein than non-users (65.3 ± 6.9 vs 60.7 ± 5.6). It could therefore be conceived that HAART-use improves protein metabolism by improving the CD4 count [34], although it could not be established if the lower serum protein levels in HIV/AIDS patients in the present study were related to CD4 count. Reduced loss of protein in diarrhoea and catabolism in HAART users may also be a factor. However, with HIV progression protein loss may be more pronounced as it has been shown that about 0.6-1.2g of protein per kilogram body weight per day are lost in adults due to infection as a result of mobilisation of amino acids from skeletal muscles in response to the release of cytokines such as interleukin-1 (IL-1) and tumour necrosis factor-alpha (TNF-α) [21]. These losses have been found to be highest in diarrhoea and dysentery, which are common in HIV infection.

The finding of mean serum total protein within the reference range in diabetics patients in this study should be interpreted with caution because our samples included diabetics on drugs as the possibility of glycaemic control having effect on protein metabolism cannot be completely ruled out. The normal serum total protein in diabetic patients as compared to significant decrease in HIV/AIDS patients suggest that protein losses in diabetics is lower, probably due to increased intakes and reduced losses through the gastrointestinal tract.

Although no literature on comparative study of serum electrolytes, total protein, calcium and phosphate in
HIV/AIDS and diabetes mellitus was encountered, the results of this study show that diabetic patients experience greater electrolyte disturbances than persons living with HIV/AIDS. These findings need to be validated, as understanding the basic metabolic differences between the two conditions may have implications in the context of coexisting diabetes and HIV/AIDS in HIV/AIDS patients on HAART. However, we recommend strict monitoring of serum electrolytes in the two conditions as early detection and treatment of these abnormalities will enhance the quality of life of patients.

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