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# Hydration Status and Glycemic Indices of Patients with Type 2 Diabetes Mellitus and HIV Comorbidities in South-South Nigeria

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**Abstract— Recently there have been an increasing trend of HIV positive patients surviving longer due to increased availability and compliance with antiretroviral therapy. Some of these patients tend to develop type 2 diabetes mellitus (T2DM) as a result of exposure to certain antiretroviral drugs as well as increasing age of the patients. HIV and T2DM could increase the risks of dehydration in these patients. This study was designed to assess the hydration status of patients having HIV and T2DM comorbidities in Akwa Ibom State, South-South Nigeria. In this study 128 participants aged 18 to 59 years were recruited consecutively from December 2023 to May 2024 from designated hospitals in Akwa Ibom state and grouped into normal, diabetic, HIV and diabetic/HIV with each group made up of 32 individuals. Blood samples were taken for on-the-spot blood glucose estimation, glycated haemoglobin, haemoglobin concentration, serum electrolytes, urea and creatinine. Urine was collected for urinalysis. Serum osmolarity and anion gap were calculated. Blood urea nitrogen concentration as well as blood urea nitrogen/creatinine ratio were also determined. The results showed a significantly higher mean chloride level in the normal and diabetic groups compared to others and a higher bicarbonate level in the diabetic group. Urea and creatinine levels were significantly higher in the diabetic and diabetic+HIV groups when compared with others. Serum calcium was significantly higher in the diabetic and HIV groups compared to others. BUN and BUN/creatinine ratio were significantly higher in the diabetic only group compared to others with serum anion gap, osmolarity, FBS/RBS and HBA1C levels being significantly higher in the diabetic group compared to others. It is concluded that T2DM increased the risk of dehydration which is exacerbated by diabetic/HIV comorbidity.**

***Index Terms*—Hydration, dehydration, glycaemic indices, glycated haemologlobin, type 2 diabetes mellitus, HIV, highly active anti-retroviral therapy (HAART).**

## 1. Introduction

HIV and type 2 diabetes mellitus (T2DM) are individual illnesses affecting the immune and endocrine systems respectively, individuals diagnosed with these illnesses are usually placed on medications for life [1]. HIV patients usually tend to have increased gastrointestinal symptoms resulting in frequent passage of watery stool as well as vomiting especially in advanced stages while type 2 diabetes is characterized increased urinary frequency (polyuria), increased thirst (polydipsia) and increased food intake (polyphagia) which results in increased cellular dehydration with reduced glucose uptake by the cells. This may result in acidosis and eventually coma which could be fetal. Patients having HIV and type 2 diabetes comorbidities have a double whammy effect and a higher risk of dehydration [2]. This study was therefore designed to ascertain the hydration status and glyceamic indices of patients with type 2 diabetes mellitus and HIV comorbidities using specialized biochemical markers.

## 2. Method

### *A. Research Design*

This is a case-control study. The sample size determination was done using the formula shown in Equation 1.

$$N = \frac{z^2 pq}{d^2} \quad (1)\ [3]$$

N = the desired sample size, Z = the standard normal deviate, usually set at 1.96 which corresponds to the 95 % confidence interval. p = the proportion in the study population estimated to have both HIV infection and diabetes.

### *B. Recruitment of Participants*

HAART experienced HIV and T2DM patients aged 18-59 years who gave informed consent were included in this study while pregnant women, patients with complaints of dysuria, pyuria and fever as well as those who refused consent were excluded from this study. Normal patients without type 2 diabetes mellitus and HIV were included as control.

### *C. Study Area*

The study was conducted in designated hospitals in Akwa Ibom State. Akwa Ibom is a State in the South-South zone of Nigeria with a land area of 7,249 square kilometers. It lies between Latitudes 4032’ and 5033’ North and Longitudes 7035’ and 8025’ East. It is bounded by Rivers State, Cross River State, Abia State and the Gulf of Guinea on the East, West, North and South respectively. It has an estimated

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population of 7.2 million with an annual growth rate projected at 3.2 %.

### *D. Study Population*

The study population were HIV-seropositive adult patients on HAART who were also diabetics seen within the study period attending the HIV/AIDS clinics as well as normal patients from designated hospitals in Akwa Ibom State.

### *E. Study Period*

The study was carried out over a period of six months, from December 2023 to May 2024.

### *F. Collection and Treatment of Samples*

The socio-demographic profile of the patients were obtained with the aid of an interviewer-administered questionnaire and this included age, sex, occupation, marital status and educational status. A focused medical history, family history, and physical examination was also done before sample collection.

### *G. Anthropometric Measurements*

The height of the participants was measured with a stadiometer stabilized against a vertical wall or with tape without shoes or caps with the patients standing erect on a hard surfaced of the stadiometer, head, buttocks and feet touching the vertical wall, with the head level with the horizontal plane [4]. The participants were asked to place their legs together, bringing the ankles or knees together, whichever came together first (often they came together simultaneously). The height was read to the nearest 0.5 cm. The weight was measured with a digital weighing scale. The participants stood over the center of the scale with their body weight evenly distributed between their feet without shoes. The arms were made to hang freely by the sides of the body, with palms facing the thighs, the head held up and face forward. The weight was read to the nearest 0.5 kg. The body mass index was calculated from weight/height$^2$ (Kg/M$^2$).

The blood pressure (BP) was measured on the left arm using the mercury sphygmomanometer at the heart level using appropriate cuff size. The subjects were allowed to relax for 5 minutes in a sitting position before measuring their blood pressure. Blood pressure readings were recorded to the nearest whole number, and the average of the three recordings computed.

### *H. Laboratory Investigations*

The patients were educated on the procedure for vene-puncture and some of the complications which include some pain at the insertion site, tingling sensation if a nerve is penetrated mistakenly and a wheal at the surrounding area due to oedema. They were re-assured of caution and carefulness in the procedure. For each patient, after selecting the site in the upper limb with prominent veins, a 10 mL syringe with needle was used to collect the blood. Eight milliliters of blood was collected from every case and control for laboratory analysis.

### *I. Analyses of Samples*

Blood samples of the patients were analyzed using different methods.

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### *K. Determination of Electrolytes (Sodium, Potassium, Chloride) and Bicarbonate in Plasma*

Serum concentration of sodium andpotassium were determined by spectrophotometry method while chloride was determined by colorimetric method.

### *L. Determination of Urine pH, Specific Gravity and Osmolarity*

The pH of the urine was measured using a pH meter while the specific gravity of the urine was determined using copper sulphate method. The osmolarity was calculated from Equation 2 [5].

$$\text{Osmolarity} = 2(Na+) + 2(K+) + \text{Glucose} + \text{Urea (all in mMol/L} \quad (2)$$

### *M. Calculation of Serum Anion Gap*

The anion gap was calculated from specific cations (Na+ and K+) and specific anions Cl- and HCO3) as shown in Equation 3 [6].

$$\text{Anion Gap} = (\text{sodium} + \text{potassium}) - (\text{Chloride} + \text{Bicarbonate}) \quad (3)$$

### *N. Determination of Serum Creatinine in Serum (Jaffe's Method)*

Creatinine reacts with picric acid in an alkaline medium to form a red-orange complex. The absorbance of this complex will be measured photometrically at 492 nm and compared with a standard. The absorbance is directly proportional to creatinine concentration [7]. This creatinine method used is traceable to Isotope Dilution Mass Spectrometry (IDMS), hence the creatinine is standardized.

### *O. Urea Assay (Direct Method)*

Direct method for urea determination complex urea with an aldehyde or ketone under strong acidic conditions to form a red to yellow colored product, which is then measured either colorimetrically or with liquid chromatography [8]. Blood urea nitrogen is the nitrogen component of urea (the blood or serum Urea nitrogen ie BUN or SUN). The BUN is roughly one half (28/60 or 0.446) of the blood urea [9].

### *P. Statistical Analyses*

Data obtained was analyzed using both descriptive statistics and inferential analyses. The values obtained were reported in the form Mean±standard deviation while significant difference in means was examined using One-way Analysis of Variance (ANOVA). Also, further analyses were carried out to separate the means using

Duncan test and data analyses were facilitated using Statistical Package for Social Sciences (SPSS version 20.0) and Graphpad Prism 7.0.

### *Q. Ethical Issues*

Ethical approval for this study was obtained via a written request to the Human Research and Ethics Committee of Akwa Ibom State Ministry of Health with protocol no HREC No. AKHREC/22/2/24/213. Armed with the ethical approvals, the Heads of the various hospitals involved were consulted and their permission obtained. Written informed consent was obtained from each patient, signed and thumb-printed. Patients were free to withdraw from participating in the study at any point without any negative consequence.

## 3. Results

### *A. Biochemical Markers of Hydration Status of HIV/Type 2 Diabetes Mellitus Patients*

The results in Table 1 shows that there was no significant difference in the serum sodium and potassium levels among the groups ($p > 0.05$). It also reveals that the mean chloride was significantly higher in the normal and diabetic groups than in the HIV and diabetic+HIV groups ($p < 0.05$) while between the normal and diabetic groups, there was no significant difference in their chloride concentration ($p > 0.05$). The result also shows that between HIV and diabetic and diabetic+HIV groups, there were no significant difference in their chloride concentration ($p > 0.05$). It shows that the mean bicarbonate between HIV and diabetic+HIV groups were not significantly different ($p > 0.05$) while in the diabetic group, a significant higher level of bicarbonate was obtained compared with other groups ($p < 0.05$). In the normal group, the bicarbonate level was significantly higher than that obtained in HIV and diabetic+HIV groups ($p < 0.05$). Table 1 further shows that the mean urea concentration in the normal and HIV groups were not significantly different ($p > 0.05$). It also revealed that between diabetic and diabetic+HIV group, there was also no significant difference in the urea concentration ($p > 0.05$). The level of urea in diabetic and diabetic+HIV group were significantly higher than that of other groups ($p < 0.05$).

The mean creatinine in diabetic+HIV group and diabetic groups were significantly higher than that obtained in other groups while that obtained in the normal group was significantly higher than that of the HIV group ($p < 0.05$). Furthermore, there was a significant increase in the serum calcium concentration in the diabetic and HIV groups compared with other groups ($p < 0.05$) while the calcium level in the normal group was significant higher than that of the diabetic+HIV group ($p < 0.05$). There was also no significant difference in the calcium concentration between the diabetic and HIV groups ($p > 0.05$). The result also shows that there was a significant increase in BUN in diabetic group when compared with other groups ($p < 0.05$) while in diabetic+HIV group the BUN level was significantly higher than that obtained in normal and HIV groups ($p < 0.05$). There was also a significant increase in the BUN level in HIV group than in the normal group ($p < 0.05$).

### *B. Serum Anion Gap of Participants*

From Figure 1 the serum anion gap in the normal and diabetic groups were found to be significantly lower than that of the HIV and diabetic + HIV groups ($p < 0.05$) while between the normal and diabetic groups, there was no significant difference in their serum anion gap ($p > 0.05$).

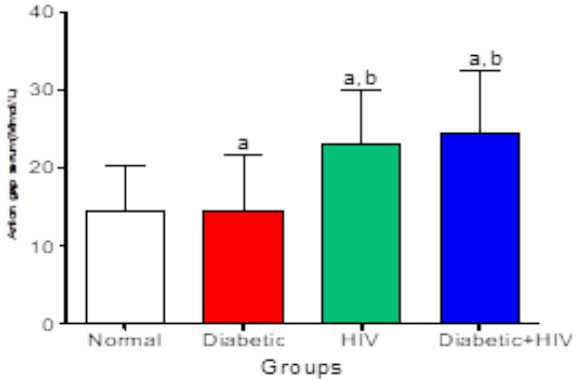


Fig. 1. Serum anion gap of participants in various groups

### *C. Serum Osmolarity of Participants*

The result in Figure 2 shows that there was a significant higher level of serum osmolarity in the diabetic and diabetic+HIV groups when compared to the normal and HIV groups ($p < 0.05$) while between the normal and HIV groups there was an insignificant difference in serum osmolarity ($p > 0.05$).

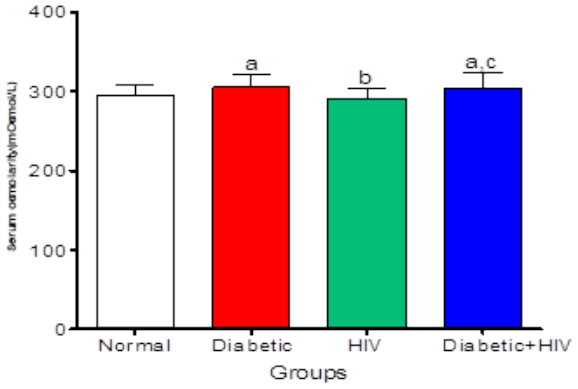


Fig. 2. Serum osmolarity of participants in various groups

Table 1
Biochemical markers of hydration status of HIV/Type 2 diabetes mellitus patients

| Parameters | Normal | Diabetic | HIV | Diabetic + HIV |
|---|---|---|---|---|
| Sodium (Na) | 138.75±5.61[a] | 139.38±5.99[a] | 136.38±6.08[a] | 137.50±9.14[a] |
| Potassium (K) | 3.92±0.48[a] | 3.86±0.71[a] | 3.97±0.67[a] | 4.13±0.70[a] |
| Chloride (Cl) | 156.56±27.79[b] | 145.25±28.88[b] | 15.59±3.27[a] | 157.58±31.83[b] |
| Bicarbonate (HCO3) | 26.13±2.11[b] | 26.84±2.92[b] | 24.16±2.70[a] | 24.69±2.18[a] |
| Urea | 4.18±1.32[a] | 4.71±1.94[b] | 4.17±0.97[a] | 5.28±2.24[b] |
| Creatinine | 82.68±15.39[b] | 115.93±25.14[c] | 70.81±9.68[a] | 102.24±25.85[c] |
| Calcium | 2.12±0.35[b] | 2.48±0.54[c] | 2.55±0.39[c] | 1.81±0.49[a] |

### *D. Blood Urea Nitrogen (BUN) Concentration of Participants*

Figure 3 shows that there was a significant increase in BUN in Diabetic group compared with other groups ($p < 0.05$) while in diabetic+HIV group the BUN level was significantly higher than that obtained in normal and HIV groups ($p < 0.05$). There was also a significant increase in the BUN level in HIV group than in the normal group ($p < 0.05$).

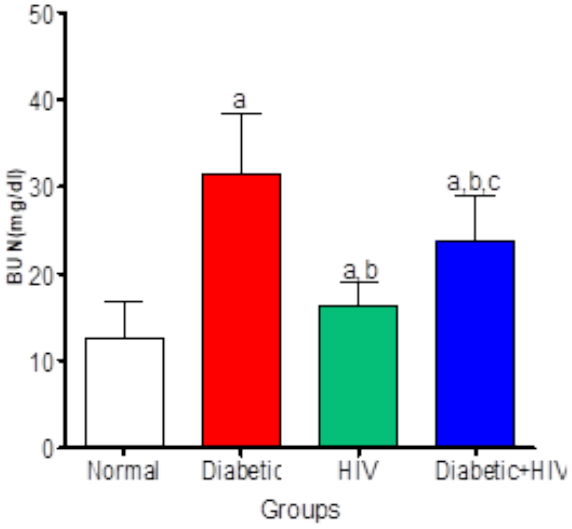


Fig. 3. Blood urea nitrogen (BUN) concentration of participants in various groups

### *E. Blood Urea Nitrogen/Creatinine Ratio of Participants*

Figure 4 shows that the blood urea nitrogen/creatinine ratio in diabetic group was found to be higher than other groups while between HIV and diabetic+HIV, an insignificant difference in the blood urea nitrogen/creatinine ratio was obtained ($p > 0.05$). The result also indicates that the normal group reported the lowest significant level of blood urea nitrogen/creatinine ratio compared with that obtained in other groups.

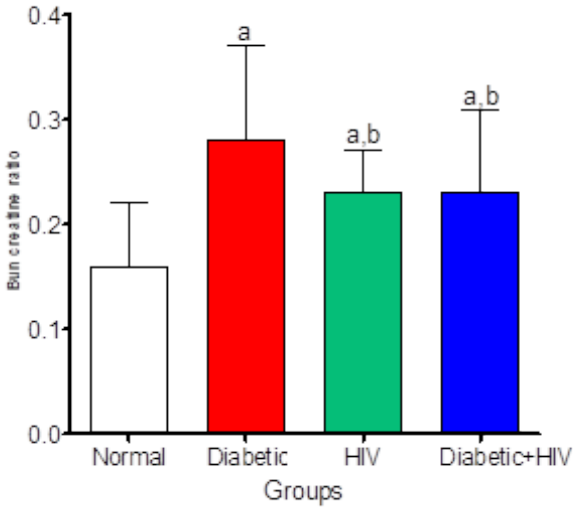


Fig. 4. Blood urea nitrogen/creatinine ratio of participants in various groups

### *F. Urine pH of Participants in Various Groups*

Figure 5 shows that there was no significant difference in the urine pH among the various groups.

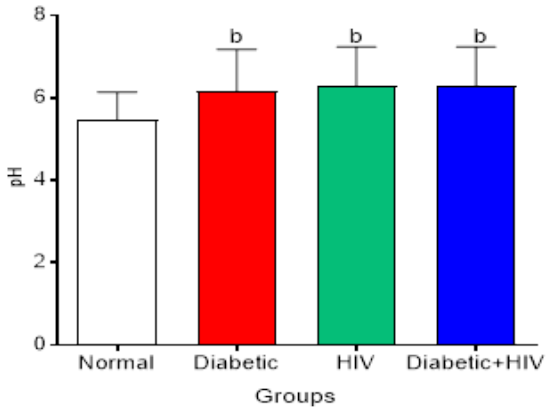


Fig. 5. Urine pH of participants in various groups

### *G. Urine Specific Gravity of Participants*

The result in Figure 6 shows that there was no significant difference in SG among the groups ($p > 0.05$).

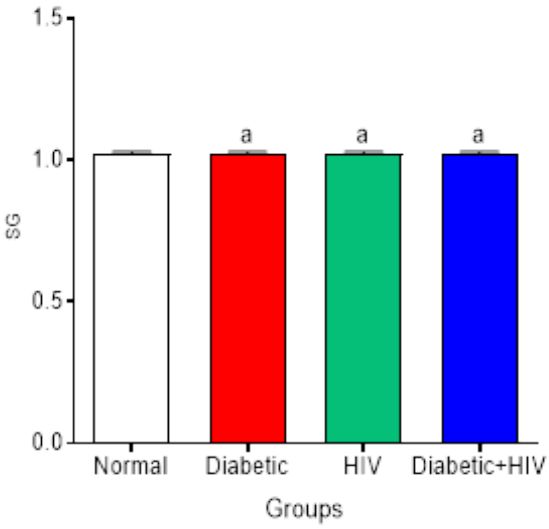


Fig. 6. Urine specific gravity of participants in various groups

### *H. Fasting/Random Blood Sugar Level of Participants*

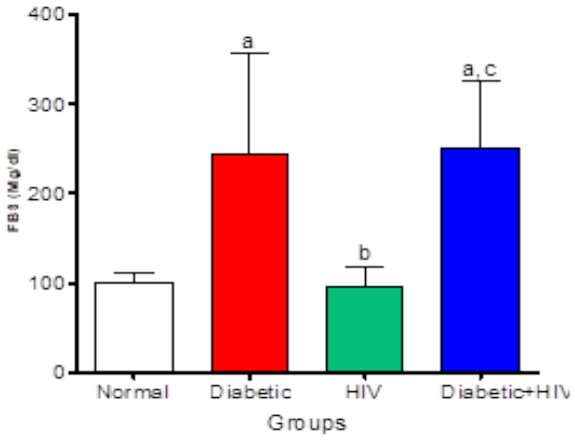


Fig. 7. Fasting/random blood sugar level of participants in various groups

Figure 7 shows that the result of the mean FBS/RBS in diabetic and diabetic+HIV groups were significantly higher than that obtained in other groups ($p < 0.05$) while between normal and HIV, there was no significant difference in their FBS/RBS ($p > 0.05$).

*I. Glycated Haemoglobin (HBA1C) Level of Participants*

Figure 8 reveals that the mean HBA1C level in the diabetic and diabetic+HIV groups were significantly higher than that obtained in other groups ($p < 0.05$) while between normal and HIV, there was no significant difference in their HBA1C level ($p > 0.05$). The mean values of HBA1C in the HIV and normal groups were significantly lower than that obtained in diabetic and diabetic+HIV groups ($p < 0.05$).

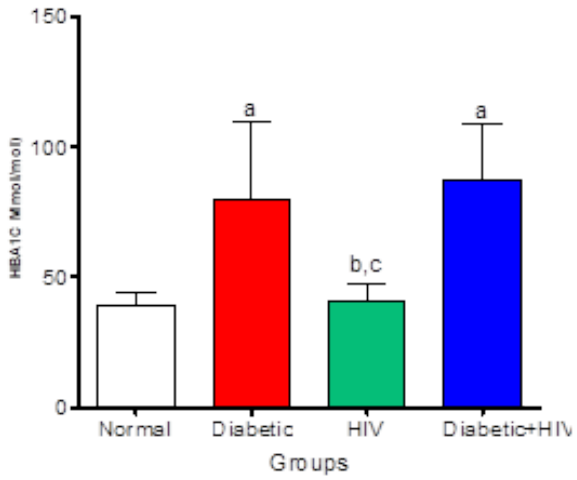


Fig. 8. Glycated haemoglobin (HBA1C) level of participants in various groups

## 4. Discussion

The present study shows an insignificant reduction in the mean serum potassium level in the diabetic only group as against the diabetic+HIV group with the highest mean serum potassium level and this is in agreement with a previous study in which hypokalemia was found as a possible risk factor for type 2 diabetes mellitus [10], where hypokalaemia was associated with dysglyceamia irrespective of diuretics use.

In another study diabetes mellitus was linked to both hypo and hyperkalemia and also hypo and hypercalcemia reflecting the coexistence of hyperglycemia related mechanisms, which tend to change serum potassium and calcium to opposite directions. This also correspond with the significantly increased serum calcium found in this study as well as the increased urine calcium in the diabetic group compared to the control group. In contrary, another study showed that the serum potassium was significantly higher in diabetic patients while sodium, chloride, creatinine and urea were insignificantly higher in the diabetic patients compared to the non-diabetic patients [11]. However, in this study sodium and chloride were insignificantly higher with urea and creatinine being significantly higher in diabetic group compared to the control.

This study also shows significant decrease in all the electrolytes levels except for serum calcium which was significantly higher in the HIV only group when compared to other groups that had significantly higher electrolytes but lower calcium, the same pattern of reduced electrolyte was also found in the urine sample of HIV only group, though they were within normal range however these electrolytes were significantly higher in other groups. These findings disagrees with findings from another study hypocalcaemia and hyponatraemia were the most frequent electrolyte abnormalities and occurred more frequently in persons living with HIV and type 2 diabetes mellitus (PLWH/DM) compared with HIV-uninfected patients with diabetes mellitus [12] and this was traced to increased glycated haemoglobin level in diabetic and diabetic+HIV group when compared to the HIV only group. This is also at variance with another study that showed no significant difference in serum sodium, potassium, chloride and bicarbonate of HIV HAART experienced and naïve groups when compared to the control [13]. Another study also found out that. Decrease in serum sodium and chloride levels were observed to be statistically highly significant (p-value less than or equal to 0.05) in uncontrolled diabetes while that of potassium and magnesium showed insignificant alterations. This was traceable to increased glycated haemoglobin levels.

The general decrease in both serum and urinary electrolytes except calcium in the diabetic group as well as the increase urea and creatinine levels is likely due to hyperglyceamia with increased HBA1C stimulated by increased inflammatory responses and stasis possibly mediated by heightened oxidative stress with resultant increased serum creatinine levels seen in this study.

From this study the serum anion gap was significantly increased in the HIV and diabetic+HIV group. Increased anion gap is associated with acidosis and dehydration. Al-Aly et al. [14], reported that HIV positive patients usually show polyclonal increases in immunoglobulins which was attributed to increase in anion gap in the HIV patients and also linked to renal tubular acidosis [15]. However, this finding is contrary to another study which showed that a reduction in the anion gap is most commonly due to decreased albumin concentration as albumin is the primary unmeasured anion [16]. Anion GAP in the diabetic only group in this study was normal and this could be due to the normal bicarbonate concentration in the diabetic group in this study. This further supports the findings of higher serum anion gap in the HIV only group and implies that HIV plays a greater role in increasing the anion gap.

Serum osmolarity is the amount of solutes in one liter of solvent while osmolality is the amount of solutes per kg of solvents however they are used interchangeably and the term osmolality is now replacing osmolarity. From this study, the serum osmolarity is reduced in the HIV group compared to other groups, this corresponds with the low sodium level seen in this study. Belloso et al. [17], also found that HIV patients had a significant reduction of serum sodium and osmolarity compared with the control group. Sultan [18], found out that sodium, potassium, glucose and osmolarity were increased in diabetics compared to non-diabetics, this agrees with the significantly increased serum osmolarity in the diabetic+HIV and in the diabetic when compared to that of the HIV group as

seen in this study. This was further supported by a previous study where significant correlations were found between blood glucose level with serum osmolality, sodium and potassium concentrations [19].

The level of blood urea nitrogen found in the different groups in this study is similar to the findings of Achu et al. [20], that HAART experienced patients had a significantly higher mean BUN level when compared to the other groups and this was also linked to prolonged duration of diabetes and possibility of developing diabetic retinopathy [21]. Most of the diabetic patients in this study were significantly older than the normal and HIV groups with prolonged duration of diabetes. This was further supported by another study in which BUN level was in tandem with glucose variations seen in elderly hospitalized diabetic patients [22]. So, age of the patients as well as duration of diabetes are likely responsible for the increased BUN level in the diabetic group in this study.

In this study the diabetic and diabetic+HIV groups were found to have significantly higher fasting/random blood sugar levels which also corresponded with the increased glycated haemoglobin. This agrees with the findings of increased glycated haemoglobin level in the diabetic and diabetic/HIV comorbid patients where it was also linked to the presence of hypocalcaemia and hyponatreamia [23]. Poor glycaemic control noted by increased HBA1C level in the diabetic and diabetic+HIV groups as found in this study is also noted to be associated with critically ill patients [24]. Therefore, the higher the glycated haemoglobin level the worst the prognosis.

## 5. Conclusion

From the foregoing, it is concluded that type 2 diabetes mellitus increases the risks of dehydration which is worsened in patients with HIV/diabetic comorbidities. This is supported by the increased BUN, increased BUN/creatinine ratio in the diabetic and HIV groups in this study as well as the significantly lower anion gap in the diabetic group and higher anion gap and serum osmolarity in the HIV/diabetic comorbid group. This is further supported by a worsening electrolyte profile in the diabetic and HIV/diabetic groups compared with other groups.

## 6. Limitation of Study

This study is limited to HIV and type 2 diabetic patients in hospitals in Akwa Ibom State in southern Nigeria. Similar studies should be carried out by non-governmental organization to cover the entire country or other specific regions.

## Acknowledgements

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## Authors Contributions

The study was conceived and designed by Itoro Lawrence Ikpe, Christopher Edet Ekpenyong, Nsikak E. Udokang and Uduak A. Inwang who also wrote the original draft. Samson Timothy Kayode analyzed and interpreted the data.

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