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ERRATUM:

This article was inadvertently republished under Volume 2, No. 2 (July–December 2022) following a redesign and restructuring of the journal website. The correct bibliographic designation for this article is Volume 5, No. 8 (January–June 2020), under which it was originally published. This correction affects only the volume, issue, and publication-period metadata. The article content, DOI, authorship, pagination, and publication date remain unchanged.

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FROM THE EDITORIAL DESK

You are welcome to our rejuvenated Pioneer Medical Journal. On behalf of the Publisher and the Editorial team, I apologise for the absence of the journal from the committee of journals for these past six years. It was due to circumstances beyond our control. We are back and ready to serve you better. The new edition continues with Volume 5 having stopped in Volume 4.

During the period of its absence from the stable, a reorganisation was undertaken with the appointment of a new Editor-in-Chief and the editorial team.

A website was created to interface with the public and online access is being worked on. Our web page is www.pioneermedicaljournal.com.

The editorial team promises to make the journal visible and much sought after by authors to publish articles. We are presently still publishing twice a year, and will, within the next two years publish four times a year.

We thank the Management of the hospital for support in seeing that this journal resurrected. The Editorial team also thanks the Chairman, the entire executive and members of the Medical and Dental Consultants' Association of Nigeria, Federal Medical Centre, Umuahia for their wonderful support.

Our watch word is that Pioneer Medical Journal has come to stay. Once again, thank you and God bless.

Prof Maxwell U. Anah
Editor-in-Chief

WHAT IS ON THIS EDITION

We are glad to publish several interesting topics in this edition. Most of the manuscripts are studies done in Umuahia and its environment. They are interesting and varied.

The Corona Virus disease 2019 (COVID-19) pandemic is raging and it is now the new normal as virtually all sectors have been affected. A review of this has been added. Expect more from us in the next edition.

GENERAL INFORMATION FROM THE EDITOR-IN CHIEF

ALL articles to be submitted to the email address:

pmjumu@gmail.com,

THE Pioneer Medical Journal of FMC Umuahia accepts manuscripts from Nigeria and beyond in areas of basic medical sciences; clinical sciences and related fields. Publication for now is semi-annually.

The journal expects all Manuscripts submitted to her to conform to the widely cited "*Uniform Requirements for Manuscript Submitted to Biomedical Journals*"

Papers in the following categories are accepted: Original Scientific Articles, Case Reports, Brief Communications, Letters to the Editor, and Images in Medical Practice. Review articles are usually accepted. Articles should normally not exceed 3,000 words, while for Case reports, Letters, it is 1,500 words. Images in medicine should not exceed 1,000 words.

Although the journal tries not to present wrong or distracting data, it must be emphasized that the **DATA AND INFORMATION APPEARING IN ARTICLES & ADVERTISEMENT ARE THE OPINIONS AND RESPONSIBILITIES OF THE CONTRIBUTORS**. The journal, therefore *does not* accept liability or inaccurate information. All articles\manuscript are peer-reviewed by two different assessors and all works are acceptable for publication on the condition that is has not been accepted for publication elsewhere.

Certification from authors is not acceptable; hence, all collaborating authors will be expected to show the role they played in the respective article.

MANUSCRIPTS:

A copy of the manuscript should be sent to the Editor-in-chief via the e-mail: pmjumu@gmail.com, copy to maxgen@yahoo.com. Authors are entitled to a free copy of the journal. Original articles should be prepared in the following format: Title Page (title of article, names of authors; Name of institution where work was done and address of corresponding author, including e-mail) Summary (maximum of 300 words in structured form but highlight introduction, methodology, result and conclusion); Introduction Methodology, Result (with tables and diagrams), Discussion, Conclusion, Acknowledgement and References.

Clinical Photographs should be disguised, as not to give away patients' identity.

REFERENCES should follow the *Vancouver* style.

Competing interest should be declared.

Articles once accepted, remain the property of the journal. They may not be reproduced elsewhere without the approval of the Editor-in-Chief.

Publication attracts administrative cost as or approved by the MDCAN.

Yours truly,
Prof. Maxwell U. Anah

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ELECTROLYTE ABNORMALITIES IN HIV INFECTED CHILDREN IN CALABAR, NIGERIA.

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ABSTRACT

Background: HIV infected patients and particularly those with AIDS are predisposed to a host of different water, electrolytes and acid base disorders. Electrolytes and acid-base disorders have been reported in patients with HIV/AIDS with or without treatment. This study was aimed at determining the prevalence of electrolyte abnormalities in HIV infected children in Calabar, Nigeria.

Subjects and methods: A descriptive cross sectional study of 146 consecutive HIV infected children seen at the paediatric HIV clinics of General Hospital Calabar and University of Calabar Teaching Hospital, aged 6 weeks to 15 years, carried out from 1st February to 30th September, 2015. Demographic and clinical data were obtained by interviewing parents/guardians of each subject, who met the inclusion criteria such as treatment with or without highly active antiretroviral therapy (HAART) including Zidovudine and Stavudine. Children who had vomiting and diarrhoea were excluded. Clinical examinations, anthropometry were done and blood samples taken for serum electrolytes (Potassium, Sodium and bicarbonate). Serum electrolytes were analyzed using ion selective electrode spectrophotometry. In this study, electrolyte abnormalities were defined as thus: Hyponatraemia (Serum Sodium level < 130mEq/L), hyponatraemia (Serum Sodium level < 130mEq/L), hyperkalaemia (Serum Potassium > 5.5mEq/L), hypokalaemia (Serum Potassium < 3.5mEq/L) and metabolic acidosis (Serum bicarbonate < 20mEq/L). Data were analysed using SPSS version 20 and p-value ≤ 0.05 was significant.

Results: Out of the 146 children recruited, 85 (58.2%) were males giving a male: female ratio of 1:0.7. The mean age was 100.8±45.3 months and most 104 (71.2%) were in the age group 5-14 years. Majority, 119 (81.5%) of children were on HAART and 133 (91%) had vertical transmission from mother-to-child transmission. Most subjects had non-advanced diseases and 85 (58.2%) were in middle social class.

Electrolytes disorder showed one (0.7%) subject with hyponatraemia, one (0.7%) with hypernatraemia and 3 (2.2%) with hyperkalaemia and no subject had hypokalaemia, while 21.9% had low serum bicarbonate (metabolic acidosis). There was no relationship between acidosis and drugs taken as well as the CD4 counts (P>0.05).

Conclusion: Metabolic acidosis was the commonest electrolyte abnormality seen in HIV infected children especially those on HAART containing Zidovudine and Stavudine. Routine electrolyte estimation should be done in children with HIV/AIDS to prevent progress to severe renal disease.

Keyword: Electrolytes abnormalities, HIV, HAART, Renal disease

INTRODUCTION

An estimated 1.8 million children under age 15 years were living with Human Immunodeficiency Virus in 2015¹. In Nigeria about 260,000 children 0-14 years were living with HIV/AIDS as at 2015². Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome (HIV/AIDS) has emerged as a major cause of morbidity and mortality worldwide.

However, the use of highly active antiretroviral therapy (HAART) has had a dramatic impact on the natural history of HIV/AIDS with a significant reduction in morbidity and mortality. With more HIV infected patients being on HAART, there are increasing reports of HIV and HAART related metabolic disorders involving the kidney, liver and cardiovascular system.³

Renal diseases in HIV patients present with a wide spectrum of disease of which electrolytes and acid base disorder has been reported.⁴⁻⁸ HIV infected patients, and particularly those with AIDS are predisposed to a host of different water, electrolyte and acid base disorders, since they have a modified renal physiology including free water clearance. Exposure to infections, inflammatory, endocrinological, oncological and pharmacological variables, further alter their homeostatic capacity.⁴

Hyponatraemia and hypokalaemia are the two major electrolyte disorders that may be associated with HIV infection. They are more likely to occur in sicker patients with the higher rate in those who are hospitalized.⁵ Hyponatraemia occurs in as many as 35-55% of hospitalized HIV infected patients, but it can also be seen in ambulatory patients.^{6,7} Peters⁸ in a study to determine renal dysfunction and electrolyte disorders reported a prevalence of 28.4%, 17.5% and 4.7% rate of hyponatraemia, hypokalaemia and hyperkalaemia without renal failure respectively. Hyponatraemia is due to excessive salt loss from gastrointestinal tract, or skin, salt wasting from tubulointerstitial renal disease and adrenal insufficiency while hypernatraemia is less common and may result from dehydration. Hypokalaemia may result from excessive vomiting or diarrhoea or because of potassium wasting from amphotericin therapy,⁹ and severe acute malnutrition, while hyperkalaemia has been reported in patients on pentamidine therapy and patients on high dose of trimethoprim and sulphamethoxazole given for *pneumocystic jiroveci* infection.¹⁰ Patients on antiretroviral therapy may develop a variety of electrolyte disturbances including hyponatraemia, hypokalaemia, hypocalcaemia and others.¹¹ For instant, hypocalcaemia has been associated with foscanet, didanosine and pentamidine therapy.¹² Hypercalcaemia and hypouricaemia have also been reported in HIV patients. In addition, acid-base

disturbances including alkalosis, acidosis or their combination have been reported.¹³ Metabolic acidosis can be classified depending on its pathophysiology as; respiratory acidosis (CO² retention), normochloremic or high anion metabolic acidosis (bicarbonate conversion), and hyperchloremic or normal anion gap metabolic acidosis (bicarbonate loss). As majority of electrolyte disorders are clinically silent, a high index of suspicion and awareness is required, especially in HIV patients with late diagnosis, concomitant inflammatory and opportunistic diseases because they can contribute to both morbidity and mortality in HIV patients.¹⁴ Therefore, this study was carried out to determine the burden of electrolyte disorders in HIV infected children in Calabar, Nigeria.

SUBJECTS AND METHODS

A descriptive cross sectional study of 146 consecutive HIV infected children seen at the paediatric HIV clinic of General Hospital Calabar and University of Calabar Teaching Hospital, aged 6 weeks to 15 years, was carried out from 1st February to 30th September, 2015. Both centres are situated in Calabar, the capital city of Cross River State in the South-South Geographical zone of Nigeria. Both centres serve the whole of Cross River State and neighbouring states. Ethical approval was obtained from Ethical committee of the University of Calabar Teaching Hospital and Cross River State Health Research/Ethics committee respectively. Written informed consent from parents and guardians/assent for those >7 years was obtained.

Demographic and clinical data were derived through parental interviewing and this was entered into a data collected from Information extracted included; biodata, likely mode of transmission, social class (as described by Olusanya *et al*¹⁵), age at diagnosis, and types of Antiretroviral (ARV) drugs used. These drugs were catergorised into nephrotoxic HAART,

non-nephrotoxic HAART and non-ARV drugs. The duration of therapy and CD4⁺-count were established. The CD4⁺-count was used to stage HIV disease according to the revised WHO paediatric immunological staging criteria.¹⁶ Patients that had diarrhoea and vomiting within two weeks of study were excluded.

Anthropometry (weight and height) was taken for each subject with standard equipment and Body Mass Index (BMI) calculated. The BMI was plotted against age on WHO- BMI for age growth charts for boys and girls respectively to obtain z-score and categorised subjects into severe thinness, thinness, normal, overweight and obesity.¹⁷

Clinical examination of each subject was done and was used for staging of HIV disease according to revised WHO paediatric clinical staging criteria.¹⁸

Blood samples were collected from each subjects in a plain bottle and allowed to stand for 20-60 minutes before being put in a centrifuge machine and spun at 300 rpm for 5 minutes. The supernatant was later transferred to appropriate tube and serum electrolytes were analysed using ion selective electrode spectrophotometry, which was carried out by laboratory scientist in the chemical pathology laboratory'

In this study, electrolyte abnormalities were defined as thus: Hypernatraemia (Serum Sodium level <130mEq/L), hyperkalaemia (Serum Potassium > 5.5mEq/L), hypokalaemia (Serum Potassium < 3.5mEq/L) and metabolic acidosis (Serum bicarbonate <20mEq/L)

Data were analysed using SPSS version 20 and p-value ≤0.05 was significant.

RESULTS:

SOCIO-DEMOGRAPHIC CHARACTERISTICS OF STUDY POPULATION

One hundred and forty-six HIV-infected subjects consisting of 85 (58.2%) males and 61 (41.8%) females, with a Male: Female ratio of 1:0.7 were recruited. Median age was 99 months with mean of 100.8 ± 45.3 months ranging from 22 to 180 months (Table 1).

Table 1: Age groups and sex distribution of study population (N=146)

Variable	Frequency	Percentage
Sex		
Male	85	58.2
Female	61	41.8
Total	146	100
Age group (years)		
< 5	34	23.3
5 to 9	53	36.3
10 to 14	51	34.9
> 14	8	5.5
Total	146	100

One hundred and forty-six HIV-infected subjects consisting of 85 (58.2%) males and 61 (41.8%) females, with a Male: Female ratio of 1:0.7 were recruited. Median age was 99 months with mean of 100.8 ± 45.3 months ranging from 22 to 180 months (Table 1).

CLINICAL CHARACTERISTICS OF STUDY POPULATION

Nutritional Status

One hundred and fifteen subjects (78.9%) had normal weight, while 13 (8.9%), 4 (2.8%), 10 (6.8%) and 4 (2.7%) were severely thin, underweight, overweight and obese, respectively (Table II).

Mode of Transmission

One hundred and thirty-three subjects (91.1%) had Mother-To-Child Transmission (MTCT) as mode of HIV transmission, of which 116 (79.5%) had maternal HIV status confirmed, and 17 (11.6%) were suspected based on clinical presentation (Table II). Only two subjects (1.4%) had blood transfusion. The rest (7.5%) had combinations of causes.

Duration of ARV Drugs

One hundred and nineteen (81.5%) subjects were receiving ARV drugs. Among subjects receiving antiretroviral therapy (ART), mean duration on ARV drugs was 4.2 ± 2.7 years ranging from 0.5 to 12 years. Most subjects 91(76.5%) had received ARV for less than 6 years while 28 (23.5%) has received ART for longer than 6 years. (Table II).

Distribution of classes of HAART

Among subjects receiving ARV, majority 114, (95.8%) received only non-nephrotoxic, while

5 (4.2%) received both nephrotoxic and non-nephrotoxic ARVs. NVP-AZT-3TC 97, (85.0%) was the commonest non-nephrotoxic ARV regimen received, followed by EFV-AZT-3TC 7, (5.9%) and ABC-AZT-3TC 3, (2.6%).

Clinical staging of study population

Many subjects 60(41.1%) were in clinical stage 2, 48(32.9%) in stage 1, 27 (18.5%) in stage 3 and 11(7.5%) in stage 4 (table II).

Mean CD4 count was 785 ± 596 cells/ml ranging from 16 to 2,801 cells/ml. Thirty-one (21.2%) subjects had CD4 count below 200 cells per ml.

Table II: Clinical characteristics of study population (N= 146)

Table II: Clinical characteristics of study population (N= 146)		
Variable	Frequency	Percentage
Nutritional status		
Severe thinness	13	9.1
Underweight (thinness)	4	2.8
Normal weight	115	78.3
Overweight	10	7.0
Obese	4	2.8
Total	146	100
Mode of HIV transmission		
MTCT confirmed	116	79.5
MTCT suspected	17	11.6
Blood transfusion	2	1.4
*Others	11	7.5
Total	146	100
Receiving ART		
Yes	119	81.5
No	27	18.5
Total	146	100
Duration on ART(years)		
≤3	59	49.6
4-6	32	26.9
7-9	25	21.0
10-12	3	2.5
Total	119	100
Type of HAART		
Both non-nephrotoxic and nephrotoxic (TDF*)	5	4.2
Non-nephrotoxic	114	95.8
Total	119	100
Non-nephrotoxic HAART		
NVPAZF3TC	97	85.0
EFV-AZF3TC	7	6.1
ABCAZF3TC	3	2.6
ABCNVP3TC	2	1.8
EFV-3TC	2	1.8
LPV-AZF3TC	2	1.8
ABGEFV-LPV	1	0.9
Total	114	100
Clinical stage		
1	48	32.9
2	60	41.1
3	27	18.5
4	11	7.5
Total	146	100
Immunologic stage		
No immunodeficiency	90	61.6

*TDF-Tenofovir; NVP-Nevirapine; AZT-Zidovudine; 3TC-Stavudine; ABC-Abacavir; EFV-Efavirenz; LPV-Lamivudine

*Others - circumcision out of the hospital, use of unsterilized instrument and IV drug use.

PATTERN OF SERUM ELECTROLYTES AMONG SUBJECTS

Mean serum sodium concentration was 136.8 ± 3.6 mmol/L ranging from 127.7 to 150.5 mmol/L. One subject each, had hyponatraemia (0.7%) and hypernatraemia (0.7%), while all others 144 (98.6%) had serum sodium concentrations within normal limits (table III).

Mean serum potassium concentration was 4.5 ± 0.43 mmol/L ranging from 3.5 to 6.3 mmol/L. Three subjects (2.1%) had hyperkalaemia, while 143 (97.9%) had serum potassium concentrations within normal limits.

Mean serum bicarbonate concentration was 23.6 ± 4.5 mmol/L ranging from 11.1 to 33.2 mmol/L. Alkalosis, acidosis and normal serum bicarbonate concentrations were found in 12 (8.2%), 32 (21.9%) and 102 (69.9%) of subjects respectively (Table III).

When acidosis, the commonest bicarbonate abnormality was subjected to statistical analysis in relation to the type of ART taken and level of CD4, there were no statistically significant differences, $P > 0.05$ (Table IV).

Table III: Pattern of serum electrolytes (N=146)

Table III: Pattern of serum electrolytes (N=146)		
Electrolytes	Frequency	Percentage
Sodium (mmol/L)		
Mean Sodium (136.8 ± 3.6)		
Hyponatraemia	1	0.7
Normonatraemia	144	98.6
Hypernatraemia	1	0.7
Total	146	100
Potassium (mmol/L)		
Mean Potassium (4.5 ± 0.43)		
Normokalaemia	143	97.9
Hypokalaemia	0	0
Hyperkalaemia	3	2.1
Total	146	100
Bicarbonate (mmol/L)		
Mean Bicarbonate (23.6 ± 4.5)		
Alkalosis	12	8.2
Normal bicarbonate	102	69.9
Acidosis	32	21.9
Total	146	100

TABLE IV: THE RELATIONSHIP BETWEEN ART, IMMUNOLOGIC STAGE AND ACIDOSIS IN THE STUDY POPULATION

VARIABLE	ACIDOSIS		TOTAL (%)	TEST STATISTICS	p-value
	PRESENT (%)	ABSENT (%)			
ART					
HAART	27(18.5)	92(63.0)	119(81.5)	$\chi^2 = 0.224, df=10.636$	
NO HAART	5(3.4)	22(15.1)	27(18.5)		
Total	32(21.9)	114(78.1)	146(100.0)		
IMMUNOLOGIC STAGE					
CD4> 200 Cells/ml	23(15.8)	92(63.0)	115(78.8)	$\chi^2 = 1.164, df=10.281$	
CD4<200 Cells/ml	9(6.1)	22(15.1)	31(21.2)		
Total	32(21.9)	114(78.1)	146(100.0)		

DISCUSSION

In this study, electrolytes abnormalities were uncommon with one subject each having hyponatraemia and hypernatraemia giving a prevalence of 0.7%. Surprisingly, no subject had hypokalaemia while 2.2% had hyperkalaemia. In contrast, other studies^{7,13,19} reported higher prevalence of hyponatraemia and hypokalaemia. Tolaymate *et al*¹⁹ and Verma and Singh¹³ reported a prevalence of hyponatraemia of 20% and 61% respectively. The low prevalence rates of hyponatraemia, hypernatraemia, hypokalaemia and hyperkalaemia seen in this study may be explained by the fact that majority of our subjects were stable and over 90% had no symptom. Most were in early stages of HIV infection with 78.8% of subjects having CD4⁺ count of 200 cells per ml and above. All our patients were on routine clinic check-ups as we excluded those hospitalized and those that presented within two weeks of vomiting and diarrhoea. It could be recalled that hypokalaemia is found in setting of gastrointestinal infection leading to vomiting and diarrhoea as well as severe acute malnutrition. In addition, only 12% of our subjects had low BMI, an evidence that the prevalence of severe HIV was low.

In these other studies,^{13,19} hyponatraemia was found associated with co-morbidity like AIDS encephalopathy, cardiomyopathy, oral diuretics use, opportunistic infection and gastroenteritis. Their CD4⁺ counts also had a positive correlation with hyponatraemia.

In this current study, the prevalence of metabolic acidosis was 21.9%. This is similar to

the study by Nilima *et al*²⁰ who reported a prevalence of 31.8%. A particular type of non-hypoxic lactic acidosis (type B) has been described with use of antiretroviral drugs such as zalcitabine, stavudine, didanosine and zidovudine. This entity is explained mainly by mitochondrial toxicity and reveal hyperlactaemia with lactic acidosis to overt life threatening lactic acidosis.^{21, 22} Interestingly, most of our subjects (81.5%) in this study were on first line HAART which contain zidovudine and stavudine. These are non-nephrotoxic drugs and ordinarily should not cause problems but are culprits in academia.²³ Didanosine and stavudine has been associated with a high risk for lactic acidosis in HIV infected patients.^{23,24} Reported risk for developing lactic acidosis includes; female, obesity, pregnancy, having a low CD4 + nadir before starting regimens and regimens containing NRTI.²⁵

In this study there was no significant association between metabolic acidosis and use of HAART. This was similar to finding by Bonnet *et al*.²⁶ This may be due to the fact that metabolic acidosis in HIV infected patients has multiple factors such as exposure to nephrotoxic drugs, age, opportunistic infection, renal dysfunction which were not studied. Furthermore, there was no significant association between metabolic acidosis and low CD4+ count (CD4+ <200cells/ml). This was similar to report by Geddes *et al*.²⁷ Few subjects with low CD4 + and small samples size may possibly explain this.

In conclusion, metabolic acidosis is the commonest electrolytes abnormalities seen in HIV infected children especially those on HAART containing zidovudine and stavudine in this study. The other electrolytes are common.

Limitation of study

This study is limited by the small sample size and this could not allow for comprehensive analysis to correlate electrolyte abnormalities with risk factors such as age, sex, CD4+, count,

viral load and associated use of nephrotoxic drugs (non ARV)

Conflict of interest: None

Funding: None

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