(RESEARCH ARTICLE)

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Assessment of serum electrolytes levels among sickle cell patients in South-Eastern Nigeria

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Abstract

Background: Sickle cell disease is a common genetic disorder mainly characterized by vascular occlusion and haemolysis and it constitutes a major public health problem. The aim of this study is to assess the serum electrolyte levels in sickle cell patients attending the University of Nigeria Teaching Hospital, Enugu.

Materials and methodology: A total of 66 subjects, ages 18 – 40 years, were recruited for this study with thirty sickle cell subjects (female = 16, Male = 14) as test subjects and thirty non-sickle cell subjects (female = 21, male = 9) as control subjects. A total of 5mls of venous blood was collected from each subject. The serum obtained from each sample was analyzed for serum electrolytes (sodium, potassium, chloride, and bicarbonate) by potentiometry using a sensacore autoanalyzer. The data were analyzed using Statistical Package for the Social Sciences (SPSS) version 22.

Results: Anthropometric results obtained from this study showed a significant decrease ($P < 0.05$) in mean ± SD of systolic blood pressure, diastolic blood pressure, and body mass index (BMI) in the test subjects compared to the control subjects respectively. The electrolyte analyses showed a significant increase ($P < 0.05$) in mean ± SD of potassium and chloride in the test subjects compared to the control subjects respectively. The control subjects have a non-significant increase ($P > 0.05$) mean ± SD of sodium compared to the sickle cell subjects while the sickle cell subject has a non-significant increase ($P > 0.05$) mean ± SD of bicarbonate compared to the control subjects. There was a positive correlation between sodium and bicarbonate, while in the other parameters; no significant correlation existed.

Conclusion: This study concludes that sickle cell anaemia subjects are predisposed to electrolyte variations, hence, the need to check these electrolyte values in sickle cell subjects.

Keywords: Electrolytes; Haemoglobin SS; Sickle cell; Haemoglobinopathy

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1. Introduction

Evidence has shown that diseases associated with genes seem to be more rampant globally than other types of diseases, with over 7 million babies being born each year with genetic abnormalities [1]. Sickle cell disease (SCD), is a genetic disease associated with the human blood and it is one haemoglobinopathy that is most common among the other haemoglobinopathies, and hence, a major public health problem with over 200,000 babies born per year with SCD in Africa [2,3].

Human blood is made up of hemoglobin which is responsible for the shape of red blood cells. It usually appears like doughnuts but with a thin center rather than a hole [4]. Hemoglobin is a tetramer composed of two α globin and two beta globin chains in normal adults [5]. These chains work in conjunction with heme which reversibly binds with oxygen and transports it throughout the body.

In addition to the transport of oxygen, Haemoglobin is also a carbon dioxide carrier, gives the red color to the blood, acts as a buffer, and interacts with other ligands [6]. In conditions involving abnormal hemoglobin, such as sickle cell anemia, the abnormal shape of the red blood cells can lead to problems [4]. These problems are referred to as haemoglobinopathies. Sickle Cell Disease (SCD) is a haemoglobinopathy in which there is the substitution of a single amino acid in the beta chain of adult hemoglobin resulting in hemoglobin S, C, D, or E depending on amino acid substitution [7].

Nigeria is the most sickle cell endemic country in Africa with 2-3% of the total population affected [8], with an estimated 24% prevalence of sickle cell trait, 100,000 annual SCD births, and 100,000 annual SCD infant deaths [9]. The most common clinical phenotype is the homozygous form (HbSS or sickle cell anemia) [1]. Compound heterozygous SCD includes HbSC, HbSD, HbSO-Arab, and HbS/beta-thalassemia [10].

Heterozygotes are generally less symptomatic than homozygous [1]. This homozygous form results from the substitution of the amino acid, valine (GTG), for glutamic acid (GAG). Glutamic acid is an amino acid in the sixth position in the globin chain of the adult hemoglobin (HbA) [11].

This genetic defect results in the fragility of the red blood cell which deforms when the oxygen pressure decreases. Under conditions of deoxygenation (that is when the hemoglobin is not bound to oxygen), Hb tetramers that include two of these mutant sickle globin subunits (that is, HbS) can polymerize and cause the erythrocytes to assume a crescent or sickle shape from which the disease takes its name [12].

Sickle cell anemia is the most common form of sickle cell disease [13]. It is characterized by chronic hemolysis and painful vaso-occlusion, which often results in organ dysfunction. Sickling, which is associated with hemoglobin S (HbS) alongside vascular occlusion and erythrocyte hemolysis, affects the overall biochemical balance in sickle cell patients [14] and will lead to various biochemical abnormalities like cell dehydration in the case of body electrolytes.

Electrolytes such as sodium (Na^+), potassium (K^+), chloride (Cl^-), and bicarbonate (HCO_3^-) play various vital roles in the body and are required for the optimal functioning of cells and organs [15,16]. Sodium is one of the major cations and functions in regulating the total amount of water in the body [17]. It also plays a vital role in electrical communication in many systems, especially the nervous and muscular systems. However, potassium is responsible for regulating heartbeat and muscle function and is important for the overall functioning of the cell [18]. Chloride helps maintain a normal balance of body fluids [15]. Bicarbonate, on the other hand, plays a role in maintaining the blood pH levels, that is, acid-base balance [19]. Disturbances in these electrolytes pose a threat to the normal functioning of the cell.

Disturbances, such as an increase or decrease in these electrolytes can lead to detrimental effects [20]. Owing to the sickling of the cell, the cellular membrane integrity becomes altered leading to abnormally high red cell permeability. This leads to an efflux of potassium from the cell and an influx of sodium favoring red cell dehydration. The K-Cl co-transport is one of the pathways through which potassium is lost; which is abnormally activated by low intracellular magnesium. In principle, K^+ and Cl^- ions are rapidly and irreversibly lost with a very significant amount of water following, as a result of osmosis [18]. However, Airhomwanbor et al. [21], in their report, noted that sex is a factor in the estimation of sodium and bicarbonate level in sickle cell patients with females presenting with metabolic alkalosis (increased HCO_3^-) while the males present with metabolic acidosis (decreased HCO_3^-).

Sickle cell disease has long been a disease of medical concern because it is a genetically acquired disease and causes severe damage to red blood cells if not managed well. The deoxygenation of sickle cells leads to increased erythrocyte permeability [22-24] and this causes the loss of some important electrolytes like potassium and this result in an

electrolyte imbalance in the body system. Findings from this research will help determine whether electrolytes estimation will be a vital routine test to be carried out on sickle cell patients.

Aims and objectives

This study is aimed to assess the serum electrolytes levels of patients suffering from sickle cell disease, measure the serum sodium, potassium, chloride, and bicarbonate in the sickle cell subjects and normal individuals, and determine if there are variations in the electrolyte level in sickle cell subjects. We also aim to statistically compare these biochemical parameters in the sickle cell subjects with normal individuals and hence proffer approaches to its treatment and management. The result from this current study will also highlight if variation in electrolyte levels will be used as biomarkers of SCD.

2. Material and methods

2.1. Study Area

The cross-sectional study was carried out at the University of Nigeria, Teaching Hospital (UNTH) Ituku-Ozalla. The subjects were recruited from UNTH and the University of Nigeria, Enugu Campus, (UNEC).

2.2. Study Population and Design

A total number of sixty (60) participants were recruited for the study. They comprised 30 sickle cell anemia patients (16 females, 14 males) receiving treatment at the Sickle Cell Unit at the UNTH, as test subjects, and 30 students (21 females, 9 males) of the UNEC, as control subjects. The age range of the participants is between 18-40 years.

Prior to the collection of the blood samples from the respondent, each respondent was notified and made to understand why the study is being carried out. A structured questionnaire was used to get necessary data about the participants.

2.3. Ethical Consideration and Informed Consent

An ethical clearance certificate was obtained from the University of Nigeria Teaching Hospital Research and Ethical Committee with Ref no: UNTH/CSA/329/VOL.5. Informed consent was as well obtained from each of the participants before the commencement of the study.

2.4. Inclusion and Exclusion Criteria

2.4.1. Inclusion criteria

- Subjects who are diagnosed as having sickle cell anemia.

2.4.2. Exclusion criteria

- Hypertensive subjects
- Subjects taking drugs that contain electrolytes
- Subjects with any other haemoglobinopathy
- Subjects with records of recent blood transfusions

2.5. Sample Collection

A total of 5mls of venous blood was collected aseptically from the respondent and dispensed into plain containers properly labeled with the respondents' names and laboratory numbers. They were allowed to clot and subsequently centrifuged at 3000rpm for 5 minutes. The serum was extracted and dispensed into another labeled plain tube for immediate analysis.

2.6. Biochemical Analysis

2.6.1. Estimation of Serum Electrolytes

Sodium, Potassium, Chloride, and bicarbonate estimation were done using a Sensacore Electrolyte Analyser (Telangana, India.) strictly following the manufacturer's operational guideline.

2.7. Statistical Analysis

Data analysis was done using Statistical Package for the Social Sciences (SPSS) version 22. The results of the biochemical assays were reported as mean ± SD (standard deviation).

3. Results

Table 1 Anthropometric Parameters of Sickle Cell Subjects and Non-Sickle Subjects

Groups	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	BMI (Kg/m²)
Sickle Cell Subjects N = 30	100.83 ± 2.17	69.27 ± 3.69	19.33 ± 0.45
Non-Sickle Cell subjects N =30	110.73 ± 3.06	81.20 ± 4.15	23.28 ± 3.51
t-Statistics	13.35	11.63	5.97
P – Values	0.000	0.000	0.000

(Values are given as mean ± SD)

Table 2 The Electrolyte Levels of Sickle Cell Subjects and Non-Sickle Subjects

Groups	Sodium (Na^+)	Potassium (K^+)	Chloride (Cl^-)	Bicarbonate (HCO_3^-)
Sickle Cell Subjects N = 30	135.12 ± 3.49	4.65 ± 0.53	107.09 ± 2.05	22.80 ± 6.8
Non-Sickle Cell subjects N =30	136.43 ± 2.28	3.85 ± 0.29	100.20 ± 3.98	21.47 ± 1.41
t-Statistics	1.879	-7.070	-7.546	1.028
P – Values	0.070	0.000	0.000	0.313

(Values are given as mean ± SD)

Table 3 Correlation of the Parameters of the Test Groups

Parameters	r (Pearson)	P Values
Systolic vs Diastolic	0.320	0.085
Systolic vs BMI	0.181	0.337
Systolic vs Sodium	0.074	0.698
Systolic vs Potassium	-0.007	0.969
Systolic vs Chloride	0.171	0.365
Systolic vs Bicarbonate	-0.116	0.540
Diastolic vs BMI	0.001	0.994
Diastolic vs Sodium	0.076	0.691
Diastolic vs Potassium	0.173	0.359
Diastolic vs Chloride	0.213	0.258
Diastolic vs Bicarbonate	0.034	0.857
BMI vs Sodium	0.000	1.000

BMI vs Potassium	0.023	0.905
BMI vs Chloride	0.239	0.204
BMI vs Bicarbonate	-0.090	0.635
Sodium vs Potassium	-0.101	0.596
Sodium vs Chloride	0.122	0.520
Sodium vs Bicarbonate	0.480	0.007**
Potassium vs Chloride	-0.010	0.960
Potassium vs Bicarbonate	0.030	0.876
Chloride vs Bicarbonate	-0.087	0.648

(** shows significance)

4. Discussion

Imbalance homeostasis of electrolytes including sodium, potassium, and chloride [15], has been described in relation to sickling and increased dehydration in sickle cell patients [18] in Nigeria and other parts of the world.

In table 1, there was a significant decrease ($P < 0.05$) in mean ± SD of systolic blood pressure (P = 100.83 ± 2.17, 110.73 ± 3.06), diastolic blood pressure (P = 69.27 ± 3.69, 81.20 ± 4.15) and BMI (P = 19.33 ± 0.45, 23.28 ± 3.51) in the test subjects compared to the control subjects respectively. This observation is in line with previous studies by [25-28]. The decrease in blood pressure in the sickle cell subjects could be a result of low serum sodium levels, haemolytic anemia, dehydration, and inadequate food intake which can occur due to anemia.

In contrast to this study, studies by Benneh-Akwasi Kuma *et al.,* [29], indicated the risk of relative systemic hypertension and hypertension in sickle cell subjects. Benneh-Akwasi Kuma *et al.* [29] corroborate studies of sickle cell subjects with low blood pressure adding that relative systemic hypertension appeared in male subjects with a steady increase in age, whereas, hypertension is uncommon and appears in subjects having a medical history of hypertension. The decreased BMI could be a result of micro-nutrient deficiencies, loss of appetite, increase demand from high metabolic rates due to increased red blood cell turnover due to hyper haemolysis, reduced absorption, and increased degradation of nutrients that occurs in sickle cell subjects. This is consistent with studies by [30-32]. On the other hand, it is in contrast with the study by Hall *et al.* [33], who recorded a high body mass index in high-income countries.

In table 2, there was a significant increase ($P < 0.05$) in mean ± SD of potassium (P = 4.65 ± 0.53, 3.85 ± 0.29) and chloride (P = 107.09 ± 2.05, 100.20 ± 3.98) in the test subjects compared to the control subjects respectively. The control subjects have a non-significant increase ($P > 0.05$) mean ± SD of sodium (136.43 ± 2.28) compared to the sickle cell subjects (P = 135.12 ± 3.49). The results here are in line with studies by [15,34,35]). Almost similarly, Agoreyo and Nwanze [36], in their report, observed a significant difference in sodium levels between their control group and sickle cell patients that are in the active crisis stage. The sickle cell subjects have a non-significant increase ($P > 0.05$) mean ± SD of bicarbonate (22.80 ± 6.8) compared to the control subjects (21.47 ± 1.41). In sickle cell anemia, the haemolysis that occurs causes a release in the K^+ which is an intracellular cation into the extracellular environment resulting in an increase in potassium with a concomitant decrease in Na^+. There is also an abnormal activation of the potassium chloride (K^+-Cl^-) co-transport system and Gardos channel [15]. The abnormal activation of this system results in an increase in potassium and chloride with a resultant effect of increased sodium. This is in line with Nnodim *et al.* [37], in their study, stating that sickling is accompanied by an intra-erythrocytic loss of potassium and gain of sodium.

Excessive potassium losses and concomitant gain of sodium from the intracellular fluid to the extracellular fluid were a result of dehydration and deoxygenation which often occurs in a sickle cell. The abnormal activation of the Gardos channel resulting in a rise in the erythrocyte concentration of calcium levels (although not reported in this study) in sickle cell patients contributed to higher efflux of potassium accompanied by chloride.

A higher bicarbonate level in sickle cell subjects, when compared to control subjects, is seen in this study, though not significant ($P = 0.313$). This could be a result of dehydration which occurs in vomiting and/or diarrhea. There could be an increased acidic content in the blood which caused an increased level of bicarbonate in comparison to that of the control subjects. This is in contrast to studies by [38,39]. In line with this study, Airhomwanbor *et al.* [21], in their study,

reported a high level of bicarbonate in the blood of female subjects which can be from metabolic alkalosis in contrast to metabolic acidosis experienced in males (though not indicated in this study).

In table 3, there was a positive correlation between sodium and bicarbonate. This could be due to disturbances in acid-base balance. This is in line with the study of Feldman *et al.* [40], on the correlation between Serum Chloride and Bicarbonate Concentrations.

Limitation

The sample size of the study was small, hence cannot be projected to the whole population. Follow-up cases can give better insights into the serum electrolytes values and other biochemical variables.

5. Conclusion

This study was able to show imbalances in the levels of serum electrolytes of sickle cell subjects in comparison to non-sickle cell subjects. These imbalances play a vital role in the pathophysiology of sickle cell disease, hence, the complications in an individual with sickle cell disease. Rehydration is a very important remedy to these imbalances as dehydration encourages sickling. It is recommended that hydration through water drinking be practiced by sickle cell subjects. Electrolytes must be measured regularly in sickle cell patients while they are managed. Further research on serum electrolytes relative to sex and age should be conducted. This will indicate if there are age-related factors and sex-related factors affecting the serum electrolyte level of sickle cell subjects. Finally, further research on acid-base balance in sickle cell subjects should be conducted, as this will help give a better understanding of the mechanism behind an acid-base imbalance in sickle cell patients.

Compliance with ethical standards

Disclosure of conflict of interest

We declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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