

*Full Length Research Paper*

# Electrolyte profile and prevalent causes of sickle cell crisis in Enugu, Nigeria

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One hundred sickle cell patients aged between 6 - 25 years in steady state who attended Sickle Cell Clinic at University of Nigeria Teaching Hospital, Enugu, Nigeria were selected for this study. Out of this number, only thirty who were eventually admitted in crisis state within one year of this study were selected for subsequent investigations. They included 20 females and 10 males. We also selected thirty apparently healthy hemoglobin AA subjects, (17 males and 13 females) aged between 6 and 32 years to serve as secondary control. Samples were collected on the patient's initial visit to the hospital (stable state). Samples were also collected on admission and 24 h after infusion therapy. Serum electrolytes, malarial parasite count, widal agglutination, blood and urine cultures were done using standard methods. The results showed a statistically significant decrease ( $p < 0.05$ ) in mean sodium and potassium levels in crisis when compared with those in steady state. The electrolytes were assayed 24 h after rehydration of the patients in crisis. There were significant increases ( $p < 0.05$ ), in mean sodium and potassium levels. Considering the prevalent causes of crisis, 63% of the subjects in crisis had malarial parasitaemia. 16.7% had bacterial infection and 13.3% were infected with Hepatitis B while 7% had both malaria and bacterial infection. The significance of this study is to highlight the fact that sickle cell patients who receive hydration therapy attain electrolyte balance within 24 h of re-hydration and therefore should not be over-enthusiastically challenged especially in those localities where there are no facilities for monitoring hydration therapy. In addition, the study revealed that malaria is the major precipitating cause of sickle cell crisis in Enugu, Nigeria and governments should take a holistic approach towards the fight against malaria.

**Key words:** Sickle cell anaemia, electrolytes, crisis, prevalent causes, malaria.

## INTRODUCTION

### Epidemiology

Although the effects of sickle cell disease (SCD) on general morbidity and mortality have been studied extensively (Gladwin et al., 2004; Prasad et al., 2003), much work has not been done in determining the prevalent causes of sickle cell crisis especially in this part of the

world. There is high prevalence of sickle cell disease in Africa and elsewhere (Oheme-Frempong et al., 1994). The disease is most common among people living in or originating from Sub-Saharan Africa (Akinyanju, 1989). The disorder also affects people of Mediterranean, Caribbean, Middle Eastern and Asia origin (Npat, 2002). The sickle cell gene is most common in areas where mosquito is endemic (Meremiku, 2008). Sickle cell trait affects 30% of Africa's tropical population (Oheme-

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Frempong, 1994). It also affects an estimated 1 - 2% (120,000) of newborns in Africa annually. About 178 babies (0.28/1000 conceptions) are affected by sickle cell disease in England annually (Hickman et al, 1999). Besides, about 72,000 in USA (NIH, 2004) and 10,000 in the United Kingdom suffer from the disease (Davies et al., 1997).

Sickle cell disease refers to a group of disorders caused by inheritance of a pair of abnormal haemoglobin genes including sickle cell gene (Meremiku, 2008). It is an inherited blood disorder characterized primarily by chronic anaemia and periodic episodes of pain. The underlying problem involves haemoglobin, a component of red blood cells. Haemoglobin molecules in each red blood cell carry oxygen from the lungs to the organs and tissues and bring carbon dioxide back to the lungs. In sickle cell anaemia, the haemoglobin is defective. After haemoglobin molecules give up oxygen, some may cluster together and form rod-like structures. These structures cause red blood cells to become stiff and assume a sickle shape. Unlike normal red cells which are usually smooth and donut-shaped, sickled red cells cannot squeeze through small blood vessels. Instead, they stack up and cause blockages in arterioles thereby depriving organs and tissues of oxygenated blood. This process produces periodic episodes of pain and ultimately damage tissues and vital organs including liver, spleen, kidney, heart, bones, etc, thus leading to high morbidity and serious medical problems (NIH, 2004). Normal red cells live about 120 days in the blood stream but sickled red cells die after about 10 - 20 days. Because they cannot be replaced fast enough, the blood is chronically short of red blood cells, a condition called anaemia.

## Pathophysiology

Sickle cell disease is an inherited disorder associated with abnormal haemoglobin in the homozygous state (Sergeant, 1992). The genetic abnormality is a point mutation arising from the substitution of glutamic acid by valine at the sixth position on the beta polypeptide chain (Ureme et al., 2003) . It is accompanied with various clinical manifestations such as jaundice, cutaneous ulcer, skeletal changes and episodes of intravascular sickling and thrombosis resulting in painful crisis and infarcts in various organs (Kabins, 1970). Sickle cell pain crises are precipitated by infection, dehydration and hypoxia. Intercurrent infections particularly of respiratory tract, fever, abdominal, skeletal pain, haematologic and bone pain crisis are the main causes of morbidity in sickle cell patients (Kaine, 1983). The patients may have fever, pulmonary infarction that presents as acute chest crisis and dehydration. One of the ways of managing sickle cell crisis is by re-hydration. Hydration is done using various grades of electrolytes such as 5% dextrose saline, normal saline, Darrow's solution and oral rehydration solution (ORS).

It has been demonstrated that sickling is accompanied by an intraerythrocytic loss of potassium and gain of sodium, thus creating disequilibrium in the ionic strength across the cell membrane (Status et al., 1971). Chem et al. (1981) reported that haemolysis, intravenous potassium administration, blood transfusion among others, increase serum potassium level. This elevated potassium concentration may lead to cardiac excitability and ventricular fibrillation, weakness and ascending paralysis. There is also conformed weight loss throughout the acute phase of crisis and a negative water balance. However, the administration of fluid early in crisis not only achieved positive water balance but largely prevented weight loss from occurring. Conversely, re-hydration of patients with varying strengths of electrolytes may precipitate a shift in membrane potential and a rise to abnormal level. Infections can precipitate crisis due to underlying functional asplenia in most adults with sickle cell anemia, leading to defective immunity against encapsulated organism. An infectious disease is one caused by the invasion and multiplication of organisms (Gossel et al., 1980). The infection could be of bacterial, viral or protozoan origin. The bacterial infection may be due to *Haemophilus influenza*, *Streptococcus pneumonia*, *Staphylococcus aureus*, *Neisseria meningitidis* and *Escherichia coli* among others. The protozoan infection can be due to plasmodium species leading to the so-called "malaria attack" (Gossel, 1980).

The objective of this study was to follow-up 100 sickle cell patients who reported at the sickle cell clinic, University of Nigeria Teaching Hospital, Enugu, Nigeria, within one year to determine frequency of crisis and the precipitating factor in addition to assessing electrolyte balance within 24 h.

## MATERIALS AND METHODS

### Subjects

A total of one hundred (100) sickle cell patients who attended sickle cell clinic at University of Nigeria Teaching Hospital were selected for this study. Out of this number, only thirty (30) who were later admitted in crisis state within a period of one year was selected for further investigations and monitoring. They included 20 female and 10 male subjects aged between 6 - 25 years. Thirty apparently healthy hemoglobin AA individuals (17 males and 13 females) aged between 6 - 32 years were assessed and they served as secondary control. Ethical clearance was obtained from the Ethics Committee, University of Nigeria Teaching Hospital, Enugu while informed consent was obtained from the subjects and parents of the minors. Children below six years were excluded from this study because of the volume of blood required.

### Sample collection

Blood samples were collected in EDTA bottles for Hb electrophoresis (control subjects) and malarial parasite count. Brain heart infusion (BHI) was used to collect samples for blood culture, sterile containers for urine culture while plain tubes were used for the collection of samples for Widal agglutination reaction and electrolyte

**Table 1.** Sodium and potassium levels of HbAA, HbSS in stable state, HbSS in crisis before, and 24 h after rehydration.

<b>(A) Comparison of the Na<sup>+</sup> and K<sup>+</sup> values of HbAA and HbSS stable state</b>		
	<b>Sodium</b>	<b>Potassium</b>
HbAA	138.37 ± 3.52	4.29 ± 0.47
HbSS stable state	136.22 ± 3.19	3.56 ± 0.42
P-value	P < 0.05	P < 0.05
<b>(B) Comparison of Na<sup>+</sup> and K<sup>+</sup> values of HbSS stable state and crisis before re-hydration</b>		
	<b>Sodium</b>	<b>Potassium</b>
HbSS stable state	136.22 ± 3.19	3.56 ± 0.42
HbSS Crisis before rehydration	135.17 ± 2.77	3.28 ± 0.35
P-value	P < 0.05	P < 0.05
<b>(C) Comparison of Na<sup>+</sup> and K<sup>+</sup> values of HbSS crisis during rehydration and 24 h after rehydration</b>		
	<b>Sodium</b>	<b>Potassium</b>
HbSS crisis before	135.17 ± 2.77	3.28 ± 0.35
rehydration HbSS 24 h after	137.57 ± 2.15	4.42 ± 0.15
rehydration P-value	P < 0.05	P < 0.05

profile. For sickle cell patients in crisis, blood and urine samples were collected on admission prior to fluid administration and another blood samples collected 24 h after re- hydration of patients. For the HbAA subjects, blood samples were collected for electrolyte estimation only. Thirty- five milliliters of blood were collected from the subjects depending on their age and state of health.

#### Sample analysis

The blood samples for electrolytes were allowed to clot and sera separated after centrifuging at 3000 rpm for five minutes. Sodium and potassium concentrations were analyzed using Gallenkamp flame photometer by means of flame emission. We also used quality control sera manufactured by Quimica Clinica Aplicada S.A. (QCA) for the analysis. Urine culture was done using MacConkey ager and sterile wire loop calibrated to deliver 0.01 ml of urine. Blood culture was done according to WHO standard by adding 1 ml of blood per 10 ml of BHI (Vandepitte et al., 1983). Subcultures were done on Chocolate and MacConkey agar and incubated in carbon dioxide atmosphere and aerobically respectively. Hemoglobin electrophoresis was done using cellulose acetate paper in a chamber connected to the zip-zone power supply and electrophoresed for 5 - 10 min at 350 volts. Widal agglutination reaction was carried out by tube agglutination using Chromatest kit while FIBH-Tech kit was used for Australia antigen (Vaisman et al., 1960).

#### Statistical analysis

This was done using Z-score. Calculations were done at 5% level of significance while figures were analyzed using Microsoft Excel worksheet.

## RESULTS

The mean and standard deviation (mean ± SD) of sodium and potassium of control HbAA and HbSS (stable state)

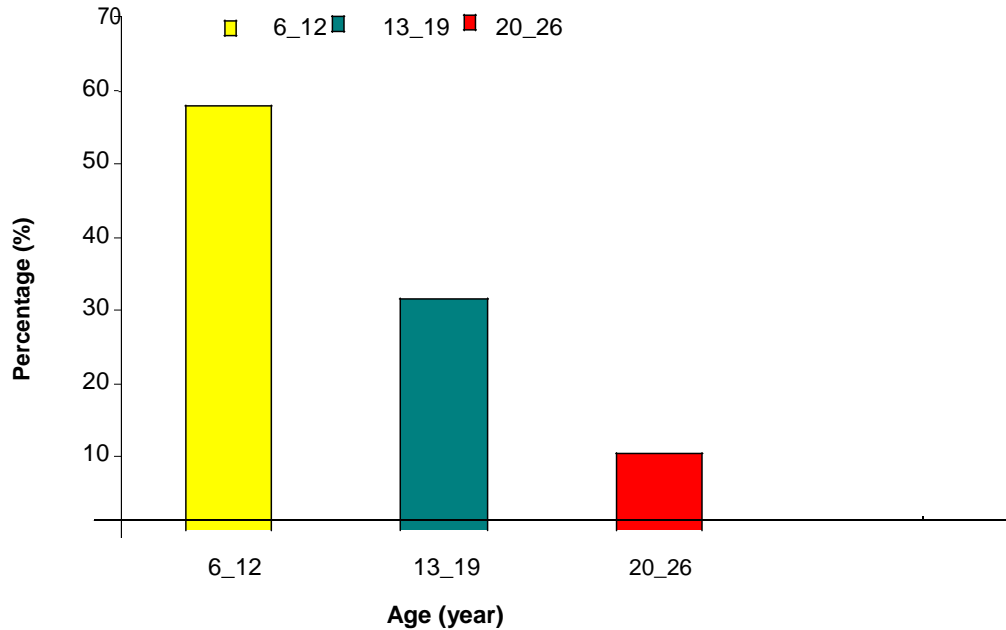
were compared as shown in Table 1A. There were significant differences in mean values of both parameters. The mean values of sodium and potassium were also compared in HbSS (stable state) and crisis before hydration (Table B) and 24 h after re-hydration as presented in Table 1(C). There was significant decrease in values in HbSS (crisis) and an increase in the values of both parameters 24 h after re-hydration (p < 0.05).

Figure 1 represents the malarial parasite count in sickle cell disease in relation to age. This analysis was done based on the fact that plasmodiasis was a major observed factor in sickle cell crisis. Children between 6 - 12 years had malarial parasite count greater than 300 parasites per microlitre of blood (57.9%). Those 13 - 19 years old had 210 - 300 parasite count per microlitre (31.6%) while those 20 - 26 years old had 101 - 200 parasite count per microlitre (10.5%).

Table 3 represents bacterial isolates in blood and urine cultures and widal agglutination test in steady state and crisis. Out of the 10 patients (stable state) who presented with bacterial infections, 60% had *Salmonella* infection, 20% (*E. coli*) 10% (*S. aureus* and *S. pneumonia*) respectively. Out of the 7 patients who eventually went into crisis as a result of bacterial infection, 57% had *Salmonellosis*, 29% (*E. coli*) while 14% were infected with *S. pneumonia*.

## DISCUSSION

There was high incidence of sickle cell crisis as observed in the University of Nigeria Teaching Hospital, Enugu. In sickle cell anaemia, there are increased and continued obligatory losses of body fluids and electrolytes which ra-



**Figure 1.** Represents malarial parasite count in sickle cell disease in relation to age.

**Table 2.** Prevailing causes of crisis in Enugu and age relationship.

Age(years)	Percentage	MP	HbsAg	Bacterial	Mixed infections
6 = 12(n = 13)	43.3	10	-	3	
13 - 19(n = 10)	33.3	7	-	3	
20 - 36(n = 7)	23.4	2	4	1	
Prevalence in Enugu		63%	13%	17%	7%

**Table 3.** Bacterial isolates (steady state) and (crisis).

Source (stable state)	<i>S. aureus</i>	<i>S. pneum</i>	<i>E. coli</i>	<i>S. para C</i>	<i>S. typhi</i>	<i>S. para B</i>
Urine	1	-	2	-	-	-
B. culture	-	1	-	-	-	-
Widal test	-	-	-	1	1	4
Titre				80	80	160
Crisis state						
Urine	-	-	2	-	-	-
B. culture	-	1	-	-	-	-
Widal test	-	-	-	-	1	3
Titre					160	160

rapidly result in dehydration. Besides, there is suppression of appetite and patient may not drink. There is also high skin loss of electrolytes coupled with the obligatory urinary losses from inability to concentrate urine. For this reason, Physicians are at liberty to give intravenous electrolyte fluid continuously and it has been documented that this could cause heart failure (Serjeant, 1992). Dehydra-

tion causes salt (sodium, chloride) and other electrolyte imbalance (HCl org, 2008). It further promotes sickling, sequestration and haemolysis. Consequently, more water and electrolytes are lost from the body (NIH, 1995). Avoiding dehydration is a good way to decrease the likelihood of pain crisis. Therefore, getting plenty of fluid is extremely important, (Lewis et al., 2008).

The results showed decrease in sodium and potassium concentrations during crisis when compared with the steady state and apparently healthy HbAA subjects ( $p < 0.05$ ) as represented in Table 1. The decreased levels of electrolytes are due to reduced fluid intake, accelerated influx and outflux of sodium and potassium, increased insensible loss and high incidence of hyposthenuria (NIH, 1995). Similar reports recorded in this study were made by Tosteston et al. (1955). Brugnara and cohorts observed marked decrease in potassium and chloride levels in painful crisis in the USA (Brugnara, 2000). The loss of potassium is also associated with calcium-activated potassium channel in the kidneys (Gardos pathway). There is excessive accumulation of calcium in sickle cell disease. The excessive accumulation of calcium activates the Gardos channel which then expels potassium into the renal tubules. The disturbance of electrolyte and water equilibrium has to be corrected to maintain a balance in order to ensure the normal functioning of the body system. And the major way of correcting this disturbance is by re-hydration therapy. In the course of correcting this imbalance, the patient may be overenthusiastically challenged especially in the rural and semi-urban settings where there are no facilities for monitoring hydration therapy.

Moreover, the study showed a higher malarial parasite concentration in children between 6 - 12 years old (>300 parasites per microlitre blood). This could be as a result of lowered immunity and relatively small blood volume when compared with the older age groups (Figure 1). There was also prevalence of malarial-induced crisis (63%) in relation to bacterial and viral infection, (Table 2). This could be as a result of parasite resistance to drugs as most of these patients could be indulging in self medication with monotherapy before reporting to hospital. This report differs from the findings of Buchanan who reported that bacterial infection was the most common cause of death in children with sickle cell disease in America (Buchanan et al., 1989). However, in all those who had bacterial infection, Salmonellosis was more prevalent (Table 3). The prevalence of malaria could be attributed to the endemic nature and unhealthy environment coupled with the low social standard of most people in this part of the world.

## Conclusion

There was increase in electrolyte levels after re-hydration. It is therefore suggested that hydration (oral or intravenous) be monitored closely to avoid iatrogenic congestive cardiac failure and electrolyte imbalance which may result if the patient is over-challenged with different grades of electrolytes. The high incidence of sickle cell disease in Africa makes it a public health problem in many countries, but it is often not recognized as such because so many cases go undiagnosed before or even after death. Malaria and its complications further

worsen the morbidity and mortality of sickle cell disease. Management of sickle cell disease includes considerations for improvement on general health conditions such as sanitation, housing, nutrition, immunization and prophylaxis against infection. Public education and programs of early diagnosis and management are needed to help prevent early mortality.

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