ORIGINAL ARTICLE

# Digestive system complications among hospitalized children with sickle cell anaemia in Enugu, Nigeria

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ABSTRACT

**Background**: Sickle cell anaemia is a multi-systemic disease with variable clinical manifestations including those involving the digestive system. There is paucity of data on the digestive system complications of sickle cell anaemia in children in our setting.

**Objective:** To determine the pattern of digestive system complications among hospitalized children with sickle cell anaemia in University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu, Nigeria.

**Methodology**: A 7-year retrospective observational study of cases of digestive system complications among hospitalized children with sickle cell anaemia was carried out. Relevant clinical data including socio-demographic characteristics, digestive system complications diagnosed, definitive investigations applied, treatment given and possible outcomes were extracted from the case record files of selected cases using a semi-structured questionnaire. Data were analyzed using SPSS version 21.0 (IBM Corp, Armonk, NY 2012) while the level of statistical significance was set at $p<0.05$.

**Results**: There were 350 children with sickle cell anaemia attending the sickle cell clinic out of which 33 had serious digestive system complications requiring hospitalizations during the period under review. Their mean age was 9.1±4.8years (9months to 18years).Nearly half, 16(48.5%) of the affected children were of low socio-economic background. Acute abdominal crisis, which was found in 12(36.4%) of cases was the most common complication, while cholelithiasis was the least common complication, occurring in one (3.3%) of the cases studied.

**Conclusion**: Acute abdominal crisis is the most common digestive system complication in children with sickle cell anaemia in our setting. Efforts should be made to exclude other potential causes of acute abdomen which may require surgical intervention in children with sickle cell anaemia. History taking, diligent physical examination and relevant laboratory and imaging studies, would readily facilitate the diagnosis, and save lives.

***Keywords****: Acute abdominal crisis, children, haemoglobin, hospitalization, multi-systemic*

## INTRODUCTION

Sickle cell disease is the most common genetic disease affecting the structure, function or the production of haemoglobin while sickle cell anaemia (HbSS) is the most common pathological haemoglobin variant worldwide.[1,2] A wide variation of the prevalence of the sickle cell gene has been

reported in different parts of Africa, the Mediterranean, Middle East, Southern and Eastern Europe and Indian sub–continent, respectively.[3] In Nigeria, with a population of 168 million, the estimate of the sickle cell trait is about 25%,while the homozygous state (HbSS) occurs in about 1-3% of the population.[3,4,5]

Sickle cell disease (SCD), including sickle cell anaemia (SCA), is a multi-systemic disease with variable clinical manifestations determined by both genetic and environmental factors.[6] The digestive system is by no means immune from these generalized effects occurring during any sickle cell crisis.

The gastrointestinal complications of sickle cell anaemia include: acute abdominal crisis, ischaemic colitis, dyspepsia/peptic ulcer disease, amongst others.[7] Similarly, hepatobiliary involvements, also, occur commonly in individuals with sickle cell anemia either directly from the sickling process or indirectly as a result of chronic haemolysis and multiple blood transfusions, giving rise to viral hepatitis, iron overload and the development of bilirubin pigment stones. All of these, contribute either singly or in combination, to the development of liver disease, and this manifests in several clinical conditions which pose both diagnostic and therapeutic challenges to the clinician.[8,9]

The objective of the present study was to determine the pattern of digestive system manifestations and its associated factors in children with sickle cell anaemia in University of Nigeria Teaching Hospital (UNTH), Enugu, South-East Nigeria.

The findings from this study will help to highlight the common digestive system complications of sickle cell anaemia in our paediatric population and contribute to the improvement of the management of such children.

METHODOLOGY

**Study Location/Population**

This study was conducted at the Department of Paediatrics, University of Nigeria Teaching Hospital (UNTH), Ituku-Ozalla, Enugu, Nigeria. It is a 500-bed tertiary hospital serving the3 million population of Enugu State, in addition to other neighbouring South-East States of Nigeria namely Abia, Anambra, Ebonyi and Imo.[10] There are about 350 registered children attending the paediatric sickle cell clinic as at the time of this review.

**Diagnostic Criteria**

The diagnostic criteria for the different digestive system complications were as follows: For an acute abdominal crisis: sudden, unrelenting and constant abdominal pain - the pain may or may not be localized in any part of the abdomen; nausea, vomiting and diarrhoea that could occur; and Other causes of acute abdomen should have been excluded by laboratory and/or imaging studies including plain abdominal x-rays and abdominopelvic ultrasonography.[11]

For acute hepatic crisis: variable severity of right upper quadrant abdominal pain, low grade fever, and vomiting; laboratory evidence of leukocytosis (evidence from full blood count and blood film); laboratory evidence of mild to moderate elevations of the liver enzyme and conjugated bilirubin levels (using liver function tests), with or without liver biopsy findings of patchy hepatic cell necrosis and cellular infiltration of the lobular parenchyma.[8,12]

Hepatic sequestration crisis was defined as acute hepatic enlargement presenting with a right upper quadrant abdominal pain associated with severe pallor and / or shock and a laboratory evidence of severe anaemia with elevated reticulocyte count and bilirubin levels.[13]

Acute cholecystitis was defined as an episode of right upper quadrant or epigastric pain with fever or positive Murphy's sign, and radiological imaging consistent with acute

cholecystitis (abdominopelvic ultrasound demonstrating gall stones, gall bladder thickening and peri-cholecystic fluids).[14]

Also, cases of chronic liver disease arising from hepatitis B or C virus infection were confirmed using standard serological tests (i.e. positive serum hepatitis B surface antigen positivity for at least six months; or anti – hepatitis C) with liver function tests results.

Functional recurrent dyspepsia: this was defined using Rome III diagnostic criteria for functional gastrointestinal disorders.[15,16]Here the diagnostic criteria includes one or more of the following: bothersome postprandial fullness, easy satiation, epigastric pain or burning in the absence of any structural disease (including at upper endoscopy) that is likely to explain the symptoms and criteria fulfilled for at least for three months with symptom onset at least six months prior to diagnosis.[15,16] The Rome III criteria is an evidence based approach for the diagnosis of functional gastrointestinal disorders based on the consensus of numerous experts, using standard methods and yes- no decision trees, and all end in specific diagnoses, providing clinicians with the best diagnostic strategies currently available.

**Study Design**

This was a retrospective observational study on children with SCA who had digestive system complications and were admitted over a 7-year period (1st January, 2008 and 31st December, 2014) at the UNTH, Enugu.

**Subjects Selection**

All cases of SCA whose status had been previously determined using cellulose acetate haemoglobin electrophoresis at the Department of Haematology, (UNTH) Enugu were selected from the paediatric ward admission registers. Patients with incomplete data set were, however, excluded.

Relevant clinical data retrieved from patients' folders included biodata: age, gender, highest educational attainments and occupations of the parents or caregivers from where their respective socio-economic classifications were estimated using Oyedeji's criteria.[17] In this method, the social class of each child was determined based on the educational attainment and occupational status of both parents. The average of the four scores (two each for the father and mother, that is, occupational status and educational attainment) to the nearest whole number was the social class of each child selected for the study.

The highest score is I while the lowest is 5. Social classes I and II; III; IV and V were respectively classified as high, middle and low socioeconomic classes. In cases where one of the parents is already dead the social class of the child is assessed by that of the living parent.

Other information sought from the medical records of the subjects included the various digestive system complications, method(s) of diagnoses, treatment given and outcomes using a semi-structured questionnaire.

**Ethical Clearance**

Ethical approval for the study was obtained from the Health Research Ethics Committee of UNTH, Enugu.

**Data Analysis**

Data were entered and analyzed using the statistical package for social sciences, SPSS, (IBM Corp, Armonk, NY 2012) version 21.0. Categorical variables were presented as frequencies and percentages while statistical significance of association between variables was assessed using *Chi-square* test. The level of statistical significance was set at $p<0.05$.

RESULTS

There were 350 children (215 males and 135 females) that attended the sickle cell clinic of the Department of Paediatrics, University of Nigeria Teaching Hospital (UNTH), Enugu as at the time of the review. Also, a total of 13, 769 paediatric admissions were registered over the period of study. Thirty-three of the SCA cases had serious digestive system

complications requiring hospitalizations giving a prevalence of *0.24%*.

Incidence of digestive system complications was 94.3 per 1000 children, and of the 33 children, 15 (45.5%) were males while the rest were females. Their mean age was 9.1± 4.8years(9months –18years).Nine (27.3%) of the patients belonged to the upper socioeconomic class, 8(24.2%) to the middle class while 16 (48.5%) were from the low social class.

The most common complication was acute abdominal crisis, seen in 12(36.4%) of the patients, followed by acute sickle cell hepatic crisis, 6 (18.2%). The least common complications were acute intestinal obstruction, cholecystitis/cholelithiasis and acute hepatic sequestration, each seen in 1(3.0%) of the admitted children, *see Table 1.*With *Chi-square* analysis, there was no significant socioeconomic predisposition to any of the digestive system complications (*p>0.05*).

Abdominal crises were the more common complication in those aged 10years and below, whereas hepatitis and peptic ulcer disease were more common in those above 10years, *see Table 1.* There was only one death (pre-operatively), in a teenage female, with acute intestinal obstruction giving a case fatality rate of 3% due to septic shock.

Diagnosis was made using imaging studies (plain abdominal x-ray and abdominopelvic ultrasonography). The child was initially managed as a case of presumed vaso-occlusive crisis (abdominal crisis) at home and only presented late in the disease. She was being co-managed with the paediatric surgical team in the hospital.

**Table 1.Trend of gastrointestinal and hepatobiliary complications of sickle cell anaemia among subjects according to age**

| Complication | 1 – 5 years | 6–10 years | >10 years | Total | Percentage |
|---|---|---|---|---|---|
| Acute abdominal crisis | 5 | 5 | 2 | 12 | 36.4 |
| Acute hepatic crisis | 1 | 4 | 1 | 6 | 18.2 |
| Viral Hepatitis B(CLD) | 1 | 0 | 3 | 4 | 12.1 |
| Recurrent Dyspepsia | 0 | 0 | 4 | 4 | 12.1 |
| Viral hepatitis C (CLD) | 0 | 1 | 1 | 2 | 6.1 |
| Acute hepatic failure | 0 | 0 | 2 | 2 | 6.1 |
| Acute intestinal obstruction | 0 | 0 | 1 | 1 | 3.0 |
| Acute Cholelithiasis | 0 | 0 | 1 | 1 | 3.0 |
| Acute hepatic sequestration | 0 | 1 | 0 | 1 | 3.0 |
| **Total** | **7** | **11** | **15** | **33** | **100** |

*Key: CLD- Chronic Liver Disease*

DISCUSSION

This study highlights the digestive system manifestations of this common genetic disorder, sickle cell anaemia (SCA), in our environment. The incidence of the digestive system complications in the present study was 94.3 per 1000 children. However, this was the first attempt to report comprehensively the digestive system complications of SCA) in our setting. Some isolated reports of single complications like acute hepatic crisis had been previously reported in Enugu.[12]

Acute abdominal pain crisis appeared to be the most common complication, necessitating hospitalization, among SCA children in the present study and it has also been reported to be quite common in this age group, by other workers.[7] The pain, which can either be generalized or solitary, has been attributed to ischaemia arising from vaso-occlusion of the mesenteric vessels.

Generally, when such cases of abdominal pain present, it is pertinent to exclude other possible differentials of acute abdominal pain including acute splenic sequestration, splenic

infarction/abscess, hepatobiliary conditions, ischaemic colitis, acute surgical abdominal causes including acute appendicitis, intestinal obstruction in addition to functional gastrointestinal disorders.[7,15,18]

It is recommended that, in order not to miss any of the above possible differential diagnoses particularly in solitary abdominal complaints with its likely morbidity and mortality consequences, a thorough history taking, specific physical examination in addition to appropriate laboratory and radiological imaging studies should be applied. A case of acute surgical abdomen who presented late was reported which was diagnosed with the aid of radiological imaging. However, the child died following a complicated acute intestinal obstruction.

Some cases of recurrent functional dyspepsia were observed. Diagnosis of recurrent dyspepsia were based on Rome III criteria as paediatric oesophageo-gastrointestinal endoscopy is not readily available in our setting.[15]Both conditions of recurrent dyspepsia and other ulcer-like conditions like peptic ulcer have been reported in SCA populations. The aetiology of ulcers in SCA has been attributed to the reduced mucosal resistance following repeated ischaemic infarction during crisis episodes.[19]

Children with haemoglobinopathies are known to develop pigmented gallstones and the risk increases with advancing age, and inheritance of HbSS.[20]Although only one case of cholelithiasis was reported in our study, some studies have observed frequencies of 4.1-16% among children/adults populations with SCD.[20,21,22]African literature suggests that cholelithiasis is uncommon among native African populations on account of their staple diet known to be rich in carbohydrates and fibres and less in lipids.[3]However, with increasing globalization and high consumption of 'westernized' fast food diets rich in fats, it is possible that the risk of cholelithiasis in the general Nigerian population, including SCA children, may have been on the increase.

Sickle cell anaemia is a chronic haemolytic anaemic state with recurrent acute exacerbations/crises requiring blood transfusions. Repeated transfusions increase the risk of development of transfusion related infections.[8] Emechebe, *et al,* and Ejiofor and colleagues working independently reported a prevalence of 8.1% and 8.3% for hepatitis B and C, respectively, in paediatric populations.[23,24] Some of our cases had hepatitis B or C infection resulting from possible blood transfusions and its attendant risks of chronic liver disease and cirrhosis. However, with the recent introduction of hepatitis B vaccination in the routine immunization schedule of the national programme on immunization the incidence of hepatitis B may be on the decline, including in SCA populations.

Also, repeated blood transfusions increase the chances of development of hepatic iron overload.[25] But, since chronic blood transfusion programme is not commonly obtainable in our setting, cases of hepatic iron overload may not be commonly reported.

Cases of acute sickle cell hepatic crisis were reported in the present study, just as in earlier studies by Kaine and Udeozor in Enugu over two and half decades ago.[12] The aetiology of acute hepatic crisis is not clear but, it has been postulated to be due to stagnation of sickled red cells within the liver sinusoids with resultant decrease in circulation in hepatic sinusoids.[26]

## CONCLUSION

Acute abdominal pain crisis is the most common digestive system complication of sickle cell anaemia in our setting. Efforts should be made to exclude other potential causes of acute abdomen requiring surgical intervention in children with sickle cell anaemia by ensuring a thorough history taking, diligent physical examination and relevant laboratory as well as imaging studies in order to save lives.

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