IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 7 Ver. 13 (July. 2018), PP 61-64
www.iosrjournals.org

Ultrasonographically Determined Autosplenectomy Rates In Nigerian Sicklers And The Predictors Running Title: Splenic Changes In Nigerian Sicklers

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Abstract
Background*: At birth, the spleen in sickle cell anaemia patients (SCA) is normal in size and function. With increase in age, there are repeated vaso-occlusions, multiple infarctions and splenic fibrosis resulting in atrophy and autosplenectomy. Early monitoring and detection are enhanced by ultrasonography of the spleen because the spleen responds to different pathologic states such as fever and SCA by dimensional and parenchymal changes.*
Objective*: This study aims to determine the prevalence of autosplenectomy by abdominal ultrasonography in SCA patients in Calabar, Nigeria.*
Methods*: A prospective study of 120 patients was carried out between January to June, 2018. Sociodemographic data was collected on each patient prior to physical examination. Abdominal ultrasonography examination was performed on all the recruited patients. Splenic longitudinal and transverse dimensions were measured and echogenicity documented.*
Results*: The median of age of the sickle cell subjects was 14.5% years. Out of the 120 sickle cell subjects 69(57.5%) were males while 51 (42.5%) were females. The prevalence of autosplenectomy was 32.5% and was higher with increasing age. There was no difference in splenic size by gender. Only 1(0.83%) of the study had splenomegaly and 3(2.5%)had splenic atrophy. The youngest patient with SCA was 9 years old.*
Conclusion*: Autosplenectomy is a common finding in SCA patients and it increases with age. As survival improves in SCD in Nigeria, autosplenectomy rate is increasing. A review of the vaccination programme forsicklers with possible booster doses of vaccines such as the pneumococcal vaccine in adolescentsand adulthood is recommended.*
Key Words*:Autosplenectomy, Sickle Cell Anaemia, Ultrasonography.*

Date of Submission: 12-07-2018 Date of acceptance: 27-07-2018

I. Introductions

Sickle cell disease (SCD) is a common autosomal recessive genetic disorder of the blood characterized by a defective form of haemoglobin (Hb) synthesis with production of an abnormal form known as sickle haemoglobin (HbS).[1,2] It is among the most common of the inherited haemoglobinopathies.

The spleen is the most frequently affected organ in SCD mainly due to its reticuloendothelial function and complex anatomy.[3,4] It has a slow tortuous microcirculation that favours sickling of red blood cells and as a consequence splenic infarctions are very common.[5,6]With increase in age, there are repeated vaso-occlusions, multiple infarctions and splenic atrophy.[7] The spleen is eventually reduced to a siderofibrotic mass. This process occurs at about 6-8years and is known as auto-splenectomy. Usually by the eight-year, most SCA patients do not have a clinically palpable spleen.[7]

In the tropics however, splenomegaly may persist into adulthood due to tropical splenomegaly syndrome resulting from the malaria parasite.[8]

Focused clinical follow-upand the gradual introduction of a broad range of life saving measures (including penicillin prophylaxis, vaccination for common bacterial diseases, training of parents to detect splenic sequestration events and provision of disease-modifying treatment with hydroxy-urea) andvaso-occlusive episodes and have led to an increased life expectancy among people with SCD in many affected countries. Hence, older people with complications are now seen.[9,10]It is important therefore to define changes in the spleen in this emerging scenario.

The aim of this study was to determine the prevalence of autosplenectomy among SCA patients in the University of Calabar Teaching Hospital, Calabar, Nigeria. Findings from the study are expected to help define splenic changes among sicklers in this region and inform management decisions.

II. Patients And Methods

This was a prospective study conducted over a 6 month period (January to June, 2018) to determine the prevalence of autosplenectomy by abdominal ultrasonography in homozygous sickle cell disease patient in Southern Nigeria.Patients of all ages who were attending the Sickle Cell and Haematology clinics at the University of Calabar Teaching Hospital, Calabar, Nigeria were consecutively recruited into the study. Demographic data including anthropometry were obtained from theparticipants prior to a physical examination done under conditions of privacy.

The study population was made up of non-pregnant SCA patients in steady state and who had not had surgical splenectomy. Informed consent was obtained from all subjects in the study.

Ultrasound examination was performed using B-mode Mindray Ultrasound machine with a 3.5 – 5.0 MHz probe. Transabdominal ultrasonography was done with the patient at the rightlateral decubitus position in the coronal plane because of the superior advantage of obtaining easily the longest dimension of the spleen and reproducibility of measurements. Longitudinal size measurement was measured between the supero-medial and the most inferolateral points of the spleen. The transverse dimension was measured between the hilumand the most superolateral margin of the spleen.Autosplenectomywas defined as the non visualization of the spleen; while splenomegaly meant that the long axis of the organ is longer than 130 mm.[7] Splenomegaly was defined as "mild" if the two measurements exceeded the upper limit of normal by less than 10%; "moderate" when the measurement was 10% to 20% greater; and "marked" when the measurement exceeded the upper limit of normal by more than 20%.[8] A shrunken spleen was defined as the long axis of the spleen measured less than 50 mm. Spleen sizes were measured two times, and the mean values were recorded. The measurement of the splenic dimensions was made during deep inspiration.

Ethical clearance was obtained by the Health Research Ethics Committee of the University of Calabar Teaching Hospital, Calabar.

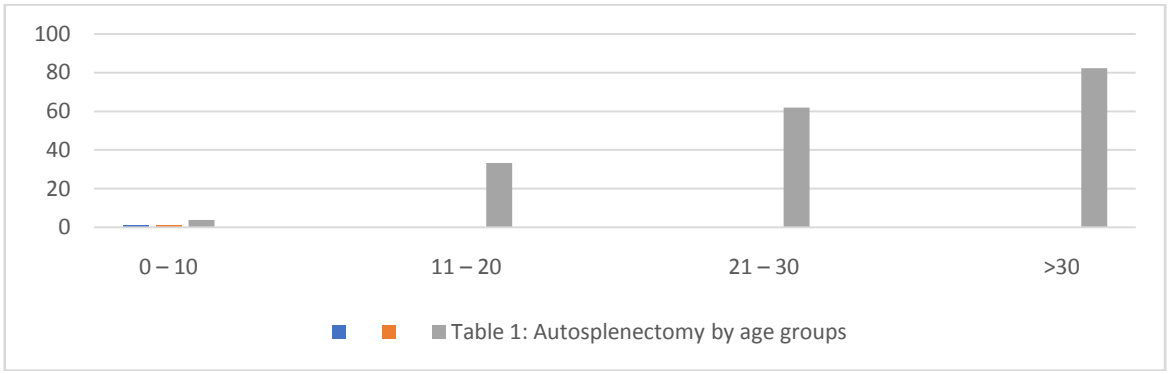
III. Statistical Analysis

The data were analysed with the Statistical Package of Social Sciences (SPSS) software version 18 for window. Simple proportions, percentages and graphs were used to analyse the data. Chi-square test was used to test difference between categorical variables. Student's 't' test was used to compare continuous variables odd ratio and multiple regression analysis were used to identify predictors of gall bladder stones. p value of <0.05 was regarded as significant.

IV. Results

One hundred and twenty confirmed SCA patients aged 1.5-55 years were studied. The median age was 14.5 years(IQR 6-25 years). Fifty-two (43.3%) were aged below 10 years; 30 (25.0%) between 11 and 20 year; 21 (17.5%) between 21 and 30 years and 17(14.2%) more than 30 years. There were 69 (57.5%) males and 51(42.5%) females. The prevalence of autosplenectomy was 32.5% (95%CI 24.2%-41.7%).This prevalence was much higher in individuals more than 10 years old – 54.4% (95% CI 41.9 – 66.5%). It was less common in those less than 10 years of age, 3.8%(95% CI 0.5-13.2%). The largest number with autosplenectomy was in the age group 30 years and above (Table 1).The youngest subject with autosplenectomy was nine years. By the age of 20 years, about a third of SCA patients already had autosplenectomy, and by the age of 30, 61.9% had autosplenectomy.Only 1(0.83%) of the study population had splenomegaly.

There was no difference in splenic size by gender. Three (2.5%) had splenic atrophy.



$\chi^2 = 47.01$; p = 0.000

Figure 1: Autosplenectomy Rates among 120 sicklers

V. Discussion

The spleen is the main filter for blood-borne pathogens and antigens: a key organ for iron metabolism and erythrocyte homeostasis as well as maintaining immune and hematopoietic functions.[11] A reduction in size of the spleen affects these major functions The spleen in sickle cell anaemia at birth is normal in size and functiondue to the abundance of fetal Haemoglobin (HbF).[12] With gradual but progressive replacement of HbF with HbS splenic manifestations (splenomegaly, splenic atrophy and autosplenectomy) begin to set in.[13]

In this study, the overall prevalence rate of autosplenectomy in the study population was 32.5%(95% CI 24.2 – 41.7%) as determined by non-visualization of the spleen during ultrasonography. This is at variance with a study by Babadoko et al[19] in Zaria Nigeria who reported the prevalence of autosplenectomy as 55.4% and Attalla et al[20] reported 47.8%. Reports from Jamaica and the US documented autosplenectomy in most adult patients with SCD.[8,13]

The low rate of autosplenectomy in our environment could be attributable to geographical variation since studies have shown that variations exist in splenic size and parenchymal echo-texture of SCD patients due to differences in race, haplotype, ethnicity and clime.[14,16,17] However, autosplenectomy was higher in our study compared to the reports from Saudi Arabia by Al-Salem et al[18] where out of 363 studied patients, only 24 (6.6%) of patients had autosplenectomy.The prevalence of autosplenectomy in our study is much higher in individuals more than 10 years old(54.4%) and less common in those less than 10 years of age. By the age of 20 years, about a third of SCA patients already have autosplenectomy and by age 30 61.9% had autosplenectomy. The youngest SCA patient with autosplenectomy was 9 years in this study.

Thus, autosplenectomy is usually increasedwithage as also reported by Esan2 et al and Babadoko et al.[14] There was no appreciable difference in splenic size by gender in our study and splenic atrophy was seen in 2.5% of the study population. Babadoko et al[14] reported splenic atrophy in 23(31%) out of the 74 subjects studied. Similarly, Awotua-Efebo et al[16] and Ahmed et al[17] documented higher rates of splenic atrophy. The lower incidence of splenic atrophy in our study could be attributedto differences in study protocol, clime and haplotype.The low rate of splenomegaly in our study 1(0.83%) when compared to the 21.1% rate in a study conducted by Ma'aji et al[19] in Sokoto, Nigeria may be due to the younger age group in their study.

VI. Conclusion

Autosplenectomy is a common finding in SCA patients and it increases with age. As survival improves in SCD in Nigeria, autosplenectomy rate is increasing. A review of the vaccination programme for sicklers with possible booster doses of vaccines such as the pneumococcal vaccine form early adolescence is recommended.

Acknowledgement

We are grateful to Dr. Nchiewe Ani and Dr. Affiong Ngaji of the Department of Radiology, University of Calabar, for their immense support in carrying out this study. We also appreciate Dr Joan Ikobah of the Department of Paediatrics and Dr. Marcus Inyama of the Haematology Department, University of Calabar for their contribution.

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Ekanem EE"Ultrasonographically Determined Autosplenectomy Rates In Nigerian Sicklers And The Predictors Running Title: Splenic Changes In Nigerian Sicklers."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 7, 2018, pp 61-64.