SOCIODEMOGRAPHIC AND CLINICAL FACTORS PREDICTIVE OF POOR HEALTH-RELATED QUALITY OF LIFE OF CHILDREN WITH SICKLE CELL ANAEMIA IN THE GAMBIA.

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Abstract

Background: Children with sickle cell anaemia (SCA) experience recurrent vaso-occlusive crises and complications, often impacting on their health-related quality of life (HRQoL). This study determined HRQoL of 130 children aged 5 - 15 years with SCA and compared to 130 age- and sex-matched apparently healthy haemoglobin AA children in The Gambia. It also determined the impact of sociodemographic and clinical data on HRQoL of these children.

Method: HRQoL was determined using Pediatric Quality of Life Inventory (PedQL). HRQoL score <69.7 was defined as poor HRQoL. Sociodemographic and clinical factors predictive of poor HRQoL were determined by binary logistic regression analysis.

Results: The two groups had similar means ages 9.83 ± 2.79 years for HbSS and 9.65 ±2.84 years for HbAA group, p=0.598, with a male: female ratio 1.1:1. There was significant underweight (p = 0.019) and stunting (p = 0.045) among children with SCA than HbAA. The mean HRQoL scores were also significantly lower in SCA than HbAA children in the physical, emotional, social, school and overall health domains, p<0.001. Seventy-five (57.7%) of SCA patients had poor HRQoL. Significant pain >3 episodes in the preceding 12 months (OR=1.9; 95% CI=1.392 – 2.201; *p*=0.028); late diagnosis (OR=1.8; 95% CI=1.697–1.957; *p*=0.012); and clinical stroke (OR=69.3; 95% CI=1.337–89.36; *p*=0.037) were identified as significant independent predictors of poor overall HRQoL among children with SCA.

Conclusion: SCA has a negative impact on all domains of HRQoL. Frequent significant pain crises, late diagnosis and stroke were independent predictors of poor HRQoL among Gambian children with SCA.

Keywords: Children, Health-related quality of life, Sickle cell anaemia, The Gambia, Clinical factors, Predictors.

INTRODUCTION

Sickle cell anaemia (SCA), the most severe form of sickle cell disorders, is caused by mutation in the sixth amino acid of the β-globin gene. It is inherited in an autosomal recessive pattern [1,2]. Sickle haemoglobin (HbS) results from a single base pair replacement of adenine with thymine, at the sixth codon of the β-globin gene [1,2]. This point mutation leads to the replacement of glutamine with valine at the sixth position of the β-globin molecule [1-3].

Children with SCA often start manifesting symptoms by six months of life, due to the protective effects of foetal haemoglobin (HbF) which gradually reduces at about this age. However, manifestations could be as early as 4 months of age depending on the level of decline of HbF [4,5]. These manifestations include vaso-occlusive crises such as dactylitis (hand foot syndrome), bone pain and abdominal pain crises. Others include features of chronic haemolysis, increased susceptibility to infections particularly malaria and pneumococcal infections and multi-organ damage [4,6].

It is estimated that about 400,000 babies are born each year with SCA globally; 75 percent of these babies are born in the tropical regions of sub-Saharan Africa which are home to most of the over 25 million people who live with SCA globally [7]. In The Gambia, using Hardy-Weinberg equilibrium, Grosse *et al.* in 2011 estimated newborn prevalence of sickle cell anaemia in the country from two previous studies as 1.2 percent and 0.8 percent respectively [8-10].

The term Health Related Quality of Life (HRQoL) is often described as the health aspects of quality of life and is generally considered to reflect the impact of disease and treatment on ability and daily functioning [11]. It has also been considered to reflect the impact of perceived health on an individual's ability to live a fulfilling life [11].

Sickle cell anaemia being a chronic disorder will potentially affect physical, mental, emotional and psychological domains of children and adolescents as well as that of their parents and caregivers. Children with SCA have been reported to have significantly lower HRQoL compared to their healthy counterparts without the SCA [12]. However, to the best of the investigator's knowledge, there is paucity of studies on SCA in children and adolescents in The Gambia and none has been done on the effects of the disease on HRQoL in Gambian children. In addition, socio-demographic and clinical factors that may be associated with the HRQoL may differ from one region to another, and these have not been explored in The Gambia.

This study aimed to determine the HRQoL of children aged 5 – 15 years with SCA and to compare such to their age- and sex-matched apparently healthy haemoglobin AA counterparts. It also determined the socio-demographic and clinical factors associated with HRQoL in these children.

METHODOLOGY

Study Design: This study was a hospital based comparative cross-sectional study.

Study site: The study was carried out at the Paediatric Department of Edward Francis Small Teaching Hospital (EFSTH), Banjul, the only tertiary hospital in The Gambia.

The Paediatric Haematology Clinic is one of the paediatric specialist clinics in the hospital. This once-a-week clinic offers general and specialist care to children with SCD and it is run by a Consultant Paediatrician assisted by a Senior Registrar and two Registrars. There are over 300 children with SCD on the clinic register, out of which an average of 30 patients are reviewed weekly. Haematinics, antimalarial and penicillin chemoprophylaxis are prescribed routinely. Some of the patients are also on hydroxyurea.

Study Population: The population for this study was children with SCA in steady state aged 5 – 15 years who were attending the SCD clinic for routine follow up visit. Age and sex-matched apparently healthy children with Hb AA (comparison group) comprised children on routine pre-school entry care medical tests, or those for follow up after minor illness and whose haemoglobin genotype has been confirmed as AA in the laboratory unit of EFSTH. These children (controls) were recruited from the Paediatric Outpatient Department of the hospital as shown in Figure 1.

Figure 1: Flow chart showing recruitment of the study participants.

Children aged 5 to 15 years confirmed to have haemoglobin SS genotype by alkaline cellulose acetate electrophoresis, in steady state and whose parents gave written consent and older children (7 years and above) gave assent were included in the study. Steady state was defined according to Ballas SK *et al.* [13] as a period during which a child with SCD is free of crisis (painful or haemolytic), infection or any other acute illness for at least four weeks after the last episode of

crisis and at least three months after the last transfusion. Children with haemoglobin AA whose parents gave written consent and older children (7 years and above) gave assent were included in the study. Children with SCA and HbAA with chronic illness were excluded from the study.

Sample size calculation:

The minimum number (n) of patients needed for the study was calculated using the formula for comparing two independent means in a case-control study [14].

Minimum sample size n was = 127; which was approximated to 130. Hence, 130 children with sickle cell anaemia and 130 children with Hb AA were recruited for this study.

ETHICAL CONSIDERATION

Ethical approval for this study was obtained from the Research Ethics Committee of the EFSTH, Banjul, The Gambia. The investigator explained the purpose and aim of the study to the participants and their caregivers in the language they understood. This was done according to participant information sheet and written informed consent and/or assent which were obtained before recruitment. The procedure and scope of the study, purpose, benefits were explained to the children as well as to their parents/caregivers.

The identity of participants was concealed by assigning participants' initials, and not full name to the collected data. The proforma were safely kept, while the electronic copies of the data were held on password-protected computers. The study was at no cost to the participants.

Data Collection

Consecutive children with SCA who fulfilled the inclusion criteria were recruited until the desired sample size was reached. Also, the comparison group was selected consecutively after matching for age and sex, until sample size was reached. A data proforma was used to obtain information

about socio-demographic characteristics such as age at last birthday, sex and socio-economic class of participants as described by Ogunlesi [15]. It was graded on a score of 1 to 5; 1 being the highest (Class I) and 5 the lowest (Class V). Classes I and II were further classified as upper social class, class III as middle social class, while IV-V were classified as lower social class.

Information on the age at diagnosis of SCA was documented. This was dichotomised into early diagnosis, if the diagnosis was made in the first year of life, or late diagnosis, if diagnosis was made after infancy. Information on the use of hydroxyurea was also obtained. Data on SCD complications such as stroke, acute chest syndrome, avascular necrosis of head of femur/ humerus (AVN), priapism, leg ulcer, osteomyelitis/septic arthritis, etc. were collected historically and verified by checking medical charts in the SCD registry of EFSTH. Significant painful episode was defined according to Ballas et al [13] as pain episode that requires hospital visit and the use of analgesia.

Anthropometry, including weight and height of all study participants was measured. The participants' weights were checked using SECA Digital weighing scale (model 345621 4567). The weighing scales were standardised daily using a mass of known weight, and the scales adjusted to zero before taking each measurement, recorded to the nearest 0.1 kilograms. The participants' heights were measured to the nearest 0.1cm using an RGZ-160 stadiometer by Leaidal Medical Ltd, United Kingdom (UK). The participants were made to stand erect without shoes and headgears, with both feet placed together, the heels, the calves, the buttocks and the occiput touching the wall and the participants looking straight ahead or in the Frankfurt plane.

The nutritional status of the children was derived from their anthropometry and interpreted based on the WHO Z-scores for age and gender. Children with Z-score values between -2 Standard Deviations (SD) and +2SD were regarded as normal. Stunting was defined as Z-score height for

age below -2SD. Underweight was defined as a weight below -2SD for age and gender. Wasting was defined as a weight below -2SD for height and gener. Overweight was defined by BMI-Z > 2 SD but ≤ +3 from the mean; and obese if BMI-for-age Z-score was >3 from the mean. Normal weight was BMI-for-age Z-score within the mean ±2 [16]. Calculation of Body Mass Index (BMI) was done using the formula, weight in kilograms/ height^2 (kg/m^2).

Subsequently, the venepuncture site was disinfected with methylated spirit, and one millilitre of venous blood was collected into the EDTA bottle for haematological indices at the Paediatric laboratory of the hospital. Analysis of the sample was done using ABX micro ES 60 automated haemoanalyser (Siemens, Vienna Austria) within three hours of blood collection.

Assessment of Health-Related Quality of life (HRQoL)

This was done using the Pediatric Quality of Life Inventory (PedsQL) – Child/Adolescent Report Version 4 Questionnaire. This instrument was chosen because the questionnaire is brief, easy to administer, culturally appropriate and has ability to distinguish between healthy children and children with chronic health conditions such as SCA. Health-related quality of life has a high internal consistency and reliability for the Total Scale Score (Cronbach's alpha = 0.88 child report)[17].The scale was translated verbally back and forth in the three major languages in The Gambia: Mandinka, Fula and Wolof.

Four domains and overall (also known as total) HRQoL scores were determined. Eight parameters were scored for physical functioning domain, while five parameters each were scored for the three psychosocial functioning domains – emotional, social and school functioning domains. In all, 23 parameters were scored. Scores for each parameter ranged from 0 to 4, with 0 score for event that

never happened, 1 for those that almost never happened, 2 for events that sometimes happened, 3 for those that often occurred and 4 for those always experienced.

To allow for ease of interpretability, with higher scores denoting higher HRQoL, reversed scoring was subsequently done to transform 0 – 4 scale items to 0 – 100, such that 0 became 100; 1 became 75; 2 was scored 50; 3 was scored 25; and 4 scored 0 [17].

For each participant, the domain score was the average scores of all parameters in that domain, i.e., the sum of the items scored divided by the number of items answered. When more than 50% of the items in the scale are missing, the domain scale score would not be computed. The overall HRQoL score was the average scores of physical, emotional, social and school functioning HRQoL, i.e., sum of the four domains HRQoL divided by four. From a previous study, the established cut off below which a child is considered to have poor quality of life is when the overall HRQoL is <69.7 for children 5 years and above [18].

Data analysis

Data were checked by the investigator for correctness and consistency and analysed using SPSS for windows version 22 statistical software (IBM Corp., Armonk, NY, USA). Categorical variables like age group, sex and socio-economic classes were summarised using percentages and proportions and were compared using Pearson's chi square test. Continuous variables like age, weight, height, and HRQoL scores were summarised using mean and standard deviations after they were tested for normality using the Kolmogorov-Smirnov test which revealed normal distribution. Age at diagnosis was however described with median and interquartile range, IQR, because it was not normally distributed. Comparison of the mean (SD) of HRQoL scores between children with SCA and comparative group HbAA children was determined using student (independent sample) t-test. Association between sociodemographic characteristics and HRQoL

of children with SCA was determined by comparing the mean HRQoL between gender, age groups, ethnic groups and social classes using independent sample t-test or ANOVA, as appropriate.

Participants were classified as having poor or good scores based on the established cut-off overall HRQoL score of 69.7. Poor HRQoL was the primary outcome measured [11]. Study, or predictive factors included sociodemographic variables (gender, age group, socioeconomic class) and nutritional status. Other factors such as disease-related data (age at diagnosis, number of significant painful episodes, transfusion, hospitalisation in 12 months preceding the study), and use of HU. They were also included in the binary logistic regression model used to determine the independent predictors of poor HRQoL among the children with SCA. Effect size was interpreted as mean difference or odds ratio, while P-values < 0.05 was considered statistically significant at 95% Confidence interval (CI).

RESULTS

The 260 children studied were recruited over a seven-month period. These comprised 130 children with SCA who routinely attend paediatric SCD clinic and another 130 apparently healthy children with confirmed haemoglobin AA who visited the paediatric outpatient department for routine medical pre-school entry tests or those for follow up after minor illness.

Socio-demographic characteristics of the 260 study participants

Table I shows the socio-demographic characteristics of the 260 study participants. There was an overall male preponderance (53.1%) with a male to female ratio of 1.1:1. There were 69 (53.1%) males and 61 (46.9%) females in each arm.

The ages of the 260 study participants ranged from 5 to 15 years with a mean (SD) age of 9.74 ± 2.81 years. Also, the mean ages of the two groups were similar, 9.83 ± 2.79 years for HbSS, and 9.65 ± 2.84 years for HbAA group, $t = -0.529$, $df = 258$, $p = 0.598$. Children in the age group 8 – 10 years, 99 (38.1%) and Mandinka ethnicity, 120 (46.2%) had the highest representation. Other major ethnic groups included Wolof (17.7%), Fula (14.2%) and Jola (8.9%). The ethnic group distribution was not significantly different between HbSS and HbAA arms, $\chi 2 = 5.617$, $df = 4$, $p = 0.230$.

Only 15 (5.8%) of the total 260 children in this study belonged to the upper socioeconomic class (i.e., classes I and II). The 15 comprised of 3 children (2.3%) with HbSS and 12 (9.2%) HbAA children ($\chi 2 = 4.528$, $p = 0.033$). While 52 (20.0%) of all the participants were from the middle

socioeconomic class (class III), the majority, 193 (74.2%) were from the lower socioeconomic class (classes IV and V).

Table I: Sociodemographic characteristics of study participants

Anthropometry and nutritional status of the 260 participants.

The weight of the children with SCA ranged from 12.4 – 70.0 kg, with a mean of 26.69 ± 9.72 kg, which was significantly lower than 30.97 ± 13.25 kg for those with HbAA, t = 2.835, p = 0.005. Weight range of children with HbAA was 13.4 – 56.0 kg.

The height of the children with HbSS was 132.81 ± 15.27 cm, ranging from 93.0 – 170.3 cm. For HbAA children, height ranged from 106.7 – 170.0 cm, and the mean ± SD was 117 ± 25.7cm. There was no significant difference in the mean height of both groups, t = 0.478, p = 0.663.

Table II shows that underweight and stunting were more prevalent among children with HbSS than those with HbAA (29.2% vs. 16.9%, t = 5.547, p = 0.019; and 14.6% vs. 6.9%, t = 4.002, p = 0.045 respectively).

Table II: Nutritional status of the study participantsAge at diagnosis of sickle cell anaemia and use of hydroxyurea

The age of diagnosis of SCA ranged from 9 months to 14 years, with median (IQR) of 3.0 (2.0, 6.0) years. None of the children was diagnosed in the newborn period or before the first 9 months of life. Twenty-four (18.5%) were diagnosed between age of 9 and 12 months. The majority, 68 (52.3%) were diagnosed when aged 1 – 5 years and remaining 38 (29.2%) after age of five years.

Ninety (69.2%) of the 130 children with SCA were using hydroxyurea at the time of recruitment.

ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE

In addition to the overall HRQoL scoring, HRQoL was also assessed in the four domains, viz: physical, emotional, social and school functioning. Supplementary data I to IV show mean ± SD HRQoL scores of assessed individual parameters in these domains as well as the domain's average score. Table III shows the overall HRQoL scores.

Physical functioning HRQoL

The mean scores for the eight individual parameters and the average physical functioning HRQoL are shown in supplementary Table I. The mean ± SD overall physical functioning HRQoL score was 76.99 ± 27.78 for all the study participants (both HbSS and HbAA groups). As shown in the Table, the mean HRQoL scores were significantly lower among children with SCA in all parameters of physical functioning, $P < 0.001$ in all instances. Among children with HbSS, the scores were poor for "I hurt or ache" (45.77 ± 24.14), "I find it hard to do sports/exercise" (46.88 ± 33.35) and "It is hard for me to run" (47.87 ± 34.80). The highest score for this group of children was in the area of taking bath or shower by self (76.01 ± 34.69).

Emotional functioning HRQoL

Supplementary Table II shows the mean scores of the assessed five parameters and the average emotional functioning scales. The mean average emotional functioning HRQoL score was 86.15 ± 21.73 for all the study participants. In all the assessed parameters, the mean HRQoL scores were significantly lower among SCA group than haemoglobin AA, $p<0.001$.

Social functioning HRQoL

From Supplementary Table III, the mean social functioning HRQoL scores were significantly lower among SCA group than haemoglobin AA in all the five assessed parameters, $p<0.001$. The average social functioning HRQoL score for all the study participants was 84.94 ± 23.14. This

average score was also significantly lower among children with SCA (75.19 ± 25.56) than 98.27 ± 5.24 for children with haemoglobin AA, t = 11.346, p<0.001.

School functioning HRQoL

From Supplementary Table IV, the average school functioning HRQoL score for all the study participants was 76.99 ± 24.39, lower among SCA group (58.73 ± 19.84) than the HbAA group (96.93 ± 7.19), t = 19.844, p<0.001. The mean school functioning HRQoL scores were also significantly lower among SCA group than haemoglobin AA in all the five assessed parameters, p<0.001. Children with SCA had lowest mean scores for "I miss school to go to the doctor or hospital" and "I miss school because of not feeling well", 35.77 ± 23.49 and 40.58 ± 18.49 respectively.

Overall HRQoL scores of study participants

Table III shows that the overall HRQoL score for all study participants was 79.33 ± 24.08. This overall (total) health score was significantly lower among children with sickle cell anaemia (60.96 ± 21.03) than children with haemoglobin AA (98.34 ± 3.21), t = 18.931, p<0.001. The Table also shows that the mean HRQoL score was lowest (76.99) in the physical and school functioning domains. The average score in the three psychosocial functioning domains combined (Emotional, Social and School) was 82.36 ± 21.52.

Table III: The Mean Overall/Total HRQoL scores of children with sickle cell anaemia and apparently healthy children with haemoglobin AA

Supplementary data IV compared HRQoL scores between children with SCA and those with Hb AA within the age groups. In all age groups, the scores were significantly lower in children with SCA than the comparison group, p < 0.001. While physical and school functioning domains were low in all age groups, the social domain reduced progressively across the age groups.

Association between sociodemographic characteristics (age, sex, socio-economic status, ethnicity) and HRQoL among children with SCA

Table IV described association between HRQoL of children with SCA and their sociodemographic characteristics such as age group, sex, socio-economic status and ethnicity. Comparison of mean scores showed that children aged 14 – 15 years had lower mean HRQoL score in emotional and social functioning domains than other age groups, though the difference was not significant statistically. In the same way, males, although had lower mean HRQoL scores in the three psychosocial domains (emotional, social and school) than females, the differences were not significant statistically. With ANOVA, there was no statistical difference in the mean HRQoL scores among the three social classes in all domains (Table IV). The three children with SCA in the upper social class (I and II) had non-statistically significant higher mean HRQoL scores in all the four domains and in the overall score, when compared to children from other social classes. While SCA children who are of Jola ethnicity had the highest mean HRQoL scores in all domains, those who are Wolof had the lowest mean HRQoL scores.

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Table IV: Mean HRQoL and sociodemographic characteristics of children with sickle cell anaemia

Sociodemographic and some disease-relatedd events predictive of poor Overall HRQoL among the children with SCA.

Binary logistic regression analysis was undertaken to demonstrate the influence of socio-demographic and SCD-related data on poor Overall HRQoL. Using the established Overall HRQoL cut-off value of ≤ 69.7 as poor HRQoL, 75 (57.7%) of the 130 children with SCA had poor Overall HRQoL and the remaining 55 (42.3%) had good Overall HRQoL.

SCD-related data included in the logistic regression model were age at diagnosis (early or late diagnosis); nutritional status (underweight and stunting); use of hydroxyurea (HU); occurrence of

complications. Number of significant painful episodes, admissions or transfusions in the preceding 12 months were categorised into episodes >3 or ≤ 3 and were also included in the model.

Initial bivariate analysis showed that age, sex, social class and ethnicity had no significant association with HRQoL. The mean Overall HRQoL scores of those using HU was 62.52±21.04, while it was 57.58±20.89 for those not using the drug (t = -1.200, P = 0.233). Although higher proportion, 41 (45.6%) of the 90 children using HU, compared to 14 (35.0%) of the 40 not using it had good HRQoL, the difference was not statistically significant, $\chi 2 = 1.264$, P = 0.261.

As shown in Table V, significant painful episodes on more than three occasions in the preceding 12 months (OR = 1.9; 95% confidence interval, CI = 1.392 – 2.201; *p* = 0.028); late age at diagnosis (OR = 1.8; 95% CI = 1.697 – 1.957; *p* = 0.012); and clinical stroke (OR = 69.3; 95% CI = 1.337 – 89.36; *p* = 0.037) were significant independent predictors of poor Overall HRQoL among children with SCA.

Table V. **Binary logistic regression analysis showing sociodemographic and some disease related events as predictors of poor Overall HRQoL among the children with SCA.**

DISCUSSION

This study focussed attention on child/adolescent reported QoL scores and found that SCA is associated with limitations in HRQoL of Gambian children and adolescents in all the assessed domains. The study also highlighted the predictive effects of numerous pain episodes in the preceding 12 months, late diagnosis and stroke on poor quality of life.

In all domains, HRQoL scores were lower among SCA group than those found for haemoglobin AA children of the same age and sex. Other previous studies have also reported lower QoL scores among children with SCA compared to non-sickle cell children and adolescents. This has been ascribed to the chronicity of SCA with its attendant crises and complications[19]. In the USA, one previous study reported that the occurrence of acute crises in SCD was a major factor that negatively influenced all domains of both the patients and parent report of PedsQL scales [20]

HRQoL scores in the physical functioning domain was lowest in the parameters “I hurt or ache”, “I find it hard to do sports/exercise” and “It is hard for me to run”. The scores in these parameters were lower than the average physical domain score. This finding is similar to a report by Alharbi et al in 2016. They found that most children and adolescents with SCA in Mecca always felt it hard to do sports, walk or run [21].

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The impact of SCA was most on physical domain, since this domain had the lowest HRQoL score of the four domains assessed. This will undoubtedly affect the independence of the child as well as increase stress and burden of care on the caregiver. It might also contribute to the reduced scores in other domain as the child’s physical interaction to the environment is significantly limited**.** Similar findings were observed in a study by Asnani et al., although, they used the WHOQOL-BREF criteria for measuring QoL in SCD [22]. They postulated that poor physical functioning in

SCD patients accounted for more medical consultations in them when compared to other patients with chronic diseases.

Emotional and social functioning were also significantly affected with the "I cannot do things that others can do" being more affected than other items in the latter domain. School functioning was also significantly lower among children with SCA than the counterparts with the score for missing school being the lowest. Parameters "not feeling well" or "go to the doctor or hospital" were more severely affected than other items in this aspect. This negative impact, particularly in the emotional and school functions, has been linked strongly with recurrent pain episodes in individuals with SCA [23]. Robust school health programmes should therefore be developed for these children with a view to reducing the impact of frequent school absenteeism on the child's perception of self-worth[24]. School teachers should put these findings into consideration by providing additional lessons for these pupils especially when they missed school. There should be functional school health services for early detection and institution of care of children with crisis, and hence reduce school absenteeism.

In the present study, there was no significant difference in the HRQoL scores between male and female children with SCA. This is consistent with the findings of Kamble and Chatruvedi who also reported that both genders were equally affected in children [25].It is also in agreement with a study done by McClish *et al*. in the US [26] and a study done in Northern Nigeria[27].This is probably due to the fact that both groups of patients (males and females) received treatment from the same health-care providers. Another plausible reason for this finding may be because gender has been noted not be related to SCD severity[28].Alharbi *et al* in Mecca, Saudi Arabia, however reported that boys were more affected than girls, unlike some other studies that found that females were more affected[24]. In a study that examined influence of gender on SCD knowledge and QoL

in adolescents with SCD in Jamaica, the authors reported the baseline results on 76 girls and 74 boys who were recruited in a large intervention study. They found that girls had higher knowledge scores, poorer overall QoL scores (70.1 ± 19.6 vs. 77.2 ± 17.8, p = 0.02) and significantly lower scores on many QoL domain scores [28]. As previously reported, these outcomes may result from hormonal effects of puberty and differences in gender roles which also begin to occur during adolescence.

This study also did not find any significant difference in HRQoL within age groups among children with SCA, unlike Pereira and colleagues [29] who found significant difference in QoL scores between age groups 5 to 7 years (score of 72.10) and 8 to 12 years (score of 65.36). In a study on biopsychosocial predictors of QoL of adolescents with SCD at Guy's and St Thomas' Hospital and King's College in the UK, age did not independently predict HRQoL [30] Since patients recruited in this current study were from the same geographical region and attended the same SCD at EFSTH, the only teaching hospital in The Gambia, this may explain why demographic factors such as age and gender had less influence on HRQoL scores.

Although, there was no observed difference in the mean HRQoL scores across the three social classes (upper, middle and lower) using ANOVA, the three children with SCA in upper social class (I and II) had higher scores when separately compared to the other two classes. These differences were remarkable in the physical, school and overall health domains. These could be attributed to caregivers' understanding of the disease, institution of preventive care and timely access to treatment. Hence, efforts should be made to improve the social class of caregivers by creating accessible educational opportunities and increasing their earning capacities.

Late diagnosis of SCD, defined in this study as diagnosis after infancy; significant pain greater than 3 episodes in 12 months preceding the study, and at least one clinical stroke event were the identified independent predictors of poor HRQoL in this study. Early diagnosis and timely intervention is expected to reduce pain episodes and other severe complications like stroke [31].

Hydroxyurea as a treatment does not only improve health outcomes clinically and haematologically for patients with SCD by decreasing disease complications and reducing mortality; it also has a potential positive impact on mental and social wellbeing, and the overall quality of life [32,33]. In the present study, however, the drug was not found to be a protective factor against development of poor HRQoL [19], possibly because the actual duration of use and compliance to therapy could not be ascertained. Addressing barriers to hydroxyurea adherence such as continued availability and better drug perception can additionally positively strengthen the relationship between adherence and HRQoL [32]. It is also possible that those on hydroxyurea initially had low HRQoL (since those on the drug are more likely to have complications and more painful episodes), but HU use had just started improving their HRQoL. The actual influence of HU on HRQoL would indeed be more obvious in a Pre and Post-HU study design and or when a cohort of patients with SCA who has similar baseline HRQoL are randomised to either HU and no-HU therapy groups, especially when introduced early.

The result of this study unravelled significant differences in the HRQoL scores between children with SCA and those with Hb AA in all domains. These findings strengthen the need for SCD preventive programs and multidisciplinary approach, especially psychosocial intervention to the problem.The study has some limitations. First, the diagnosis of stroke as a complication of sickle cell disease was based on clinical definition, rather than by MRI, since some patients might have

been missed without MRI. Our inability to ascertain compliance to hydroxyurea among those using the drug at the time of recruitment for this cross-sectional study.

It can be concluded from this study that HRQoL scores were significantly lower in all domains of assessment among children with SCA compared to apparently healthy haemoglobin AA children of similar ages and sex distribution. Also, 57.7% of the 130 children with SCA had poor Overall HRQoL. Significant pain episodes more than three in the preceding 12 months, late diagnosis and presence of clinical stroke event were identified as independent predictors of poor overall HRQoL among children and adolescents with SCA.

It is recommended that efforts should be made to strengthen comprehensive SCD care in the country. This should include neonatal screening for early diagnosis, active prevention and management of pain episodes and lifetime complications, especially stroke, to improve HRQoL. These strategies should include continued availability of hydroxyurea and other effective stroke prevention. Also, periodic assessment of HRQoL so that appropriate care and psychosocial support could be offered.

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