East African Medical Journal Vol. 98 No. 3 March 2021
INFLUENCE OF GENDER ON QUALITY OF LIFE OF PAEDIATRIC PATIENTS WITH SICKLE CELL DISEASE ATTENDING A REFERRAL HOSPITAL IN WESTERN KENYA; A PRELIMINARY ANALYSIS
Cynthia Pauline Aluoch Auma, School of Medicine, Bachelor of Medicine and Bachelor of Surgery, with Information Technology, Maseno University, P. O Box 527 - 40105, Maseno. Eddy Johnson Owino, School of Public Health and Applied Human Sciences, Bachelor of Food, Nutrition and Dietetics, Kenyatta University, P.O. BOX 3803- 40100, Kisumu.

Corresponding author: Cynthia Pauline Aluoch Auma, School of Medicine, Bachelor of Medicine and Bachelor of Surgery, with Information Technology, Maseno University, P. O Box 527 - 40105, Maseno, Email: aluochcynthia16@gmail.com

INFLUENCE OF GENDER ON QUALITY OF LIFE OF PAEDIATRIC PATIENTS WITH SICKLE CELL DISEASE ATTENDING A REFERRAL HOSPITAL IN WESTERN KENYA; A PRELIMINARY ANALYSIS

C. P. A. Auma and E. J. Owino

ABSTRACT

Background and objectives: **Sickle cell disease (SCD) is a hereditary blood disorder common in many malaria endemic regions. It is associated with high childhood morbidity and mortality, especially in Sub-Saharan Africa. The study set out to assess the gender related differences in clinical presentation of SCD in children.**

Methods and study design: **This was a cross-sectional survey conducted at Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH). Forty children under 13 years of age with S.C.D, and their guardians were interviewed using a structured questionnaire. Data was analysed using Statistical Packages for Social Sciences (SPSS) version 23.**

Results: **Forty children, mean age 6.78 years participated in the study. Males were diagnosed earlier than females, 35 months vs 39 months. All the children had poor health related quality of life (HRQOL), with females having worse scores in all domains (physical, emotional, social) except school functioning. Almost all children were anaemic (97.5%), males having a mean haemoglobin level of 6.8 ± 2.5 g/dl compared to females 6.3 ± 1.8 g/dl. Females had more annual episodes of pain crises (3.42 vs 2.38) and hospital admissions (2.75 vs 2.00) compared to males.**

Conclusions and recommendations: **SCD negatively impacts the HRQoL of sicklers especially females, who are usually diagnosed later compared to males. More studies should be done to assess gender differences in SCD related morbidity in children.**

INTRODUCTION

Sickle cell disease (SCD) is a homozygous hereditary blood disorder that occurs following point mutation at the sixth position in the beta globin subunit whereby glutamic acid is replaced by valine (1). This results in reversible polymerization of red blood cells under low oxygen tension, a characteristic pathophysiological feature of the disease (2). Approximately 240, 000 children are born with SCD in Africa annually (2).

New-born screening and early identification of SCD can significantly reduce early disease morbidity and mortality (3). Many African countries lack an effective new-born screening program which delays SCD diagnosis to when children become symptomatic (4). In two Nigerian studies, males were diagnosed with SCD earlier than females. The mean age at diagnosis was 27.33 months (5) with males being diagnosed at 25.59 months versus 29.14 months for females (5). In a study by Chukwu et al, the mean age at diagnosis for males was 33.3 months versus 47.09 months for females (4).

SCD has been noted to have sex linked differences in mortality and morbidity. Some studies suggest increased mortality and morbidity in males with SCD compared to females. This is mainly attributed to increased nitric oxide bioavailability and responsiveness in women (6). In a study by Platt et al, the mean age at death was 42 years for men versus 48 years for women (7) while in the Helvaci et al study it was 29.1 years in females versus 26.2 years in males (8). A study of school going children in India revealed that sickle cell trait positive males had higher prevalence of anaemia and morbidities (1). This is similar to findings by Ceglie et al that revealed more pain crises and severe SCD complications in male children (9). Other studies suggest both men and women with SCD generally have similar pain experiences (10).

Studies conducted indicate that SCD adversely affects health related quality of life (HRQOL) of patients (11) (12). The pediatric quality of life questionnaire (PedsQL™) is a valuable tool in assessing HRQOL of children. Evidence supports including children's perspectives in research, as children as young as 5 years can validly self-report their HRQOL when an age appropriate tool, such as PedsQL™ questionnaire is used (13). For the child self-report PedsQL™ questionnaire, the established cut-off scores meaning poor quality of life is set at 69.7 (13). A Ugandan study revealed adolescents with SCD had poor physical, emotional, school and psychosocial functioning while social functioning was adequate (11). In a study of Saudi Arabian adolescents with SCD, their HRQoL was noted to be significantly deteriorated with females demonstrating significant deterioration in emotional wellbeing (12). Poor HRQoL scores was associated with increasing age, female gender, rural residence, low family income, presence of disease-related complications and frequent hospital admissions (12).

Despite these findings, there is limited data available on gender differences in SCD presentation among children in Africa. In addition, most of these studies were done on adults with few focusing on paediatric patients. This study set out to address the following objectives:

i. To describe quality of life of paediatric patients with sickle cell disease attending a referral hospital in Western Kenya using a standard paediatric QOL (PedsQL™) tool and selected indicators of disease severity.
ii. To compare male and female children with sickle cell disease on

QOL measures and selected indicators of disease severity.

MATERIALS AND METHODS

A cross sectional study was conducted on children with SCD admitted at Obama Children's Ward in Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH).

All children aged 0-13 years already diagnosed with SCD admitted at JOOTRH during the study period were included. Only 40 children with SCD were admitted at the time of the study. Their guardians agreed to participate in the study and provided informed written consent, which was obtained in their preferred language. Ethical approval for the study was provided by Maseno University Ethics Review Committee (MUERC).

Participants who gave written consent were interviewed using a structured questionnaire. Health Related Quality of Life (HRQoL) was assessed among the school going children, aged between 7- 13 years of age (n=22), using the pediatric quality of life questionnaire (PedsQL™). The PedsQL™ questionnaire is a 23-item questionnaire consisting of four domains: physical, emotional, social and school functioning with scores ranging from 0 (never) to 4 (almost always). The Likert scale response items were then reverse scored to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0) with higher scores indicating better HRQoL. For the child self-report PedsQL™ questionnaire, the established cut-off scores meaning poor quality of life is set at 69.7 (13). A score above 69.7 indicates good HRQoL, while a score below 69.7 indicates poor HRQoL (13). Clinical data such as current haemoglobin level and malaria test results was obtained from the patients' medical records. Data gathered was analysed using Statistical Package for Social Sciences (SPSS) version 23.

RESULTS

Demographic characteristics of the study participants: The demographic characteristics of study participants were analyzed (Table 1). The mean age of the children who participated in the study was 6.78± 3.47 years, the youngest child being 1.8 years old. Most of the children were Luo (80%), 97.5% were Christian with 42.5% coming from Kisumu County. The average age at SCD diagnosis was 3.13 ± 2.46 years.

Table 1

Demographic characteristics of study participants

		Female	**Male**	**Total**
		n=24	**n=16**	**n=40**
Current age, Years n (%)	Mean (range)	6.55 (1.8-13)	7.13 (2.5-13)	6.78 (1.8 - 13)
Age at diagnosis, Years n (%)	Mean (range)	3.28 (0.25-10)	2.92 (0.5- 8.0)	3.13 (0.25-10)
Tribe, n (%)	Luo	22 (91.7)	12 (75.0)	34 (85.0)
	Luhya	1 (4.2)	3 (18.8)	4 (10.0)
	Kisii	1 (4.2)	1 (6.2)	2 (5.0)
Religion, n (%)	Christian	24 (100.0)	15 (93.8)	39(97.5)
	Muslim	0 (0.0)	1 (6.2)	1 (2.5)
	Mother	23 (95.8)	10 (62.5)	33 (82.5)

Relation of respondent to child, n (%)	Father	0 (0.0)	5 (31.3)	5 (12.5)
	Other	1 (4.2)	1 (6.2)	2 (5.0)
County of residence, n (%)	Kisumu	13 (54.2)	4 (25.0)	17 (42.5)
	Siaya	4 (16.7)	4 (25.0)	8 (20.0)
	Homabay	5 (20.8)	3 (18.8)	8 (20.0)
	Migori	1 (4.2)	3 (18.8)	4 (10.0)
	Vihiga	1 (4.2)	2 (12.5)	3 (7.5)
Child attends SCD clinic	Yes	18 (75.0)	11 (68.8)	29 (72.5)
	No	6 (25.0)	5 (31.3)	11 (27.5)
Malaria	Positive	2 (8.3)	5 (31.3)	7 (17.5)
	Negative	22 (91.7)	11 (68.8)	33 (82.5)

Children (n=40) with SCD were enrolled into the study. Data is presented as absolute number (n) and proportions (%)

Health related quality of life (HRQoL) of children with SCD

The HRQoL of children between 7-13 years of age (n=22) assessed using the PedsQL™ questionnaire was noted to be poor in all four domains (below 69.7). Girls generally had poorer HRQoL scores in all four domains except school where they performed better than boys. However, these differences were not statistically significant (*P*>.05). The physical health summary score, psychosocial health summary score and total score for males was 52.78 ± 24.68, 64.07 ± 24.09 and 60.14 ± 24.30 respectively. For females, the scores were 49.75 ± 24.86, 61.54 ± 27.27 and 57.44 ± 26.43, respectively.

Table 2

Paediatric quality of life (PedsQoL) generic score scales

Measures		***Mean (SD)***		
Paediatric Quality of Life Inventory (PedsQL)	*Male = 9*	*Female = 13*	*P value*	*Total =22*
Physical Score	52.78 (24.68)	49.75 (24.86)	.8	50.99 (25.56)
Emotional Score	69.44 (23.15)	65.38 (30.68)	.7	67.05 (27.99)
Social Score	63.33 (28.12)	56.92 (28.13)	.6	59.55 (29.34)
School Score	59.44 (21.01)	62.31(23.00)	.8	61.14 (22.42)
Total Score	*60.14 (24.30)*	*57.44 (26.43)*	*.8*	*59.68 (26.33)*
Psychosocial health summary score (Emotional + social + school)	*64.07 (24.09)*	*61.54 (27.27)*	*.8*	*62.58 (26.58)*
Physical health summary score	*52.78 (24.68)*	*49.75 (24.86)*	*.8*	*50.99 (25.56)*

Anaemia in sickle cell disease

Almost all (97.5%) the children were anaemic. The mean haemoglobin level was 6.53 ± 2.09 g/dl, with males having a higher mean haemoglobin level, 6.8 ± 2.5 g/dl compared to females 6.3 ± 1.8 g/dl. These differences were not statistically significant (P value= .5).

Table 3

Prevalence of anaemia in sickle cell disease

	Males, n=16	**Females, n=24**	**Total, n=40**
Mean haemoglobin (SD)	6.8 (2.5)	6.3 (1.8)	6.53 (2.09)
Severe anaemia (<5g/dl)	6 (37.5)	6 (25.0)	12 (30.0)
Moderate anaemia (5.1-7g/dl)	3 (18.8)	9 (37.5)	12 (30.0)
Mild anaemia (7.1-10g/dl)	6 (37.5)	9 (37.5)	15 (37.5)
No anaemia (Hb>10g/dl)	1 (6.3)	0 (0.0)	1 (2.5)

Children (n=40) with SCD were enrolled into the study. Data is presented as absolute number (n) and proportions (%).

SCD related morbidity

During the study period, 31.3% of the males were diagnosed with malaria compared to 8.3% of the females. On average, the children had 3 episodes of pain cries, 2.5 hospital admissions, 1.6 episodes of malaria and 1.4 blood transfusions annually. Females had more episodes of pain crises and hospital admissions annually while males had more episodes of malaria and blood transfusions annually. There was no statistical significance between gender and annual malaria episodes, hospital admissions, blood transfusions and pain crises (P=.7, .2, .2, .1 respectively).

Table 4

SCD related morbidity

		Mean (SD)		
Parameters	***Male =16***	***Female = 24***	P value	***Total =40***
Annual malaria episodes	1.75(1.81)	1.50 (1.84)	.7	1.6 (1.8)
Annual hospital admissions	2.00 (1.32)	2.75 (1.87)	.2	2.5 (1.7)
Annual blood transfusions	1.88 (2.65)	1.08 (1.25)	.2	1.4 (1.9)
Annual pain crises	2.38 (1.31)	3.42 (2.36)	.1	3.0 (2.1)

DISCUSSION

Sickle cell disease (SCD) has been noted to have high childhood morbidity and mortality, especially in Sub-Saharan Africa (2). There is limited data on gender related differences in SCD presentation in children (9). Most studies focuss on sex related differences in adults, largely attributed to sex hormones (6) (7) (8) (10), which might not contribute significantly to these differences in children (9). This study assessed the sex related differences in clinical presentation of SCD in African children.

Forty children (16 males, 24 females), mean age of 6.78 ± 3.47 years participated in the study. 72.5 % of the children were on follow up, attending a SCD clinic. Malaria was diagnosed in 17.5% of the sicklers unlike in a Kilifi study where 6% had malaria (18) while 10% had malaria in a Ugandan study (11). Almost all (97.5%) the children were anaemic, a finding similar to a Ghanaian study where 98.3% of sicklers were anaemic (17). Out of these, 30% had severe anemia requiring urgent blood transfusion (Hb <5g/dl). The HRQoL among children aged 7-13 years (n=22) was

poor, averaging 59.68, quite similar to a Ugandan study where the average HRQoL was 62.98 (11). The established cut-off scores meaning poor quality of life is set at 69.7 (13). In general, these observations reveal poor quality of life and point towards limited access to long-term quality care.

The mean age at SCD diagnosis was 3.13 ± 2.46 years. Many African countries, including Kenya lack an effective new-born screening program thus SCD diagnosis is made when children present with symptoms (4). However, males were diagnosed earlier than females, 2.92 ± 2.34 years (35 months) in males, and 3.28 ± 2.57 years (39 months) in females. This is consistent with other African studies whereby males were diagnosed earlier than females. In a study by Chukwu et al, the mean age at diagnosis for males was 33.3 months versus 47.09 months for females (4) while in the Akodu et al study it was 25.59 months versus 29.14 months for females (5). An Italian study (9) also revealed that males were diagnosed earlier (1.7 years vs 4.3 years). The early diagnosis of SCD in males could be attributed to more exposure to precipitating factors of crises such as strenuous exercise and cultural preference for male children thus more concern for their health needs (4). Males could also be diagnosed earlier as they have a worse clinical course leading to further investigations (9).

The HRQoL of children between 7-13 years of age (n=22) assessed using the PedsQL™ questionnaire was noted to be poor (below 69.7) in all four domains. Several studies have revealed that children with SCD have worse HRQoL when compared to healthy children (11) (12) (14) (15). The mean overall HRQoL score was 59.68. In the Kambasu study, the average HRQoL was 62.98 (11) while it was 72.28 in the Dampier study (14). Our findings are similar to the Ugandan study as both studies involved children in third world countries who likely face similar challenges as opposed to the American study where they may have more resources. The physical health summary score, psychosocial health summary score and total score for males as 52.78 ± 24.68, 64.07 ± 24.09 and 60.14 ± 24.30 respectively. For females, the scores were 49.75 ± 24.86, 61.54 ± 27.27 and 57.44 ± 26.43, respectively. However, these differences were not statistically significant (P>.05). Females generally had poorer HRQoL scores in all four domains except school where they performed better than males (62.31± 23.0 in females, versus 59.44 ± 21.01 in males). These findings are similar with a Ugandan study where females also had poorer HRQoL than males in all domains except school score (11). In the Kambasu et al study, the physical health summary score, school score, and psychosocial health summary score for males was 57.7±21.85, 58.3±19.05 and 69.0±16.26 respectively while for females it was 57.3± 19.78, 58.5± 15.38 and 62.0± 14.77 respectively (11). Our findings of lower HRQoL among females is consistent with previous studies (11) (12) (14) (15). Other factors that negatively affect HRQoL include increasing age, rural residence, low family income, presence of disease-related complications, pain, stigma and frequent hospital admissions (11) (12). SCD pain led to over seven times increased risk of missing school and greatly disrupts social, household and recreational activities (11) (16).

Almost all (97.5%) the children were anaemic. The mean haemoglobin level was 6.53 ± 2.09 g/dl, with males having a higher mean haemoglobin level, 6.8 ± 2.5 g/dl compared to females 6.3 ± 1.8 g/dl. In a Ghanaian study, almost all the children (98.3%) with SCD were anaemic with a mean haemoglobin of 7.8 ± 1.4 g/dl (17) while in a Kenyan study, the mean haemoglobin was 7.3

± 1.3 g/l (18). These findings are quite similar to our study. A study of school going children in India revealed that sickle cell trait positive males had higher prevalence of anaemia (1) compared to females contrary to our findings.

During the study period, 17.5% of the participants had malaria, males accounting for more cases (31.3% of males vs 8.3% of females). In a study conducted in Kilifi, only 6% of the children had malaria (18). SCD seems to offer moderate protection against malaria(18). Females had more episodes of pain crises (3.42 vs 2.38) and hospital admissions (2.75 vs 2.00) annually while males had more episodes of malaria (1.75 vs 1.50) and blood transfusions (1.88 vs 1.08) annually. However, these differences were not statistically significant (*P*>.05). A study by Platt et al revealed pain frequency is higher among females (19) which is similar to our findings. Pain has been noted to negatively impact on almost all aspects of HRQoL (14) which could explain the poor HRQoL among females in our study. Some studies suggest higher blood transfusion rates lead to improvement in HRQoL (11) (20) which could explain the better HRQoL scores in males in our study. Several studies (1) (7) (8) (9) have suggested higher mortality and morbidity in males with SCD compared to females, largely attributed to increased nitric oxide bioavailability and responsiveness in women (6). In a study by Ceglie et al, males with SCD had more annual pain crises (1.6 vs 0.6) and blood transfusions (2.3 vs 1.9) compared to females (9).

This study provides some perspective on the influence of gender on the HRQoL and selected indicators of disease severity in sicklers. The use of a standard paediatric quality of life tool allows comparability of findings from one study to another. However, the study has some weaknesses in that the sample size is small and the participants were hospitalised patients which could have negatively impacted on the HRQoL.

Many studies conducted on gender differences in adult patients with SCD indicate males have worse morbidity and mortality(6) (7) (8). In the Ceglie et al (9) and Charuhas et al study (1), it was also noted that in children, boys have more morbidity compared to girls. However, our study seems to indicate that girls generally have worse morbidity and HRQoL compared to boys. Large sample size studies should be done to assess gender differences in SCD related morbidity in children. SCD adversely affects HRQoL of children; with an average HRQoL score of 59.68 being reported in our study. Assessment of HRQoL in children with SCD should be encouraged to guide further management as well as in evaluating efficacy of various treatment modalities.

REFERENCES

1. Charuhas A, Neelam S, Sanjay K, Sanjay A, Mohan K, Sanjeev C, et al. Do gender differences influence the prevalence of sickle cell disorder and related morbidities among school children in rural central India? Int J Collab Res Intern Med Public Health. 2013;5:348–58.

2. Williams TN. Sickle Cell Disease in Sub-Saharan Africa. Hematol Oncol Clin North Am. 2016 Apr 1;30(2):343–58.

3. McGann PT, Tshilolo L, Santos B, Tomlinson GA, Stuber S, Latham T, et al. Hydroxyurea Therapy for Children With Sickle Cell Anemia in Sub-Saharan Africa: Rationale and Design of the REACH Trial. Pediatr Blood Cancer. 2016 Jan;63(1):98–104.

4. Chukwu B, Ezenwosu O, Eke C, Chinawa J, Ikefuna A, Emodi I. What Factors Influence the Age at Diagnosis of sickle Cell Anemia in Enugu, Nigeria? J Blood Disord Transfus. 2014 Oct 10;5(8).

5. Akodu S, Diaku-Akinwumi I, Njokanma O. Age at diagnosis of sickle cell anaemia in lagos, Nigeria. Mediterr J Hematol Infect Dis. 2013/01/02 ed. 2013;5(1):e2013001–e2013001.

6. Gladwin Mark T., Schechter Alan N., Ognibene Frederick P., Coles Wynona A., Reiter Christopher D., Schenke William H., et al. Divergent Nitric Oxide Bioavailability in Men and Women With Sickle Cell Disease. Circulation. 2003 Jan 21;107(2):271–8.
7. Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, et al. Mortality In Sickle Cell Disease -- Life Expectancy and Risk Factors for Early Death. N Engl J Med. 1994 Jun 9;330(23):1639–44.
8. Rami Helvaci M, Ayyildiz O, Gundogdu M. Gender differences in severity of sickle cell diseases in non-smokers. Pak J Med Sci. 2013 Jul;29(4):1050–4.
9. Ceglie G, Di Mauro M, Tarissi De Jacobis I, de Gennaro F, Quaranta M, Baronci C, et al. Gender-Related Differences in Sickle Cell Disease in a Pediatric Cohort: A Single-Center Retrospective Study. Front Mol Biosci. 2019;6:140.
10. McClish D, Levenson J, Penberthy L, Roseff S, Bovbjerg V, Roberts J, et al. Gender Differences in Pain and Healthcare Utilization for Adult Sickle Cell Patients: The PiSCES Project. J Womens Health 2002. 2006 Apr 1;15:146–54.
11. Kambasu DM, Rujumba J, Lekuya HM, Munube D, Mupere E. Health-related quality of life of adolescents with sickle cell disease in sub-Saharan Africa: a cross-sectional study. BMC Hematol. 2019 May 14;19(1):9.
12. Amr MA-M, Amin TT, Al-Omair OA. Health related quality of life among adolescents with sickle cell disease in Saudi Arabia. Pan Afr Med J. 2011/02/15 ed. 2011;8:10–10.
13. Varni JW, Limbers C, Burwinkle TM. Literature Review: Health-related Quality of Life Measurement in Pediatric Oncology: Hearing the Voices of the Children. J Pediatr Psychol. 2007 Mar 8;32(9):1151–63.
14. Dampier C, Lieff S, LeBeau P, Rhee S, McMurray M, Rogers Z, et al. Health-related quality of life in children with sickle cell disease: a report from the Comprehensive Sickle Cell Centers Clinical Trial Consortium. Pediatr Blood Cancer. 2010 Sep;55(3):485–94.
15. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr Off J Ambul Pediatr Assoc. 2003 Dec;3(6):329–41.
16. Fuggle P, Shand PA, Gill LJ, Davies SC. Pain, quality of life, and coping in sickle cell disease. Arch Dis Child. 1996 Sep;75(3):199–203.
17. Boadu I, Ohemeng A, Renner LA. Dietary intakes and nutritional status of children with sickle cell disease at the Princess Marie Louise Hospital, Accra – a survey. BMC Nutr. 2018 Aug 23;4(1):33.
18. Sadarangani M, Makani J, Komba AN, Ajala-Agbo T, Newton CR, Marsh K, et al. An observational study of children with sickle cell disease in Kilifi, Kenya. Br J Haematol. 2009 Sep;146(6):675–82.
19. Platt OS, Thorington BD, Brambilla DJ, Milner PF, Rosse WF, Vichinsky E, et al. Pain in Sickle Cell Disease. N Engl J Med. 1991 Jul 4;325(1):11–6.
20. Beverung LM, Strouse JJ, Hulbert ML, Neville K, Liem RI, Inusa B, et al. Health-related quality of life in children with sickle cell anemia: impact of blood transfusion therapy. Am J Hematol. 2015 Feb;90(2):139–43.