ORIGINAL ARTICLE

Oman Medical Journal [2021], Vol. 36, No. 3: e270

Nutritional and Hematological Status of Sudanese Women of Childbearing Age with Steady-state Sickle Cell Anemia

Eltigani Hassan Ali[1], Salam Alkindi[2]*, Mohamed A. Osman[3], Wafa Hilali[4], Hind M. Mirgani[4], Gareeba Adam[5], Magdi M. Morsi[6], Izzeldin S. Hussein[7] and Kebreab Ghebremeskel[1]

[1]Lipidomics and Nutrition Research Centre, School of Human Sciences, London Metropolitan University, London, UK
[2]Department of Hematology, Sultan Qaboos University, Muscat, Oman
[3]Department of Biochemistry, Faculty of Medicine, University of Khartoum, Khartoum, Sudan
[4]Department of Haematology, Ibn Auf Teaching Hospital, Khartoum, Sudan
[5]Department of Educational Technology, Faculty of Higher Studies, Al-Zaiem Al Azhari University, Khartoum, Sudan
[6]Directorate of Planning, Ministry of Health, Muscat, Oman
[7]Department of Micronutrient, Iodine Global Network, Middle East and North Africa

ARTICLE INFO

Article history:
Received: 3 May 2020
Accepted: 11 October 2020

Online:
DOI 10.5001/omj.2021.81

Keywords:
Female; Anemia, Sickle Cell; Nutritional Status; Sudan.

ABSTRACT

Objectives: We sought to investigate the nutritional and hematological status of Sudanese women of childbearing age with sickle cell anemia (SCA). Anthropometry and hematology were used to assess nutritional status and health and disease conditions, respectively. ***Methods***: Women with steady-state (HbSS, n = 39; age = 19.0±2.7) and without (HbAA, n = 36; age, 19.8±2.7) SCA were recruited during a routine visit to the Hematology Clinic, Ibn-Auf Teaching Hospital, Khartoum, Sudan. ***Results:*** The two groups of women lived in similar environmental conditions and ate similar diets three times a day. However, despite taking regular meals, the women with sickle anemia were thinner and lighter ($p < 0.001$) and shorter ($p = 0.002$) compared with those who do not have the disease. Also, they had higher levels of mean corpuscular hemoglobin (Hb) concentration and white cell count ($p < 0.001$), mean corpuscular volume ($p = 0.003$), and platelet ($p = 0.002$) and lower packed cell volume and Hb ($p < 0.001$). There was no difference in levels of anthropometric and hematological variables between the hydroxyurea treated and untreated SCA patients ($p > 0.050$). ***Conclusions:*** The low anthropometric (height, weight, and body mass index) and abnormal hematological values in the women with SCA in steady-state reflect sustained nutritional insults inflected by the disease and poverty. Tailored nutritional counseling/advice must be an integral part of managing patients with SCA. Such advice is particularly vital for women of childbearing age because of the adverse effects of prepregnancy nutritional deficiency on birth outcomes.

Sickle cell anemia (SCA) is an inherited blood disorder. It is transmitted as an autosomal recessive gene characterized by recurrent chronic hemolytic anemia, vaso-occlusive crises, and predisposition to infections that seriously impact morbidity and mortality.[1] SCA is common in Sub-Saharan Africa, the Caribbean, Middle East, and India, and the prevalence is increasing globally because of migration.[2] The first reporting of the presence of the hemoglobin S (HbS) gene in Sudan was by Archibald.[3] Since, different studies have revealed that Sudan has a high prevalence of SCA, with HbS allele frequency that ranges between 0.8% in the Northern regions and over 30% in the Western regions of the country.[4–6] The high HbS allele frequency in the latter region is thought to be due to the high level of consanguineous marriages (40–45%), the tribal influx from West Africa, and endemic malaria.[7,8]

Despite its genetic simplicity, where SCA is a single substitution base change T>A at codon 6 of the β gene, there is significant clinical heterogeneity of the disease probably attributable to genetic, epigenetic, nutritional, and many environmental factors interacting with each other.[9] Generally, the care for patients with SCA has improved over the years due to earlier diagnosis, the widespread use of penicillin prophylaxis, vaccination, folate

*Corresponding author: ✉sskindi@squ.edu.om

supplementation, and access to comprehensive care programs including blood transfusions and hydroxyurea therapy, impacting significantly on morbidity and mortality.[10–14]

Nutritional status and growth and development are important indicators of the overall health and well-being of patients with SCA. Indeed, patients with sub-optimal nutrition status are at increased risk of hospital admission and severe morbidity and mortality. These health indicators are often compromised/impaired by a high metabolic rate caused by the disease, reduced absorption of essential nutrients, and appetite loss induced by the disease and its treatments. Also, a lack of access to nutrient-dense foods is a major problem for sickle cell patients in economically disadvantaged countries and communities.

It is widely recognised that maternal nutritional status before pregnancy is one of the main determinate factors of pregnancy outcome.[15–20] Published data are scarce on the nutritional status of women of childbearing age with SCA. Indeed, the effect of nutritional status before pregnancy on maternal and fetal outcomes has not been studied in women with the disease.

Until recently, it was a rarity to find pregnant women with sickle cell disease (SCD) in Sudan. However, because of improved disease management and the resulting increase in life expectancy, their number has increased significantly. Regardless, the country is highly underdeveloped with a rudimentary health service system and rampant poverty and malnutrition. In this highly patriarchal society, women, young children, and individuals with chronic diseases tend to bear the brunt of gross malnutrition and undernutrition.

The aim was to investigate the nutritional status and health of Sudanese women of childbearing age with SCA. Anthropometry and hematology were used to assess nutritional status and health and disease conditions, respectively.

METHODS

Women with steady-state SCA HbSS (n = 39) and without HbAA (n = 36) were recruited during a routine visit to the Hematology Clinic, University of Khartoum Ibn Auf Teaching Hospital. Unmarried women aged 16–40 years who volunteered to participate in the study and with the mental competence to give informed consent were included in the study. Women with sickle cell crisis, acute illness or blood transfusion in the previous four months, the presence of other chronic diseases or a physical disability that impairs access to food or restricts eating, and those that were pregnant were excluded from the study. Steady-state is defined absence of sickle cell crisis or acute illness for four months before and up to two weeks after blood collection for the study. A blood specimen (5 mL), detailed anthropometric, demographic data, medical history, and dietary habits were collected. We obtained ethical approval from the Ministry of Health of Sudan, University of Khartoum, Medical School, and London Metropolitan University, and signed informed consent from the participants.

Demographic data from the patients and medical history from hospital records and patients were collected using a questionnaire developed for the study.

Weight in kilograms and height in centimeters were assessed with a Seca Electronic Scale 890 (UNISCALE, Seca, Birmingham, UK) and a height-length measuring board (Schorr, Weight and Measure, LLC, Olney, Maryland, USA), respectively.

Hb concentration, packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), white blood cell (WBC) count and platelets count (PLTs) were measured using the Sysmex KX-21 N Automated Hematology Analyzer (Sysmex Corporation, Kobe, Japan).

Data are expressed as mean±standard deviation or percentages. Quantitative data were tested for normality and homogeneity of variance and subsequently analyzed with the independent *t*-test (parametric data) or the Mann-Whitney U test (non-parametric data). Categorical (sociodemographic, clinical, and laboratory characteristics) data with cell frequency of five or more were assessed with a chi-square test on the contingency platform. When the observed cell count was less than five, chi-square and Yate's correction of continuity and Fisher's exact test were used under the assumption of independence of rows and columns and conditional on the marginal totals. The significance level was set at $p < 0.050$. The data was analyzed with SPSS Statistics (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.).

Table 1: Age, clinical, and demographic parameters of the participants.

Characteristics	HbSS (n = 39)	HbAA (n = 36)	*p*-value
Age, years	19.0 ± 2.7	19.8 ± 2.7	NS
Weight, kg	39.0 ± 8.9	53.8 ± 11.0	0.001
Height, cm	151.0 ± 11.7	158.0 ± 6.7	0.002
BMI, kg/m²	17.2 ± 4.3	21.5 ± 4.2	0.001
Underweight (< 18.5)	27 (69.2)	9 (25.0)	0.001
Normal weight (18.5–24.9)	11 (28.2)	20 (55.6)	< 0.001
Overweight/ obese (≥ 25.0)	1 (2.6)	7 (19.4)	0.209
Education			
Illiterate/ primary school	24 (61.5)	3 (8.3)	< 0.001
Middle/high school	13 (33.3)	11 (30.6)	
University	2 (5.1)	22 (61.1)	< 0.001
Parental relationship			
First- and second-degree relatives	25 (64.1)	16 (44.4)	0.037
Unrelated	13 (33.3)	20 (55.6)	0.001
Siblings with sickle cell disease			
Yes	22 (56.4)	3 (8.3)	< 0.001
No	17 (43.6)	33 (91.7)	< 0.001

NS: not significant; BMI: body mass index.

RESULTS

The anthropometric and demographics characteristics of the women with (HbSS) and without (HbAA) SCA are presented in Table 1. There was no difference in age between the HbSS and HbAA groups ($p > 0.050$). However, the latter group was taller ($p = 0.002$), heavier ($p = 0.001$), and had a higher body mass index (BMI) compared with the former. The HbAA women had higher literacy and attendance of tertiary education rates ($p < 0.001$).

Most of the sickle cell patients and healthy control subjects eat regular breakfast (94.9 vs. 94.4%) and lunch (92.3 vs. 94.4%) [Table 2]. However, a significant number of the two groups do not consume dinner regularly (HbSS = 41.0% and HbAA = 61.1%, $p < 0.050$).

Of the HbSS, four had liver enlargement (4 cm, n = 2; 2 cm, n = 2) and one had spleen enlargement (6 cm). None of the patients had a scar for splenectomy. A few of the HbSS patients had a history of painful crisis with hemolysis and infection.

Table 2: Daily food consumption frequency of the participants.

Response	HbSS (n = 39)	HbAA (n = 36)	*p*-value
Regular breakfast			
Yes	37 (94.9)	34 (94.4)	NS
No	2 (5.1)	2 (5.6)	
Regular lunch			
Yes	36 (92.3)	34 (94.4)	NS
No	3 (7.7)	2 (5.6)	
Regular dinner			
Yes	23 (59.0)	14 (38.9)	NS
No	16 (41.0)	22 (61.1)	

NS: not significant.

The women with SCA compared with the healthy control had lower PCV and Hb concentration ($p < 0.001$) and higher MCH ($p < 0.001$), MCV ($p = 0.003$), WBC ($p < 0.001$), and PLTs ($p = 0.002$) counts [Table 3]. There was no difference in lymphocyte and neutrophil counts and systolic and diastolic blood pressure between the two groups ($p > 0.050$).

Of the thirty-nine patients who consented to participate in the study, 25 were on hydroxyurea treatment. Anthropometric, demographic, and hematological variable data of the hydroxyurea treated and untreated patients at steady-state are presented in Table 4. There was no difference in age, weight, height, BMI, and systolic and diastolic blood pressure between the two groups ($p > 0.050$).

The hydroxyurea treated and untreated patients had a similar history of blood transfusion rates and comparable levels of Hb concentration, PCV, MCH, MCV, WBC, PLTs, neutrophil, and lymphocyte counts ($p > 0.050$). Also, the percentages of patients who were receiving folic acid supplementation were not different (treated 100% and untreated 92.8%, $p > 0.050$).

DISCUSSION

Consanguineous, marriage between first and second cousins, is a common tradition in all Sudanese tribes. This is evident from the high percentage of parental blood relationship of the HbSS (64.1%) and HbAA (44.4%) groups. Consistent with our findings, Daak et al[5] reported high parental and self-consanguineous

Table 3: Hematological characteristics of the participants.

Characteristics	HbSS (n = 39)	HbAA (n = 36)	*p*-value
Hb, g/dL	9.2 ± 1.6	14.3 ± 1.6	< 0.001
PCV, %	25.1 ± 6.2	37.6 ± 3.3	< 0.001
MCV, FL	88.9 ± 13.5	81.4 ± 5.7	0.003
MCH, pg	34.5 ± 3.6	31.0 ± 3.0	< 0.001
White cell count, × 10^3 µL	11.4 ± 4.2	5.9 ± 2.1	< 0.001
Neutrophils, %	51.6 ± 11.3	47.9 ± 9.9	NS
Lymphocytes, %	38.8 ± 9.1	41.0 ± 9.5	NS
Platelets, × 10^3 µL	409.1 ± 121.5	328.5 ± 95.6	0.002
Systolic BP	109.5 ± 10.4	108.5 ± 9.6	NS
Diastolic BP	67.4 ± 8.4	70.4 ± 8.3	NS
Blood transfusion history, n (%)			
Yes	32 (82.1)	1 (2.8)	< 0.001
No	7 (17.9)	33 (97.1)	
Folic acid supplement			
Yes	38 (97.4)	1 (2.8)	< 0.001
No	7 (17.9)	1 (2.8)	
Hydroxyurea use			
Yes	25 (64.1)	0 (0.0)	< 0.001
No	14 (35.9)	0 (0.0)	
Omega 3 fatty acids			
Yes	4 (10.3)	0 (0.0)	NS
No	35 (89.78)	0 (0.0)	

NS: not significant; Hb: hemoglobin; PCV: packed cell volume; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; BP: blood pressure. Data presented as mean±SD unless otherwise indicated.

Table 4: Anthropometric and hematological characteristics of the hydroxyurea treated and untreated (HbSS) groups.

Characteristics	Treated (n = 25)	Untreated (n = 14)	*p*-value
Age, years	18.9 ± 2.4	19.3 ± 3.1	NS
Weight, kg	39.7 ± 9.7	37.7 ± 7.4	NS
Height, cm	151.4 ± 13.2	150.3 ± 8.5	NS
Body mass index, kg/m^2	17.50 ± 5.0	16.6 ± 2.5	NS
Systolic BP	109.0 ± 10.4	110.4 ± 10.5	NS
Diastolic BP	65.4 ± 8.2	71.1 ± 7.9	NS
Hb, g/dL	9.2 ± 1.8	9.2 ± 1.1	NS
PCV, %	25.0 ± 7.3	25.2 ± 3.8	NS
MCV, FL	92.0 ± 6.3	83.4 ± 20.2	NS
MCH, pg	35.2 ± 3.5	33.2 ± 3.6	NS
White cell count, × 10^3 µL	11.8 ± 4.2	10.7 ± 4.2	NS
Neutrophils, %	51.4 ± 10.4	52.0 ± 13.2	NS
Lymphocytes, %	37.7 ± 8.4	40.6 ± 10.5	NS
Platelets, × 10^3 µL	412.2 ± 130.2	403.0 ± 108.8	NS
History of blood transfusion, n (%)			
Yes	20 (80.0)	12 (85.7)	NS
No	5 (20.0)	2 (14.2)	NS
Folic acid supplement, n (%)			
Yes	25 (100)	13 (92.8)	NS
No	0 (0.0)	1 (7.2)	NS

NS: not significant. Hb: hemoglobin; PCV: packed cell volume; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; BP: blood pressure. Data presented as mean±SD unless otherwise indicated.

marriages in patients with SCD in Western Kordofan State, Sudan. In this study, although a significant number of the control and patients were born to parents who are blood relatives, the figure was more remarkable in the SCD group. It may be that the social stigma associated with the disease makes it very difficult for affected individuals to find a suitor (husband/wife) outside the immediate family circle. Regardless, as it is apparent from the number of siblings with SCA in the patient group, consanguinity/in-breeding would be expected to perpetuate and increase the prevalence of the disease in Sudan.

There is an urgent need for comprehensive and well-planned education, social awareness, and counseling programs targeted for patients with SCA, and the community, particularly in rural areas with deep-rooted traditions, to help reduce discrimination and stigma. In Sudan, the strong predictors of negative attitude and discrimination against SCD are lacking knowledge and low socioeconomic status.[5] Similar observations have been reported from other Sub-Sahara African countries.[21,22]

Illiteracy is almost a norm in patients with SCD, and they hardly complete high school and few attend university education. In our study, patients without formal (illiterate) and primary school education accounted for about 61.5%; only two (5.1%) had university education. Compared with their age and gender-matched classmates, an appreciable number of children with the disease are thought to under-perform drastically in school[23–25] due to disease-caused absences, neurological abnormalities resulting from silent and overt strokes, poverty, and psychological/psychiatric issues.[26–28]

There was no difference in age, ethnicity, and the frequency of daily food consumption between the two groups of women. However, the SCA group, compared with their healthy counterparts, had lower weight, height, and BMI compared to the

control women. These findings are consistent with the results of previous studies.[18–20,29–34] In contrast to our findings, high BMI and obesity in American children and adults with SCA have been reported.[35,36] It appears the anthropometric deficits commonly observed in patients with the disease in developing countries can be rectified by appropriate nutritional care and clinical management, particularly during childhood and adolescence.

The sickle cell patients who participated in this study were at steady-state, and some claimed to be on hydroxyurea (64.1%), folic acid (97.4%), and omega-3 fatty acids (10.3%). However, their hematological profiles, which were abnormal, were significantly different from that of the healthy control women. This finding was unexpected since hydroxyurea is known to improve hematological abnormalities in SCD.[37–41] It is plausible the patients might not have been taking hydroxyurea as prescribed by their physicians because of its side effects (constipation/diarrhea, hair loss, muscle and joint pain, etc.), financial difficulties (patient have to pay for their medication in Sudan), inability to understand prescription guidelines and/or the drug became unavailable in private and hospital pharmacies. Indeed, the hematological data of the hydroxyurea treated and untreated patients, which were similar, reveals that the patients were unlikely to have been taking the medication as per guidance. Since most sickle cell patients in the country are poor. The government should explore the possibility of partially or wholly subsidizing hydroxyurea. Also, doctors must regularly check that their patients are following the prescription guidelines.

Small sample size (more patients who fulfill the inclusion and exclusion criteria could not be found in the same clinic), failure to collect quantitative nutrients intake data (most of the subjects were illiterate and they were unable to record their dietary intakes reliably), and failure to perform hemoglobin F tests (lack of laboratory facility) were the main limitations of the study. Regardless of these limitations, the study has provided a good picture of the nutritional and health status of Sudanese women of childbearing age with SCA.

CONCLUSION

The low anthropometric measures (height, weight, and BMI) and abnormal hematological values of the women with SCA in steady-state reflect sustained nutrition insults inflected by the disease and poverty. Tailored nutritional counseling/advice must be an integral part of managing patients with SCA. Such advice is particularly vital for women of childbearing age because of the adverse effects of prepregnancy nutritional deficiency on birth outcomes.

Disclosure

The authors declared no conflicts of interest. No funding was received for this study.

Acknowledgements

The authors are thankful to the women for consenting to participate in the study, Mr. Abdullah Nasir of the Biochemistry Department, University of Khartoum, Medical School, for helping with blood collection and hemoglobin typing and to the technical staff of the Haematology Clinic, Ibn-Auf Teaching Hospital, Khartoum, Sudan, for hematological assay. Also, we are grateful to Dr. Omer Hassan and Miss Khadija Hassan for their help and support, particularly in the recruitment of the participants and the transport of blood samples to London, UK, for biochemical analysis.

REFERENCES

1. Weatherall DJ, Clegg JB. Inherited haemoglobin disorders: an increasing global health problem. Bull World Health Org 2001;97:704-712.
2. Weatherall DJ. The global problem of genetic disease. Ann Hum Biol 2005 Mar-Apr;32(2):117-122.
3. Archibald RG. A case of sickle cell anaemia in the Sudan. Trans R Soc Trop Med Hyg 1926;19(7):389-39.
4. Adam MA, Adam NK, Mohamed BA. Prevalence of sickle cell disease and sickle cell trait among children admitted to Al Fashir teaching hospital north Darfur State, Sudan. BMC Res Notes 2019 Oct;12(1):659.
5. Daak AA, Elsamani E, Ali EH, Mohamed FA, Abdel-Rahman ME, Elderdery AY, et al. Sickle cell disease in western Sudan: genetic epidemiology and predictors of knowledge attitude and practices. Trop Med Int Health 2016 May;21(5):642-653.
6. El-Hazmi MA, Al-Hazmi AM, Warsy AS. Sickle cell disease in Middle East Arab countries. Indian J Med Res 2011 Nov;134(5):597-610.
7. Sabahelzain MM, Hamamy H. The ethnic distribution of sickle cell disease in Sudan. Pan Afr Med J 2014 May;18(1):13.
8. Saha N, Hamad RE, Mohamed S. Inbreeding effects on reproductive outcome in a Sudanese population. Hum Hered 1990;40(4):208-212.
9. Rahimy MC, Gangbo A, Ahouignan G, Adjou R, Deguenon C, Goussanou S, et al. Effect of a comprehensive clinical care program on disease course in severely ill children with sickle cell anemia in a sub-Saharan African setting. Blood 2003 Aug;102(3):834-838.
10. Adamkiewicz TV, Silk BJ, Howgate J, Baughman W, Strayhorn G, Sullivan K, et al. Effectiveness of the 7-valent pneumococcal conjugate vaccine in children with sickle cell disease in the first decade of life. Pediatrics 2008 Mar;121(3):562-569.
11. Elderdery A, Mohamed B, Cooper A, Knight G, Mills J. Tribal distribution of haemoglobinopathies in a Sudanese patient population. J Med Lab Diagn 2011;2(4):31-37.
12. Gaston MH, Verter JI, Woods G, Pegelow C, Kelleher J, Presbury G, et al. Prophylaxis with oral penicillin in

children with sickle cell anemia. A randomized trial. N Engl J Med 1986 Jun;314(25):1593-1599.

13. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. Lancet 2010 Dec;376(9757):2018-2031.
14. Vichinsky EP. Comprehensive care in sickle cell disease: its impact on morbidity and mortality. Semin Hematol 1991 Jul;28(3):220-226.
15. Johnson W, Elmrayed SA, Sosseh F, Prentice AM, Moore SE. Preconceptional and gestational weight trajectories and risk of delivering a small-for-gestational-age baby in rural Gambia. Am J Clin Nutr 2017 Jun;105(6):1474-1482.
16. Mavalankar DV, Trivedi CC, Gray RH. Maternal weight, height and risk of poor pregnancy outcome in Ahmedabad, India. Indian Pediatr 1994 Oct;31(10):1205-1212.
17. Pan Y, Zhang S, Wang Q, Shen H, Zhang Y, Li Y, et al. Investigating the association between prepregnancy body mass index and adverse pregnancy outcomes: a large cohort study of 536 098 Chinese pregnant women in rural China. BMJ Open 2016 Jul;6(6):e011227.
18. Patel A, Prakash AA, Das PK, Gupta S, Pusdekar YV, Hibberd PL. Maternal anemia and underweight as determinants of pregnancy outcomes: cohort study in eastern rural Maharashtra, India. BMJ Open 2018;8(8):e021623.
19. Vobecky JS. Nutritional aspects of preconceptional period as related to pregnancy and early infancy. Prog Food Nutr Sci 1986;10(1-2):205-236.
20. Young MF, Nguyen PH, Addo OY, Hao W, Nguyen H, Pham H, et al. The relative influence of maternal nutritional status before and during pregnancy on birth outcomes in Vietnam. Eur J Obstet Gynecol Reprod Biol 2015 Nov;194:223-227.
21. Marsh VM, Kamuya DM, Molyneux SS. 'All her children are born that way': gendered experiences of stigma in families affected by sickle cell disorder in rural Kenya. Ethn Health 2011 Aug-Oct;16(4-5):343-359.
22. Tusuubira SK, Nakayinga R, Mwambi B, Odda J, Kiconco S, Komuhangi A. Knowledge, perception and practices towards sickle cell disease: a community survey among adults in Lubaga division, Kampala Uganda. BMC Public Health 2018;18(1):1-5.
23. Armstrong FD, Thompson RJ Jr, Wang W, Zimmerman R, Pegelow CH, Miller S, et al; Neuropsychology Committee of the Cooperative Study of Sickle Cell Disease. Cognitive functioning and brain magnetic resonance imaging in children with sickle cell disease. Pediatrics 1996 Jun;97(6 Pt 1):864-870.
24. Ogunfowora OB, Olanrewaju DM, Akenzua GI. A comparative study of academic achievement of children with sickle cell anemia and their healthy siblings. J Natl Med Assoc 2005 Mar;97(3):405-408.
25. Akenzua GI, Olanrewaju DM. School performance of children and adolescents with sickle cell anaemia (sicklers) and healthy controls. Niger J Paediatr 1995;22:18-22.
26. Crosby LE, Joffe NE, Irwin MK, Strong H, Peugh J, Shook L, et al. School performance and disease interference in adolescents with sickle cell disease. Phys Disabil 2015;34(1):14-30.
27. Ezenwosu OU, Emodi IJ, Ikefuna AN, Chukwu BF, Osuorah CD. Determinants of academic performance in children with sickle cell anaemia. BMC Pediatr 2013;13(1):189.
28. Smith KE, Patterson CA, Szabo MM, Tarazi RA, Barakat LP. Predictors of academic achievement for school age children with sickle cell disease. Adv Sch Ment Health Promot 2013;6(1):5-20.
29. Ebomoyi E, Adedoyin MA, Ogunlesi FO. A comparative study of the growth status of children with and without SS disease at Ilorin, Kwara State, Nigeria. Afr J Med Med Sci 1989 Mar;18(1):69-74.
30. Kumar DS. Study of physical growth affected by sickle cell diseases. I J M H R 2017;3:96-99.
31. Lukusa Kazadi A, Ngiyulu RM, Gini-Ehungu JL, Mbuyi-Muamba JM, Aloni MN. Factors associated with growth retardation in children suffering from sickle cell anemia: first report from central Africa. Anemia 2017;2017:1-6.
32. Ngo Um SS, Seungue J, Alima AY, Mbono R, Mbassi H, Chelo D, et al. A cross sectional study of growth of children with sickle cell disease, aged 2 to 5 years in Yaoundé, Cameroon. Pan Afr Med J 2019 Oct;34:85.
33. 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):675-682.
34. Telfer P, Coen P, Chakravorty S, Wilkey O, Evans J, Newell H, et al. Clinical outcomes in children with sickle cell disease living in England: a neonatal cohort in East London. Haematologica 2007 Jul;92(7):905-912.
35. Chawla A, Sprinz PG, Welch J, Heeney M, Usmani N, Pashankar F, et al. Weight status of children with sickle cell disease. Pediatrics 2013 Apr;131(4):e1168-e1173.
36. Farooqui MW, Hussain N, Malik J, Rashid Y, Ghouse M, Hamdan J. Prevalence of obesity in sickle cell patients. Blood 2014;124:4932.
37. Charache S, Terrin ML, Moore RD, Dover GJ, Barton FB, Eckert SV, et al; Investigators of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. N Engl J Med 1995 May;332(20):1317-1322.
38. Daak AA, Ghebremeskel K, Elbashir MI, Bakhita A, Hassan Z, Crawford MA. Hydroxyurea therapy mobilises arachidonic Acid from inner cell membrane aminophospholipids in patients with homozygous sickle cell disease. J Lipids 2011;2011:718014.
39. Nevitt SJ, Jones AP, Howard J. Hydroxyurea (hydroxycarbamide) for sickle cell disease. Cochrane Cystic Fibrosis and Genetic Disorders Group, (Ed). Cochrane Database of Systematic Reviews; 2017.
40. Rigano P, De Franceschi L, Sainati L, Piga A, Piel FB, Cappellini MD, et al; Italian Multicenter Study of Hydroxyurea in Sickle Cell Anemia Investigators. Real-life experience with hydroxyurea in sickle cell disease: A multicenter study in a cohort of patients with heterogeneous descent. Blood Cells Mol Dis 2018 Mar;69:82-89.
41. Wang WC, Ware RE, Miller ST, Iyer RV, Casella JF, Minniti CP, et al; BABY HUG investigators. Hydroxycarbamide in very young children with sickle-cell anaemia: a multicentre, randomised, controlled trial (BABY HUG). Lancet 2011 May;377(9778):1663-1672.