Nutritional and haematological status of Sudanese women of childbearing age with steady-state sickle cell anaemia

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Abstract

Objectives: To investigate the nutritional and haematological status of Sudanese women of childbearing age with sickle cell anaemia. Anthropometry and haematology were used to asses nutritional status, and health and disease conditions, respectively.

Subjects and Methods: Women with steady-state (HbSS, n=39; age =19.0 ± 2.7) without (HbAA, n=36; age, 19.8 ± 2.7) sickle cell anaemia were recruited during a routine visit to Haematology Clinic, Ibn-Auf Teaching Hospital, Khartoum, Sudan. Ethical approval from Ethics Committees of London Metropolitan University, UK, and the University of Khartoum,

Medical School and Ministry of Health of Republica of Sudan, and informed consent from the participants were obtained.

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 anaemia were thinner and lighter (p=0.000) and shorter (p=0.002) compared with those who do not have the disease. Also, they had higher levels of MCH and White cell count (p=0.000), MCH (p=0.003) and platelet (p=0.002) and lower PCV and haemoglobin (p=0.000). There was no difference in levels of anthropometric and haematological variables between the hydroxyurea treated and untreated sickle cell anaemia patients (p>0.05).

Conclusions: The low anthropometric (height, weight, body mass index) and abnormal haematological values in the women with sickle cell anaemia in steady-state are a reflection of sustained nutritional insults inflected by the disease and poverty. Tailored nutritional counselling/advice must be an integral part of the management of patients with sickle cell anaemia. Such advice is particularly vital for women of childbearing because of the adverse effects of pre-pregnancy nutritional deficiency on birth outcomes.

Keywords: Sudanese Women, childbearing age, sickle cell anaemia, nutrition.

Introduction

Sickle cell Anaemia (SCA) is an inherited blood disorder. It is transmitted as an autosomal recessive gene and characterized by recurrent chronic haemolytic anaemia, vaso-occlusive crises, and predisposition to infections that impact seriously on morbidity and mortality[1]. SCA is common in Sub-Sahara Africa, Caribbean, Middle East and India and

the prevalence is increasing globally because of migration[2]. The first reporting of the presence of HbS gene in Sudan was in by Archibald[3]. Since then, different studies have revealed that Sudan has a high prevalence of SCA, with HbS allele frequency that ranges between 0.8% in the Northern and over 30% in Western regions of the country[4–6].The high HbS allele frequency in the latter region is thought to be due to 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 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 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 a loss of appetite 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 sickle cell anaemia. Indeed, the effect of nutritional status before pregnancy on maternal and foetal outcomes has not been studied in women with the disease.

Until recently, it was a rarity to find pregnant women with sickle cell disease 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 the gross malnutrition and undernutrition.

Objectives:

The aim was to investigate the nutritional status and health of Sudanese women of childing bearing age with sickle cell anaemia. Anthropometry and haematology were used to asses nutritional status, and health and disease conditions, respectively.

Subjects and methods

Subjects- Women with steady-state (HbSS, n=39) and without (HbAA n=36)) sickle cell anaemia were recruited during a routine visit to the Haematology Clinic, University of Khartoum Ibn Auf Teaching Hospital. Inclusion criteria: unmarried women aged 16 -40 years, volunteered to participate in the study, mental competence to give informed consent. Exclusion criteria: sickle cell crisis, acute illness or blood transfusion in the previous four months, presence of other chronic diseases, a physical disability which impairs access to food or restricts eating, pregnancy. Steady-state is defined absence of

sickle cell crisis or acute illness from 4 month before, and up to 2 weeks after blood collection for the study. Blood specimen, 5 ml, and detailed anthropometric and demographic data, medical history and dietary habits were collected. Ethical approval from the Ministry of Health of Sudan, University of Khartoum, Medical School and London Metropolitan University, and informed and signed consent from the participants were obtained.

Methods- Demographic data from the patients and medical history from hospital records and patients were collected with the use of a questionnaire developed for the study.

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

Haematological variables - haemoglobin concentration (Hb), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), white cell count (WBC), and platelets count (PLTS)) - were measured with the use of Sysmex KX-21 N Automated Hematology Analyzer (Sysmex Corporation, Kobe, Japan).

Data analysis:

Data are expressed as mean ± standard deviation (SD) or percentages. Quantitative data were tested for normality and homogeneity of variance and subsequently analysed with independent t-test (parametric data) or non-Whitney U test (non-parametric data). Categorical (socio-demographic, clinical and laboratory characteristics) data with cell frequency of 5 or more were assessed with a Chi-Square test on the contingency platform.

When the observed cell count was less than 5, 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 $p<0.05$. The data was analysed with IBM SPSS Statistics for Windows, version 26 (IBM SPSS Ltd., Woking, Surrey, UK) was used for data analysis.

Results:

HbSS versus HbAA

Anthropometry and Demography - The anthropometric and demographics characteristics of the women with (HbSS) and without (HbAA) sickle cell trait are presented in Table 1.a and b. There was no difference in age between the HbSS and HbAA groups ($p>0.05$). However, the latter group were taller ($p=0.002$), heavier ($p=0.000$) and had a higher body mass index compared with the former. The HbAA women had higher literacy and attendance of tertiary education rates ($p=0.000$).

Daily food consumption frequency of the participants is shown in table 2. 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%). However, a significant number of the two groups do not consume dinner regularly (HbSS, 59% and HbAA 61.1%, $p<0.05$).

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

Haematology - The haematological variable data of the two groups of women are presented in table 3. The women with sickle anaemia compared with the healthy controls had lower packed cell volume and haemoglobin concentration ($p=0.000$) and higher mean

corpuscular haemoglobin concentration (MCH, p=0.000), mean corpuscular volume (MCV, p=0.003) and white blood cell (WBC, p=0.000) and platelet (p=0.003) counts. There was no difference in lymphocyte and neutrophil counts and systolic and diastolic blood pressure between the two groups (p>0.05).

HbSS (Hydroxyurea treated and Untreated)

Of the thirty-nine patients who consented to participate in the study, twenty-five were on hydroxyurea treatment. Anthropometric, demographic and haematological variable data of the hydroxyurea treated and untreated patients at steady-state are presented in table 4.

Anthropometry and Demography – There was no difference in age, weight, height, body mass index and systolic and diastolic blood pressure between the two groups (p>0.05).

Haematology and blood transfusion history – The hydroxyurea treated and untreated patients had a similar history of blood transfusion rates, and comparable levels of haemoglobin concentration, packed cell volume and mean corpuscular haemoglobin concentration, corpuscular volume and white blood cell, platelet, neutrophil and lymphocyte counts (p>0.05). Also, the percentages of patients who were receiving folic acid supplementation were not different (treated 100% & untreated 92.8%, p>0.05).

Discussion

Consanguineous matrimony, 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%) and HbAA (44%) groups. Consistent with our findings, Daak et al [5] have reported a high parental and self-consanguineous marriages in patients with sickle cell disease in Western Kordofan State, Sudan. In this study, although a

significant number of the controls and patients were born to parents who are blood relatives, the figure was more remarkable in the latter 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 sickle cell anaemia in the patient group, consanguinity/in-breeding would be expected to perpetuate and indeed increase the prevalence of the disease in Sudan.

There is an urgent need for comprehensive and well-planned education, social awareness and counselling programmes targeted for patients with sickle cell anaemia, and the community, particularly in rural areas with deep-rooted traditions, to help reduce discrimination and stigma. It has been reported, in Sudan, the strong predictors of negative attitude and discrimination against sickle cell disease are poor knowledge and low socio-economic status[5]. Similar observations have been reported from other Sub-Sahara African countries[21,22].

Illiteracy is almost a norm in patients with sickle cell disease and they hardly complete high school or attend university education. In the current study, the patients without formal (illiterate) and with primary school education accounted for about 61.5% and only 2 (5.1%) had tertiary 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 over strokes, poverty and psychological and 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 body mass index compared to the control women. These findings are consistent with the results of investigation of previous studies [29–3418-20]. In contrast to our findings, high BMI and obesity in American children and adults with sickle cell anaemia have been reported [35,36]. It appears the anthropometric deficits commonly observed in patients with the disease in the 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 of them had claimed to be on hydroxyurea (35%), folic acid (82%) and omega-3 fatty acids (12.8%). However, their haematological profiles, which were abnormal, were significantly different from that of the healthy control women. This finding was unexpected since hydroxyurea is known to rectify haematological abnormalities in sickle cell disease [37–41]. It is plausible the patients might have not been taking hydroxyurea as prescribed by their physicians because of its side effects (constipation/diarrhoea, 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 haematological data of the hydroxyurea treated and untreated patients, which is similar, reveals that the patients were unlikely to have been taking the medication as per guidance by pharmacist/doctor. Since most sickle cell patients in the country are very poor the government should explore the possibility of partially or wholly subsidising hydroxyurea. Also, is vital that doctors check regularly that their patients are following the prescription guidelines.

Small sample size (more patients who fulfil the inclusion and exclusion criteria could not 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 haemoglobin F tests (lack of laboratory facility) were the main limitations of the study. Regardless of these limitations, the study has provided a very good picture of the nutritional and health status of Sudanese women of childbearing age with sickle cell anaemia.

Conclusion

The low anthropometric measures (height, weight, body mass index) and abnormal haematological values of the women with sickle cell anaemia in steady-state are a reflection of sustained nutrition insults inflected by the disease and poverty. Tailored nutritional counselling/advice must be an integral part of the management of patients with sickle cell anaemia. Such advice is particularly vital for women of childbearing because of the adverse effects of pre-pregnancy nutritional deficiency on birth outcomes.

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Table 1, a. Mean age (± S.D) and clinical parameters of the participants

		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/m^2)		17.2 ± 4.3	21.5 ± 4.2	0.001

NS = not significant

Table 1, b Demographic and clinical variables of the participants

		HbSS (N=39)	HbAA (N=36)	p-Value
BMI (kg/m2)	catigories	№ (%)	№ (%)	p-Value
	Under weight (<18.5)	27(69.2)	9 (25.0)	0.001
	Normal weight (18.5 – 24.9)	11(28.2)	20 (55.5)	0.000
	Over weight / obese >=25	1(2.6)	7(19.4)	0.209
Education	*Illiterate & primary school*	24 (61.5)	3(8.3)	0.000
	Middle & high school	13 (33.3)	11(30.5)	
	University	2 (5.1)	22 (61.1)	0.000
Parental relationship	*1st & 2nd degree relatives*	25 (64.1)	16 (44.4)	0.037
	Unrelated	13 (33.3)	20 (55.6)	0.001
Siblings with SCD	*Yes*	22 (56.4)	3 (8.3)	0.000
	No	17 (43.6)	33 (91.7)	0.000

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)	p>0.05 (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

Table 3. Mean (± S.D) Haematological characteristics of the participants

		HbSS (n=39)	HbAA (n=36)	P- value
Haemoglobin (g/dL)		9.2 ± 1.6	14.3 ± 1.6	0.000
PCV (%)		25.1 ± 6.2	37.6 ± 3.3	0.000
MCV (FL)		88.9 ± 13.5	81.4 ± 5.7	0.003
MCH (pg)		34.5 ± 3.6	31.0 ± 3.0	0.000
White cell count (X 10^3) µL		11.4 ± 4.2	5.9 ± 2.1	0.000
Neutrophils (%)		51.6 ± 11.3	47.9 ± 9.9	NS
Lymphocytes (%)		38.8 ± 9.1	41.0 ± 9.5	NS
Platelets (X 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	**YES**	32 (82.1)	1(2.9)	<0.001
	NO	7 (17.9)	33(97.1)	
Folic acid supplement	**YES**	38 (97.4)	1(2.9)	<0.001
	NO	7(17.9)	1(2.9)	
Hydroxyurea use	**YES**	25 (64.1)	0(0)	<0.001
	NO	14(35.9)	0(0)	
Omega 3 fatty acids	**YES**	4 (10.3) %	0 (0)	NS
	NO	35(89.78)	0(0)	

NS = not significant

Table 4. Mean (± S.D) anthropometric and haematological characteristics of the hydroxyurea treated and untreated (HbSS) groups.

		Treated (n=25)	Untreated (n=14)	P- value
Age		18.9 ± 2.4	19.3 ± 3.1	NS
Weight		39.7 ± 9.7	37.7 ± 7.4	NS
Height		151.4 ± 13.2	150.3 ± 8.5	NS
Body mass index		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
WCC(X 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 (X 10^3) µL		412.2 ± 130.2	403 ± 108.8	NS
		№ (%)	№ (%)	
History of Blood transfusion	**Yes**	20 (80)	12 (85.7)	NS
	No	5 (20)	2 (14.2)	NS
Folic acid supplement	**Yes**	25 (100)	13 (92.8)	NS
	No	0 (0)	1 (7.2)	NS

NS= not significant