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Original Research Article

Haemoglobinopathies in the Northern Darfur state, stratified by tribes and ages

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Abstract

Background: Northern Darfur state in Sudan has a multiethnic population with a high frequency of anaemia, but little is known about the distribution of abnormal Hb in the population. The objective of this study is to appraise the frequency of haemoglobinopathies in Northern Darfur state, stratified by tribes.
Material and Methods: 526 individuals were recruited randomly from thirteen different areas of Northern Darfur. Capillary electrophoresis (CE) was used to evaluate Hb variants. For each case family histories, age, ethnicity and clinical symptoms were recorded.
Results: HbSS was found in three tribes, stratified this way: 2.9 % in the *Fur* tribe, 2.7% *Bartey* and 1.5% *Zagawa*, whereas HbAS was detected in eight tribes, stratified this way, 23% *Keneen*, 18% *Rezegat*, 13.4% Fur, 10.7 *Zagawa*, 9.5% *Bartey*, 8.3% *Ziadya*, 6.6% *Tama* and 5.4% *Tongour*. For the first time in the tribes of Northern Darfur state, the unknown Hb variant was found. Over-expression, one patients was found with HbA = 43.1%, HbS = 48.8%, HbA_2 = 2.9% and HbF = 5%. This result may represent a HbS with a mild Beta plus thalassaemia.
Conclusion: Health education and screening are suggested as ways of avoiding the risk of Hb abnormality in the future. A new Hb variant is apparent in Northern Darfur, in addition to the known abnormal Hb. Therefore further investigations including DNA sequencing are required.
Keywords: Haemoglobin disorders, HbSS, HbAS, population, Northern Darfur.

1. Introduction

Haemoglobinopathies (HBP) are the commonest recessive diseases in human populations. The WHO estimated that about 5% of the world's populations is carrier of HBP [1] with more than 1% of Africans suffering from sickle cell disease (SCD) [2].

The HbS variant (α_2/β_2^{6val}) causing SCD is prevalent in Sudan and is documented among people from Khartoum [3], Blue Nile Province [4] and the Eastern States [5]. In the Kordofan regions HbS is also reported among the Albagara, an Afro-Arab constellation of tribes with a predominant African descent [6].

Studies in a sub group of Albagara / Misseria, have shown the prevalence of the HbS trait to be 30% and 16% among immigrants from the Blue Nile province [4]. This study is meant to provide better data on the prevalence of HBP among the indigenous Sudanese population of the Northern Darfur area.

2. Materials and methods

Being a community based study, participants were recruited from thirteen different areas of the Northern Darfur state, following the probability proportionate to size (PPS) random sampling procedure [7]. All main tribal groups studied (defined geographically), are shown in **Table 1**. Five ml of venous blood was collected in K2-EDTA from 526 individuals aged from 1 to 35 years and delivered to the haematology laboratory at the Darfur Teaching Hospital. Each sample was analyzed with complete blood count (CBC) and Capillary Zone Electrophoresis (CZE) using a fully automated Sysmex KX-21N analyzer (Toa Medical Electronics, Kobe, Japan) [8] and a dedicated CZE (Sebia, Paris, France) [9] respectively.

3. Results

Results were registered as follows: HbA/A (the normal condition = 87.8%); HbA/S (the SCD trait = 10.1%); HbS/S (the sickle cell disease condition = 1. 5%) and HbA/X

(the unknown Hb variants = 0.6%). **Table 2** lists the results by tribe. The homozygous form of Hb S (HbS/S) was found in three tribes out of twelve. The heterozygous form (HbA/S) was found in eight tribes of Northern Darfur state at the following frequencies: 23% *Keneen*, 18% *Rezegat*, 13.4% Fur, 10.7 *Zagawa*, 9.5% *Bartey*, 8.3% *Ziadya*, 6.6% *Tama* and 5.4% *Tongour*. No traits or disease were found in four tribes of Northern Darfur, *Medob*, *Awlad Mana*, *Gawama* and *Shrafa.*

Table 2 also shows age comparisons within the study population. The range of ages of participants with HbAS was (15 month – 35 years), whereas it was 2 – 12 years in HbSS individuals

Figure 1 shows four representative results to demonstrate the consistencies found in the specimens under CZE. **Figure 1a** was selected from those participants for having (a) HbA/S + normal level of A_2 (A = 67%, S = 30% and A_2 3%); **Figure 1_b** represents an individual with HbS/S + F and A_2 zones (S = 84.5%, F = 12.2% and A_2 3%); **Figure 1_c** represents HbA= 91%, HbA2 = 3% and unknown Hb variant = 6%. This may not be a variant but may be an artifact on CZE. This type was found only in three ethnic groups of Northern Darfur, *Ziadya, Bartey and Zagawa* tribes at 4.2%, 1.4 and 0.8% respectively. **Figure 1_d** shows HbA = 43.1%, HbS = 48.8%, HbA_2 = 2.9% and HbF = 5%. This is probably not HbAS as the HbS is high for a carrier, this may represent a HbS with a mild Beta plus thalassaemia.

4. Discussion

This pilot study was meant to see if different frequencies were present in different areas. Due to the limited size of the cohorts this aim has been reached only partially. For the Fur, the Zagawa, and perhaps the Bartey and the Tongour tribes, the number of participants per tribe was small to show a reliable differential picture. Nevertheless, we could observe the presence of the HbS trait at a similar level in the three largest cohorts and establish an average frequency of the HbS trait for the Northern Darfur state of at least 10% (See **Table 2**).

This seems to be lower than other figures reported in the Beja tribes of Eastern Sudan [5], but it is higher than the previous studies reported from the Khartoum area [3] and Blue Nile province [4]. HbA/S frequencies are reported at high but variable levels also from other Arabic countries: Saudia Arabia 2-27% [10] , Bahrain 11.2 % [11] and Kuwait 6 % [12].

The prevalence of Hb S/S in Arabic counties are also detected in varying degrees, for instance in the Eastern province of Saudia Arabia it is 2.6% [10] and Bahrain 2.1% [11]. The frequency of SCD in this study is therefore lower at 1. 5% than findings in Saudi Arabia and Bahrain [10, 11].

Moreover, data on SCD from neighboring countries is scarce, with the exception of works on the Bantu haplotype from the Bantu-speaking tribes of Kenya [13]. Globally, the highest frequency of Hb S/S is reported in Africa (10.6%) [2], the disorder affecting 11.3% in the Sokoto region of Nigeria and 5% of the total population of The Democratic Republic of the Congo[14, 15]. These findings are both higher than the results presented here. This is may be due to low sample size in this study and therefore recruiting high number of individuals below 10 years of age might reflect high prevalence of SCD in this region, as HbA/S frequencies are found to be high.

The result reported here in Figure 1(d) shows an unknown Hb variant. This was found among four different participants of *Ziadya*, *Bartey* and *Zagawa* tribes. It was not possible to distinguish this unknown Hb variant with HbA, but it appeared as a small peak in the D zone. This small peak is too low to be a HbD carrier; further genetic studies are required.

When measuring gene frequencies one should realize that when collecting samples one should exclude relatives and count only one gene per carrier and two per patient. As consanguinity is very common in Arab communities it will be inevitable that researchers will have to deal not only with environmental but also with genetic factors such as founders effect and genetic drift that may produce different frequencies in different tribes. Moreover, the absence of affected SCD patients in a number of small cohorts is to be expected and the young age of the patients indicates probable early mortality.

Current results suggest that the interaction between age and SCA needs to be considered in both clinical and public health settings. Hence, it is important to know the extent and nature of interactions between SCA and age, especially in situations where there is a high prevalence of HbS. It is hoped this series may act as a pilot study to highlight the need to implement a screening programme for sickle patients in Darfur area.

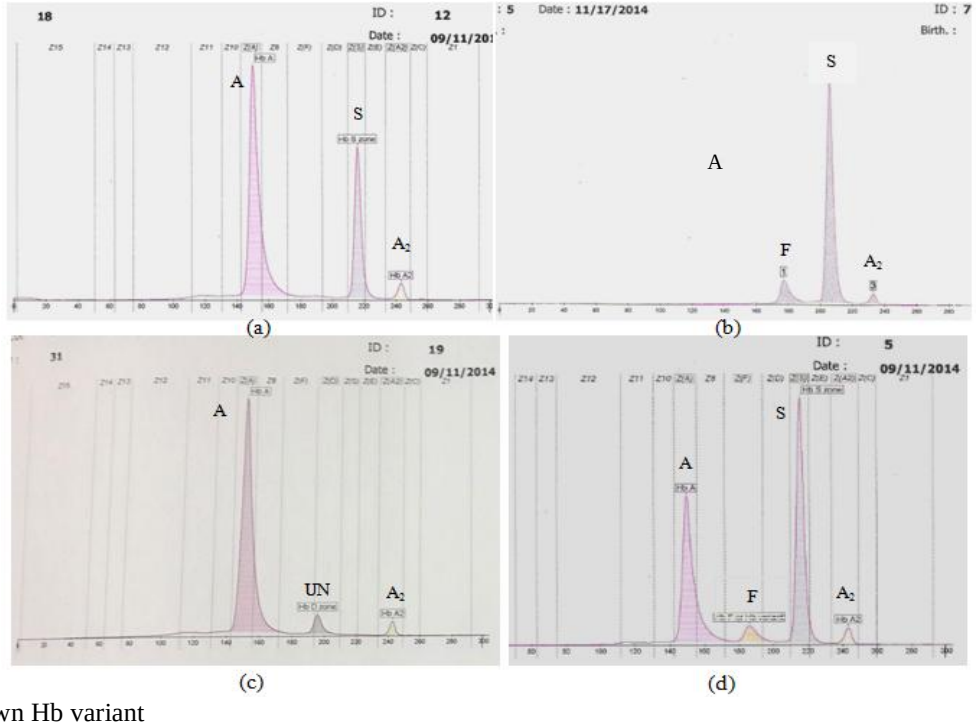
Due to the high carrier frequency and consanguinity, health education and carrier screening needs to be provided to populations at risk. Screening carried out among infants, adolescents, and young adults might provide knowledge which may become forgotten at the moment of need. However, premarital screening and partner selection as it offered in several cultures might not be accepted by younger generations. Screening the female partner early in pregnancy would be the most sensible option, followed by analysis of the male partner and prenatal diagnosis in case of a couple at risk that will have 25% chance to get a severely affected child but then again a 75% chance of an healthy one in the next pregnancy. This would promote disease control and development of a rational strategy to manage haemoglobinopathies.

Table 1: Distribution of participants according to geographical area

Residence area	Frequency (%)
Alfasher	150 (28.5)
Tawela	049 (9.3)
Korma	048 (9.1)
Dar-Alsl	041 (7.8)
Kutom	040 (7.6)
Allayeed	033 (6.3)
Alwaha	033 (6.3)
Altena	033 (6.3)
Ombaro	026 (4.9)
Alseraf	021 (3.9)
Alkoma	019 (3.6)
Karnoy	017 (3.2)
Alkoma	017 (3.2)
Total	526 (100)

Table 2: Distribution of Hemoglobin variants by tribe and age

Tribe	Number tested	HbA/S Number (%)	Age of HbAS participants Range /Y	HbSS Number (%)	Age of HbSS participants Range /Y
Keneen	17	4 (23.5)	11 - 4	-	-
Rezegat	16	3 (18.7)	10 - 16	-	-
Fur	134	18 (13.4)	-	4 (2.9)	2 - 3
Zagawa	131	14 (10.7)	4 - 30	2 (1.5)	7 –13
Bartey	74	7 (9.5)	1 - 35	2 (2.7)	5 - 7
Ziadya	24	2 (8.3)	15 month - 8	-	-
Not definable	12	1 (6.6)	16	-	-
Tama	15	1 (5.4)	7	-	-
Tongour	56	3	8 - 34	-	-
Medob	15	-	-	-	-
Shrafa	10	-	-	-	-
Awlad Mana	11	-	-	-	-
Gawama	10	-	-	-	-
Total	**526**	**53 (10.1)**		**8 (1.5)**	



Key: UN= unknown Hb variant

Figure 2: Detection of Hb variants by CZE shows three representative results to demonstrate the consistencies found in the specimens under CZE. They are selected for having (a) HbAS + normal level of A_2 (A = 67%, S = 30% and A_2 3%); (b) HbSS + F and A_2 zones (S = 84.5%, F = 12.2% and A_2 3%); (c) HbA = 91%, UN = 6% and A_2 3% (d) It is probable HbS/beta plus thalassaemia (A = 43.1%, S = 48.8% , A_2 = 2.9% and F = 5%). Comparable results were also obtained for each variant wherever they occurred among these participants.

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