The Role of Consanguinity in the frequency of Sickle cell anaemia in North Kordofan state

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المستخلص

خلفية الأسر التي بها أفراد مصابين بخضاب الدم الشاذ قد تحتاج إلى عناية صحية مناسبة من أجل سلامة أجيالهم القادمة من هذا المرض الوراثي ومخاطره.

الأهداف: تهدف الدراسة إلى التعرف على دور زواج الأقارب في انتشار مرض فقر الدم المنجلي بمنطقة شمال كردفان، والحد منه وذلك باستخدام اثنين من الدورات المختلفة وبرامج التثقيف الصحي والفحص.

الطريقة في دراسة وصفية تم أخذ عينات دم من عدد ٣٢ أسرة مصابة بمرض فقر الدم المنجلي. جمعت المعلومات وأخذت العينات من وحدة الأطفال بمستشفى الأبيض التعليمي في الفترة ما بين يونيو ٢٠١٢م – يوليو ٢٠١٢م. حللت العينات بواسطة فحص شكل خلايا الدم الحمراء، طريقة الرحلان الكهربائي إضافة إلى الاختبار الخاص بمعرفة الخلايا المتمنجلة.

النتائج خلال ورقة الاستبيان والفحوصات المعملية تم تصنيف الأسر المدروسة إلى مجموعتين. المجموعة الأولى تعبر عن آباء متزوجين من قبيلة واحدة والمجموعة الثانية آباء متزوجين من قبائل مختلفة. المجموعة الأولى شكلت حوالي ٥٦.٢% والثانية ٤٣.٨%. خارج المجموعة الأولى، ٤٠.٦% آباء علاقتهم من الدرجة الأولى (أبناء عمومة، خالات، عمات...). و١٥.٦% آباء علاقتهم من الدرجة الثانية (علاقة غير مباشرة).

الخاتمة زواج الأقارب هو ممارسة شائعة في السودان وغيره من البلدان الإسلامية ويلعب دوراً كبيراً في تزايد وانتشار فقر الدم المنجلي بمنطقة شمال كردفان. عليه توصي الدراسة بتنفيذ برنامجي التثقيف الصحي والفحص الدوري لحديثي الولادة والحوامل بغرض الحد والتقليل من انتشار المرض وسط أجيال المستقبل.

Abstract

Background: Families having offspring or other family members with abnormal haemoglobin (HB) may need appropriate health care for the safety of them and their future generations from this genetic disease and its risks .

Objective: The study aims to identify the role of inbreeding in the prevalence of sickle cell anaemia in North Kordofan State, and to minimize it by using two different courses, health education and screening programmes.

Material and methods: in a descriptive study, S gene was evaluated in freshly obtained venous blood samples from 32 Sudanese family attending the outpatient department at Elobied Teaching Hospital, North Kordofan state, Sudan, in the period between June and July 2012. The patients were surveyed for blood morphology and hemoglobin (HB) electrophoresis using a cellulose acetate method and sickling test.

Results: thirty two consanguineous and non consanguineous families in Northern Kordofan area were studied. Their ages range between (2 - 64 years). Out of studied cases, 56.2% were from one tribe and 43.8% were couples unrelated by tribe. Of couples related by tribe, 40.6% were couples who were first cousins and 15.6% were couples who were second-cousins. Alongside blood analysis, family histories and clinical information were ascertained by questionnaire. Interesting findings relating to (HB) abnormality were discovered within these families.

Conclusion: consanguineous marriage is accepted practice within Sudan and other Islamic countries, but it has a role

in the prevalence of (HB) disorders within certain tribes. Health education and screening are therefore recommended as ways of avoiding the risk of (HB) abnormality in future.

Introduction

Sickle cell anaemia (SCA) is an autosomal recessive Hb disorder with a mutation in the β globin gene. The mutation is: GAG → GTG. This leads to substitution of valine (Val) for glutamic acid (Glu) in the sixth position of the β- globin chain ***(α_2 /β_2 ^{6val})***. Despite being a small change, it can cause disastrous complications (1)**.**

Globally, SCA is the most common symptomatic haemoglobinopathy. SCA was initially reported and named by Herrick in 1910 in the UK. In 1925 Singer and Wells first explained Hb S (2). Hb S varies between ethnicities and occurs with high frequency among populations exposed to falciparum malaria (3). Hb S is known to be prevalent in the Sudan, as it was suggested to be more common in people from Kordofan and Darfur (western Sudan) (4).

Sudan is a typical Islamic country in that consanguineous marriage is commonly practiced. It shares this tradition with other countries like Saudi Arabia, Iraq, Egypt, Jordan and Kuwait, where reports on hereditary blood disorders have already been undertaken (5-8).

Such programmes should be centrally run from hospitals and should be used as an integral strategy to control those individuals according to the WHO strategy. The importance of health education and screening programs has being recognised in the management of sickle cell

anaemia (SCA). The data reported here is based on the results from blood samples taken at various families in Northern Kordofan, Elobied Teaching Hospital, paediatric department.

This building on the results have already achieved with blood morphology, cellulose acetate electrophoresis (CAE)-alkaline method and sickling test, study is concerned with the high prevalence of Hb S in a certain ethnicities. The data collected was intended to investigate the relationship between consanguinity and Hb S. So where possible, samples were also taken from the patients' parents together with information on clinical symptoms, family history and geographical data.

To assist policy-makers, the current study was carried out on patients with S gene as an example to show how genetic epidemiological data can be interpreted in terms of administrative boundaries (and/or ethnic group) and practical service indicators. A policy of detecting carriers and informing them of their risk, and possibilities for minimizing it, usually leads to a fall in births and deaths of affected children. Requirements are the same for sickle-cell disorders and other Hb abnormalities. In developed countries, the approach develops in two stages health education and screening.

These courses are suggested as ways of avoiding the risk of Hb S in Kordofan region. Health education concerns carriers of abnormal Hb, who may be from families consanguineous and non consanguineous by marriage. Patients suitable for screening programmes on the other hand, would include pregnant women and their newly

born children. This programme would also include the genetic counselling of the carriers. Health education is recommended for all known carriers of Hb abnormalities (9, 10). Accordingly, the current study aimed to know the prevalence of SCA in Northern Kordofan, encouraging the decision makers to implement the above mentioned programs.

Materials and methods

Blood morphology and CAE were performed on 32 families. The patient specimens were collected from Elobied Teaching Hospital. Ethical approval for the study protocol (conducted between March 2012 – July 2012) was obtained from the Faculty of Medicine, University of Elimam El Mahdi. Informed consent was obtained individually from all subjects. 5ml of venous blood with K_2-EDTA (anti coagulant) were collected from each participant and delivered to the haematology laboratory at the Elobied Teaching Hospital. Interviews and questionnaires were designed to collect demographic: age, sex, ethnicity (tribe), family history and clinical data.

Each sample was processed as follows:

The following blood morphology and sickling test were performed using fresh venous blood samples and CAE was applied to stored haemolysates, on cellulose paper at alkaline pH.

Blood morphology: a blood film was performed for each sample using a manual technique (11). This gives a full profile from which a case can either be diagnosed or directed for further investigation (11, 12).

Cellulose acetate electrophoresis: horizontal Hb electrophoresis was carried out on the cellulose acetate membrane (CAM) in the Tris-Borate-EDTA (TBE) buffer at pH 8.6, to identify types of Hbs by their differential mobility (11, 13).

Sickle Test: one drop of anti coagulated whole blood was added to two or three drops of the freshly prepared a solution of disodium hydrogen phosphate (Na_2HPO_4) and sodium dithionate (Na_2HPO_4). These were placed between a glass slide and a cover glass and then sealed with paraffin wax. Sickle RBCs were evident immediately in patients with HbSS, whereas sickle RBCs in HbAS patients were only evident after one to two hours and over night in some cases (11, 14).

Results

Table **1** shows the role of consanguineous marriage in the prevalence of S gene in the Northern Kordofan. From sample findings 56.2% of all Hb disorders recorded in this study were from one tribe and 43.8% were couples unrelated by tribe. Of couples related by tribe, 40.6% were couples who are first cousins and 15.6% were couples who are second-cousins.

Table 1 Frequency of consanguineous and non consanguineous marriage within the study group.

Marriage type	**No (%)**
***Couples related by tribe**	18/32(56.2)
Couples who are first cousins	13/32 (40.6)
Couples who are second-cousins and the same tribe	5/32 (15.6)
***Non consanguineous families**	14/32 (43.8)
Couple who are from the different tribes	14/32 (43.8)
Total	**32**

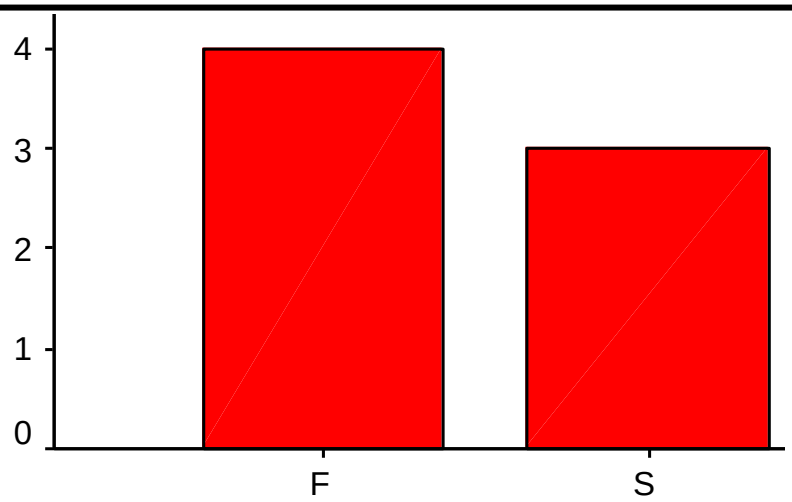
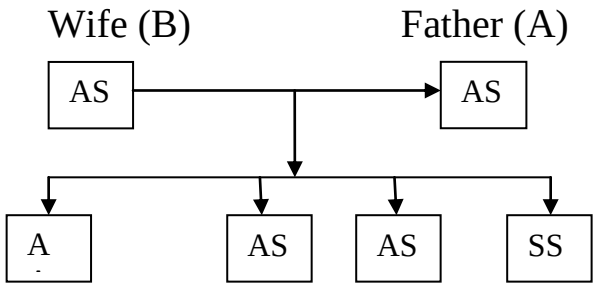


Figure 1 Frequency of first and second cousins within the study group.
***Key**: F= first degree relative; S= Second degree relative.*

Discussion

Thirty two consanguineous and non consanguineous families in Northern Kordofan area were studied. Alongside blood analysis, family histories and clinical information were ascertained by questionnaire. Interesting findings relating to Hb abnormality were discovered within these families.

The below figure, family shows the Hb S gene containing two brothers with SCT, because the father and his wife had Hb AS and their two children were with Hb AS. All families in the current study had carriers parents.



It was found that 18 out of 32 studied families (56.2%) confirmed consanguineous marriage, as depicted in Table **1**. The study was restricted to families from certain tribes of the Northern Kordofan state, but it would be fair to assume that consanguineous marriages have a role in the prevalence of Hb S throughout Northern Kordofan.

Screening should be carried out among infants, pregnant women, adolescents, and young adults - especially in remote areas. This would promote the control and development of a rational strategy to decrease the prevalence SCA.

Consanguineous marriage is accepted practice within the Sudan and other Islamic countries (5, 6, 15), but it has a role in the prevalence of Hb disorders within certain carriers (16). Health education and screening are therefore recommended as ways of avoiding the risk of Hb abnormality in the future. Health education techniques concern patients and families both consanguineous and non consanguineous by marriage, which was discussed in other published studies (17, 18). Hence, a multidisciplinary approach to the management of SCA is

crucial. This report recommends a health program management, screening in health centres and health education. Health education is especially important because inter-tribal marriage is a major factor in the prevalence of the disease, as mentioned here. As the current findings imply, a screening study is needed. Additionally, there is an urgent need to establish a screening database for SCA and malarial prevalence.

Consanguinity studies can offer fundamental data to the prevalence of Hb S. This type of abnormal Hb is common in Sudan and it is hoped that this study may prompt further molecular biology based research in the management of this abnormality.

The prevalence of S Hb can be reduced by the pre marriage diagnostic screening of carriers with hereditary disorders. At present, the majority of people in Sudan have no recorded medical history and there are currently no screening facilities. One outcome from the data reported here is that following birth all babies undergo blood morphology, CAE and sickling test screening for Hb S, and have their medical history recorded. Accordingly, this study is recommended to establish Haematology clinics and health centres specialising in SCA within Kordofan state.

Conclusion:

In conclusion, two courses of action involving health education and screening are suggested as ways of avoiding the risk of Hb abnormality. Health education is recommended for all known carriers of Hb abnormalities and patients suitable for screening programmes should include pregnant women and their newly born children. Screening should also include the genetic counselling of carriers (9, 10).

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