

قال تعالى :

{ وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ  
وَرَسُولُهُ وَالْمُؤْمِنُونَ وَسَتُرَدُّونَ إِلَى  
عَالِمِ الْغَيْبِ وَالشَّهَادَةِ فَيُنَبِّئُكُمْ بِمَا  
كُنْتُمْ تَعْمَلُونَ }

صدق الله العظيم

سورة التوبة الآية 105

# Dedication

To All We Love  
&  
Cherish

## Acknowledgment

First of all thanks for Allah that giving me the power and will to complete this study.

I would like to express my sincerest and thanks to my supervisor Dr.Tariq Elfatih Elmisbah for his close supervision, advice and endless guide.

I wish to express Acknowledgment the help provided by the staff of Albuluk, Omdurman and Khartoum Paediatric Hospitals for their help and support .

Thanks are extended to my brother Abu Algassim, my sister Afaf and my cousin Faiza Hassan for their help and support.

# Abstract

This was descriptive and cross-sectional study was carried out in Khartoum state during the period from November 2008 to January 2009.

The study was designed to determine the pattern of inheritance of sickle cell anemia in parents of patients who referred to three hospital of Khartoum State.

Hundred parents (50 mother and 50 father) were selected for this study, from Khartoum pediatric Hospitals, (2,5) ml of venous blood was taken from all parents and put it in an anticoagulant container. Complete blood count (CBC) was determined by use of Sysmex instrument N-50, and samples were investigated for HbS by use of sickling test. Hemoglobin electrophoresis was performed to determine the pattern of inheritance of sickle cell gene.

The results were as followed:

97% of samples were heterozygous form of Hb S ( $\beta\beta^S$ ) and the remaining were homozygous form of HbS ( $\beta^S\beta^S$ ). 89% red cell morphology was normocytic normochromic cells, and the remaining were microcytic normo-hypochromic cells. The means of count and cell indices in the carrier and diseased parents as follows respectively: the mean of white blood cells count(TLC) was  $8.5 \times 10^9/l$  and  $6.9 \times 10^9/l$ , the mean of red blood cell count(RBC) was  $4.6 \times 10^{12}/l$  and  $3.9 \times 10^{12}/l$ , the mean of hemoglobin(Hb) was 13g/dl and 9g/dl, the mean of hematocrit(PCV) was 41.2% and 39.3%, the mean of mean cell volume (MCV) was 86.2 and 86.3fl, the mean of mean cell hemoglobin(MCH) was 30pg and 29.1pg the mean of mean cell hemoglobin concentration (MCHC) was 31.2% (58%) and 31.3%, the mean of platelets count(PLT) was  $207 \times 10^3/\mu l$  and  $298 \times 10^3/\mu l$ .

The highest frequency of sickle cell anemia was found in Messaria tribe (40%), followed by Bargo tribe (30%), Hausa and Rezaigat (8%), Taisha and Jawama (6%), and Zagawa (2%).

# مستخلص الدراسة

اجريت هذه الدراسة الوصفية التحليلية فى ولاية الخرطوم فى الفترة من نوفمبر 2008 حتى يناير 2009 وذلك لتحديد النمط الوراثي لآباء المرض بالمترددين على ثلاثة مستشفيات بولاية الخرطوم, تم اختيار مائة من الابوين (50 أب، 50 أم) لاجراء هذه الدراسة , تم اخذ 2,5 مل من الدم فى وعاء مانع للتجلط من كلا الابوين, تم قياس صورة الدم الكامل باستعمال جهاز سيسمكس وتم إختبار العينات لهيمقلوبين S باستعمال الإختبار المنجلي, عمل الفصل الكهربائي للهيموقلوبين لتحديد النمط الوراثي وكانت النتائج كالآتى :

97% من العينات كانت تحمل الشكل الغير متجانس لهيموقلوبين S والبقية عبارة عن الشكل المتجانس للهيمقلوبين, 89% من شكل الخلايا الحمراء عبارة عن خلايا طبيعية اللون والحجم والبقية عبارة عن خلايا طبيعية-قليلة اللون وطبيعية الحجم, وكان متوسطات عدد ومعاملات الخلايا فى الآباء الحاملين والمرضى على التوالى كالآتى: متوسط عدد كرات الدم البيضاء .  $10^9 \times 5.8$  / لتر و  $10^9 \times 6.9$  /لتر ومتوسط عدد خلايا الدم الحمراء  $10 \times 4.6$   $10^{12}$  /لتر و  $3.9 \times 10^{12}$  /لتر م, ومتوسط الهيمقلوبين 13 جرام % و 9 جرام% ومتوسط الهيماتوكريت 41.2 % و 39.3% و متوسط حجم الخلية 86.3 فيمتو /لتر و 83.2 فيمتو/ لتر, ومتوسط هيمقلوبين الخلية 30 بيكو جرام و 29.1 بيكو جرلم, ومتوسط تركيز هيمقلوبين الخلية 31.2% و 31.3% . ومتوسط عدد الصفائح الدموية  $10^3 \times 207$  /ميكرولتر و  $10^3 \times 298$  ,

اعلى تكرار للانيميا المنجلية وجد فى قبيلة المسيرية (40%) تبعثها قبيلة البرقو (30%) ثم الهوسا والرزقات (8%) والتعايشة والجوامعة (6%) والزغاوة (2%) .

# Contents

| <b>Subject</b>               | <b>Page</b> |
|------------------------------|-------------|
| <b>Quran</b>                 | <b>1</b>    |
| <b>Dedication</b>            | <b>11</b>   |
| <b>Acknowledgment</b>        | <b>111</b>  |
| <b>Abstract (in English)</b> | <b>1V</b>   |
| <b>Abstract (in Arabic)</b>  | <b>V</b>    |
| <b>Contents</b>              | <b>V1</b>   |
| <b>List of tables</b>        | <b>X</b>    |
| <b>List of Figures</b>       | <b>XI</b>   |
| <b>List of plates</b>        | <b>XIII</b> |

## **Chapter one**

### **Introduction and Literature review**

|   |          |
|---|----------|
| <b>1.1. General introduction.</b>                       | <b>1</b> |
| <b>1.1.1. Anaemia.</b>                                  | <b>1</b> |
| <b>1.1.2. Evaluation and diagnosis.</b>                 | <b>2</b> |
| <b>21.1.3. Classification of anemia.</b>                | <b>2</b> |
| <b>1.1.3.1. Etiological classification.</b>             | <b>2</b> |
| <b>1.1.3.2. Morphological classification.</b>           | <b>2</b> |
| <b>1.2. Normal hemoglobin.</b>                          | <b>3</b> |
| <b>1.2.1. Discovery.</b>                                | <b>3</b> |
| <b>1.2.2. Synthesis.</b>                                | <b>4</b> |
| <b>1.2.3. Structure.</b>                                | <b>4</b> |
| <b>1.2.4. Types.</b>                                    | <b>6</b> |
| <b>1.3. The abnormal hemoglobin (hemoglobinopathy).</b> | <b>6</b> |
| <b>1.3.1. Genetics.</b>                                 | <b>7</b> |
| <b>1.3.2. Nomenclature.</b>                             | <b>7</b> |
| <b>1.3.3. Classification.</b>                           | <b>8</b> |

|   |           |
|---|-----------|
| <b>1.3.4. Prevalence and geographical Distribution.</b>       | <b>9</b>  |
| <b>1.3.5. Pattern of inheritance .</b>                        | <b>9</b>  |
| <b>1.3.6. Clinical features.</b>                              | <b>10</b> |
| <b>1.3.7. Variants.</b>                                       | <b>11</b> |
| <b>1.3.8. HbC Disorder.</b>                                   | <b>11</b> |
| <b>1.7.1.1. HbC Trait.</b>                                    | <b>12</b> |
| <b>1.7.1.2. HbC Disease.</b>                                  | <b>12</b> |
| <b>1.7.13. HbSC Disease.</b>                                  | <b>12</b> |
| <b>1.7.1.4. Clinical Features.</b>                            | <b>13</b> |
| <b>1.7.1.5. Lab Findings.</b>                                 | <b>13</b> |
| <b>1.3.7.2. HbD Disorder.</b>                                 | <b>13</b> |
| <b>1.3.7.2.1. HbD Trait.</b>                                  | <b>13</b> |
| <b>1.3.7.2.2. HbD Disease.</b>                                | <b>13</b> |
| <b>1.3.7.2.3. HbSD Disease.</b>                               | <b>13</b> |
| <b>1.3.7.3. HbE Trait.</b>                                    | <b>13</b> |
| <b>1.3.7.3.1. HbE Disease.</b>                                | <b>13</b> |
| <b>1.3.8. Lab Findings.</b>                                   | <b>14</b> |
| <b>1.2. Literature Review.</b>                                | <b>15</b> |
| <b>1.2.1. Sickling Disorders.</b>                             | <b>15</b> |
| <b>1.2.1.1. History.</b>                                      | <b>15</b> |
| <b>1.2.1.2. HbS Prevalence and Geographical Distribution.</b> | <b>15</b> |
| <b>1.2.1.3. Nomenclature.</b>                                 | <b>16</b> |
| <b>1.2.1.4. Pathophysiology.</b>                              | <b>16</b> |
| <b>1.2.1.5. Cellular Pathology.</b>                           | <b>18</b> |
| <b>1.2.1.6. Pathogenesis of Haemolysis.</b>                   | <b>18</b> |
| <b>1.2.1.7. Pathogenesis of Vaso-occlusion.</b>               | <b>19</b> |
| <b>1.2.2. Sickle Cell Disease (SCD).</b>                      | <b>19</b> |
| <b>1.2.2.1 Inheritance.</b>                                   | <b>20</b> |

|                                       |    |
|---------------------------------------|----|
| 1.2.2.2. Other factors influence SCD. | 23 |
| 1.2.2.3. Clinical Features.           | 25 |
| 1.2.2.4. Lab Findings.                | 26 |
| 1.2.3. Sickle Cell Trait(SCT).        | 26 |
| 1.2.3.1. Clinical Feature.            | 29 |
| 1.2.3.2. Diagnosis.                   | 29 |
| 1.2.4. Diagnosis of SCD&SCT.          | 30 |
| Objectives                            | 31 |

## **Chapter Two**

### **Materials and Methods**

|   |    |
|---|----|
| 2.1. Study design.                                    | 32 |
| 2.2. Study area.                                      | 32 |
| 2.3 .Study population.                                | 32 |
| 2.3.1. Inclusion criteria.                            | 32 |
| 2.3.. Exclusion criteria.                             | 32 |
| 2.4. Methods.   | 32 |
| 2.4.1. Sample collection.                             | 32 |
| 2.4.2. Methods used.                                  | 32 |
| 2.4.2.1. Complete blood count instrumentation method. | 32 |
| 2.4.2.1.1. Instrument required.                       | 32 |
| 2.4.2.1.2. Principle.                                 | 33 |
| 2.4.2.2. Sickling Test.                               | 33 |
| 2.4.2.2.1. Principle.                                 | 33 |
| 2.4.2.2.2. Procedure.                                 | 33 |
| 2.4.2.3 Hb electrophoresis.                           | 33 |
| 2.4.2.3.1. Principle.                                 | 33 |
| 2.4.2.3.2. Preparation of samples.                    | 34 |



|  |    |
|--|----|
| 2.4.2.3.3. Material and methods.         | 34 |
| 2.4.2.3.4. Procedure.                    | 34 |
| 2.4.2.3.5. Result.                       | 35 |
| 2.4.2.3.5. Peripheral smear examination. | 35 |
| 2.5. Data analysis.                      | 35 |
| <b>Chapter Three</b>                     |    |
| <b>The results</b>                       |    |
| The results                              | 36 |
| <b>Chapter Four</b>                      |    |
| <b>Discussion</b>                        |    |
| Discussion                               | 51 |
| <b>Chapter Five</b>                      |    |
| <b>Conclusion and recommendations</b>    |    |
| Conclution and Recoendations             | 53 |
| <b>Chapter six</b>                       |    |
| <b>References</b>                        |    |
| References                               | 54 |

## **Lists of tables**

|   |                |
|---|----------------|
|   | <b>Subject</b> |
| <b>Page</b>   |                |
| 1-1. Classification of anemia based on red cell measurements. |                |
| 3   |                |
| 1-2. Allelic and non allelic inheritance pattern in doubly    |                |
| 10  |                |
| Heterozygous individuals.                                     |                |

|      |               |                          |                      |
|------|---------------|--------------------------|----------------------|
| 1-3. | Common        | hemoglobinopathies       | .                    |
| 11   |               |                          |                      |
| 3-1. | Distribution  | of samples according to  | tribes.              |
| 36   |               |                          |                      |
| 3-2  | .Distribution | of samples according to  | hospitals.           |
| 37   |               |                          |                      |
| 3-3. | Frequency     | of samples according to  | sickling test.       |
| 38   |               |                          |                      |
| 3-4. | frequency     | of samples according to  | morphology of RBCs . |
| 39   |               |                          |                      |
| 3-5. | Distribution  | of patients according to | residence.           |
| 40   |               |                          |                      |
| 3-6. | Distribution  | of tribes according to   | Hb SS and Hb AS.     |
| 41   |               |                          |                      |

## Lists of figures

|   | <b>Subject</b> |
|---|----------------|
| <b>Page</b>   |                |
| 1.1. Normal and sickled RBC.  |                |
| 17  |                |
| 1.2. Inheritance of sickle gene from parent with usual and trait.                 |                |
| 20  |                |
| 1.3. Inheritance of sickle gene from parent with sickle trait.                    |                |
| 21  |                |
| 1.4. Inheritance of sickle gene from parent with trait and anemia.                |                |
| 21  |                |
| 1.5. Inheritance of sickle gene from parent with usual and anemia.                |                |
| 22  |                |
| 1.6. Inheritance of hemoglobin gene from parent with sickle trait.                |                |
| 22  |                |
| 1.7. Inheritance of sickle gene from parent with sickle cell & thalassemia trait. |                |
| 24  |                |
| 3.1. Distribution of samples according to tribes.                                 |                |
| 36  |                |
| 3.2. Distribution of samples according to hospitals.                              |                |
| 37  |                |
| 3.3. Frequency of samples according to sickling test.                             |                |
| 38  |                |
| 3.4. frequency of samples according to morphology of RBCs.                        |                |
| 39  |                |
| 3.5. Distribution of patients according to residence.                             |                |
| 40  |                |
| 3.6. Mean of leucocyte count in the parent.                                       | 41             |
| 3.7. Mean of red blood cell count in the parent.                                  |                |
| 42  |                |

|             |      |    |                                    |        |    |     |         |
|-------------|------|----|------------------------------------|--------|----|-----|---------|
| 3.8.<br>43  | Mean | of | platelet                           | count  | in | the | parent. |
| 3.9.<br>44  | Mean | of | hemoglobin                         |        | in | the | parent. |
| 3.10.<br>45 | Mean | of | haematocrit                        | (PCV)  | in | the | parent. |
| 3.11.<br>46 | Mean | of | Mean Cell Volume                   | (MCV)  | in | the | parent. |
| 3.12.<br>47 | Mean | of | Mean Cell Hemoglobin               | (MCH)  | in | the | parent. |
| 3.13.<br>48 | Mean | of | Mean Cell Hemoglobin Concentration | (MCHC) | in | the | parent. |

## List of Plates

| <b>Subject</b>  | <b>Page</b> |
|---|-------------|
| Plate.1. Sick cell anemia, Peripheral blood film showing deeply staining sick cells, target cells and polychromasia (a howell-jollybody is seen in a red cell in the top right portion of the field). | 59          |
| Plate.2.Homozygous Hb C disease, peripheral blood film showing many target cells, and spherocytic cells.  | 60          |
| Plate.3.Sickle cell anemia, painful swollen fingers (dactylitis)  | 61          |
| Plate.4. Sick cells anaemia, medial aspect of the ankle of a 15-year-old Nigerian boy showing necrosis and ulceration.  | 62          |