Hematological characteristics in Sudanese adult with sickle cell disease in Khartoum state

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Abstract: Sickle cell anemia (SCA) is a major cause of morbidity and mortality and affect hematological profile, a case control study conducted at national health laboratory in Khartoum state in period between 14 December 2011 to 20 November 2012, 80 patients with Sickle cell anemia (SCA) were enrolled, blood samples were collected in EDTA containers from each individual, Automated Cell Counter; Sysmex 21 was used to determine complete blood counts including blood cell indices, hemoglobin electrophoresis apparatus was used to estimate sickle cell genotypes using cellulose acetate alkaline electrophoresis technique. The frequency distribution of sickle cell phenotypes of study group on basis of hemoglobin electrophoresis were SS 29(36.2%), AS 49(61.2%), SC 1(1.3%), SF 1(1.3%). The mean hemoglobin concentration, mean packed cell volume, mean cell volume (MCV), mean cell hemoglobin (MCH) and mean cell hemoglobin concentration (MCHC) were 9.2 ± 3.2 gm/dl, 30.2 ± 9.2%, 76.6 ± 7.9/fl, 23.2 ± 3.0/pg, 30.1 ± 2.3gm/dl. Significant lower hemoglobin (p value <0.05), The mean TWBC, RBC and platelet counts were 11.1 x 109/L ± 8.6, 3.9 x 1012/L ± 1.3, 450 x 109/L ± 15.8, significant higher TWBC and lower RBC counts of p value <0.05 for both. the findings indicates for moderate to severe anemia.
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1. Introduction

Sickle cell disease is the most common hemoglobinopathies results from inheritance of abnormal hemoglobin S gene from parents, sickle cell disease was first described in 1910, in a dental student [1] Sickle-cell disease occurs more commonly among people whose ancestors lived in tropical and sub-tropical sub-saharan regions.[2] The clinical manifestations arise from the tendency of the hemoglobin (HbS or sickle hemoglobin) to polymerize and deform red blood cells into the characteristic sickle shape. This property is due to a single nucleotide change in the β -globin gene leading to substitution of valine for glutamic acid at position 6 of the β -globin chain (β 6glu→val or β s). [3] The homozygous state (HbSS or sickle cell anaemia) is the most common form of sickle cell disease, but interaction of HbS with thalassaemia and certain variant hemoglobins also leads to sickling. The term sickle cell disease (SCD) is used to denote all entities associated with sickling of hemoglobin within red cells [4] The normal hemoglobins are hemoglobin A (α2β2), hemoglobin A2 (α2δ2), and hemoglobin F (fetal hemoglobinα2γ2). In the adult, hemoglobin A represent<95% of the hemoglobin, A2 represents >3 to 4%, and F represents <1 to2%. In embryo is Hb-Portland (ζ2γ2), Hb-Grower1 (ζ2ε2) and Hb-Grower2 (α2ε2). Sickle hemoglobin is designated S because erythrocytes with hemoglobin S can transform into a sickle shape [5]. The genotypic designation is based upon the specific globin chains that are present. Heterozygous sickle cell would be designated α2ββs (two normal α chains, one normalβ chain, and one β chain with the sickle gene. Homozygous sickle cell anemia would be designated α2β2 [5] compound heterozygosity for hemoglobin S and hemoglobin C would be designated α2βsβ.c Hemoglobin S tends to polymerize into long rigid structures, which distort the cell into the characteristic sickle shape. Anything that causes deoxygenation of hemoglobin predisposes to sickling, including hypoxia, acidosis, and increased temperature. The polymerization of hemoglobin S is reversible, and cells that have sickled may return to normal shape with reoxygenation. However, the repeated cycles of sickling and unsickling damage the cell, and, eventually, the erythrocytes becomes irreversibly sickled. The rigid elongated sickle cells obstruct small blood vessels, resulting in tissue infarction. Sickled erythrocytes are also “sticky” and

adhere to endothelial cells, predisposing to thrombosis. Common sites of infarction include the spleen, bone and bone marrow, the medulla of the kidney, mesenteric vessels, and pulmonary vessels [6]. Sickle-cell disease may lead to various acute and chronic complications, several of which have a high mortality rate [7]. Many patients with SCA are in reasonably good health most of the time and achieving a steady state level of fitness. This state of relative well-being is periodically interrupted by crisis of which the vaso- occlusive crisis (VOC) is the most common and hallmark of patients with SCD.

The importance of early recognition and subsequent clinical and hematological assessment of the disease are greatly facilitated by familiarity with the patient's steady state. A patient with SCA is said to be in steady state when there is absence of infection, acute complicating f or acute clinical symptoms or crisis continues for at least three months [8]. Crisis refers to episodes of acute illness attributable to the sickling phenomenon in which there is a sudden deviation for the worse or a sudden exacerbation of symptoms and signs of patients with SCA who had hitherto been in stable condition [9]. Various changes in therapeutic, economic, social, technological measures have taken place [10]. Most episodes of sickle cell crises last between five and seven days. "Although infection, dehydration, and acidosis (all of which favor sickling) can act as triggers, in most instances no predisposing cause is identified [11] Patients with sickle cell disease (SCD) have varying amounts of abnormal hemoglobin called the sickle cell or "S" hemoglobin in their erythrocytes. Sickle cell anaemia (SCA) is due to the substitution of adenine with thymine in the glutamic DNA codon (GAG→GTG), which results in turn, in substitution of β 6 valine for glutamic acid. The disease accounts for over 60% of the world's major haemoglobinopathies with an estimated 2-3 million Nigerians affected by the "S" gene. [12]. Because of anemia dominates within sickling disorder; we aim to estimate hematological profile regarding as early indicator for sickle cell crisis.

2. Material and Methods

The study is a case control study conducted in period 14 December 2011 to 20 November 2012, at national health laboratory (NHL) hematology department in Khartoum town - Sudan, to determine hematological parameters of patients with sickle cell diseases. The study includes 80 male diagnosed patients with sickle cell disease (mean age 28 ± 0.35 year) and 20 healthy male individuals as control group(mean age 28 ± 0.33 year). 2ml EDTA blood samples were collected from each participant, Hb, Hematocrit, RBC, WBC, and platelets counts were estimated using hematological cells counter Symex 21. Hemoglobin electrophoresis was carried out on cellulose acetate membrane (CAM) in Tris- EDTA-Borate buffer at pH 8.6 for disease phynotyping. and quantification of A2 fraction of hemoglobin by elution method. All calculations were done using the SPSS-V19 statistical software package for analysis of the data. The data were presented as Mean ±SD, and statistical analysis was carried out using the student's paired t-test and. Differences were considered to be statistically significant at P value ⩽0.05.

3. Results

The frequency distribution of sickle cell phenotypes of study group (n 80) on basis of hemoglobin electrophoresis were SS 29(36.2%), AS 49(61.2%), SC 1(1.3%), SF 1(1.3%) Figure1. Hemoglobin, packed cell volume and mean cell hemoglobin were significant low in compared to control (P value <0.05), while mean cell volume was unaffected (P value = 0.851) Table1. Higher statistically significant levels were obtained for WBC, and lower RBC counts in patients with sickle cell disease (P value < 0.05) for both, in contrast platelet count was non-significant when compared between two groups (> 0.05) Table 2. Significant lower levels of hemoglobin, hematocrit and red cell counts and significant high values of total leukocyte and platelet counts (P value ⩽ 0.05) in comparison HbSS to HbAS genotype Table 3

Table 1. Red cell indices of study group groups case subject (n=80), control subject (n=20)

Variable	Sample	Mean ± SD	P-value
Hemoglobin g/dl	Case	9.2 ± 3.2	0.001
	Control	11.7 ± 1.9	
Packed cell volume%	Case	30.2 ± 9.2	0.133
	Control	37.7 ± 5.2	
Mean cell volume/fl	Case	76.6 ± 7.9	0.851
	Control	80.7 ± 7.7	
Mean cell hemoglobin/pg	Case	23.2 ± 3.0	0.34
	Control	24.8 ± 2.8	
Mean cell hemoglobin con g/dl	Case	30.1 ± 2.3	0.136
	Control	30.9 ± 1.3	

Table 2. Blood cell counts of study group groups (n=80), control subject (n=20)

Variable	Sample	Mean ± SD	P-value
White blood cell count $x10^9$/L	Case	11.1 ± 8.6	0.001
	Control	6.8 ± 1.8	
Red blood cell count $x10^{12}$/L	Case	3.9 ± 1.3	0.001
	Control	4.7± 0.5	
Platelet count $x10^9$/L	Case	450± 15.8	0.029
	Control	298 ± 17.1	

Table 3. Hematological values in patients with sickle cell anemia HbSS (n=29) and Hb AS (n=49)

Variable	genotype	Mean ± SD	P-value
Hemoglobin g/dl	SS	6.0 ± 1.7	0.001
	AS	11.2 ± 2.0	
Packed cell volume%	SS	20.8 ± 5.5	0.001
	AS	35.9 ± 5.7	
Mean cell volume/fl	SS	80.2 ± 8.4	0.31
	AS	84.7 ± 7.0	
Mean cell hemoglobin/pg	SS	23.2 ± 3.1	0.43
	AS	23.1 ± 3.0	
Mean cell hemoglobin con g/dl	SS	30.8 ± 1.8	0.70
	AS	30.9 ± 2.2	
White blood cell count $x10^9$/L	SS	17.2 ± 3.4	0.01
	AS	7.4 ± 2.5	
Red blood cell count $x10^{12}$/L	SS	2.6 ± 0 .83	0.02
	AS	4.8 ± 0.58	
Platelet count $x10^9$/L	SS	363.3± 16.8	0.01

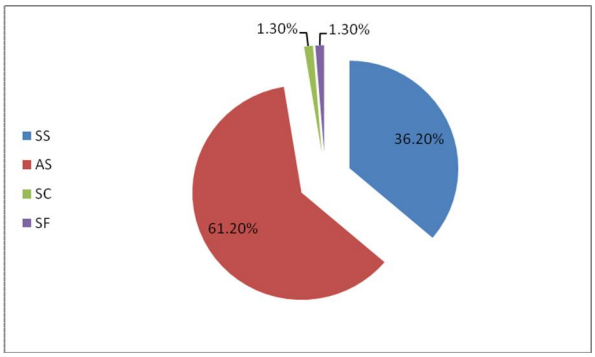

Figure1. Shwos the frequency distribution of sickle cell phenotypes of study group

4. Discussions

Hematological profile of 80 male sickle cell disease patients attending national health laboratory hematology department in Khartoum. We found the pattern of sickler genotypes by Hb electrophoresis were Hb AS 49(61.2%), HbSS 29(36.2%), HbSC 1(1.3%) and Hb FS 1(1.3%), our finding in agreement with study reported that the frequency of sickler carriers (Hb AS) has reached higher levels among populations including Nigeria and Afro-Caribbean [13]. The study revealed that Hb SS is the main form of sickle cell disease in Sudan, and Hb SC and Hb FS in less extend similar result was reported [14]. The carrier frequency ranges between 10% and 40% across equatorial Africa, decreasing to 1–2% on the North African coast and <1% in South Africa [15].

We observed no differences of mean Packed cell volume, mean cell volume (MCV) and the mean cell hemoglobin (MCH) and mean hemoglobin concentration (MCHC) in patients with SCA compared to control group mean values. We found significant lower of hemoglobin levels in patients with SCA as consequence of severe chronic hemolytic crisis accompanied with SCA patients, This is in agreement with previous studies [16].

The mean total white blood cell count (WBCC) recorded in this study for steady state, VOC and control are of similar values to those reported by other authors [16]. As expected, the total WBCs counts was significantly higher than in controls ($P<0.001$). This is expected because of the basic mechanisms which cause an increase concentration of neutrophils in venous blood of SCA patients which include intravascular neutrophils demargination accelerated release from the bone marrow. Patients with SCA are known to have significantly higher mean total WBCC than normal healthy people of AA genotype. As suggested that inflammatory response is leading to the release of cytokine mediators enhance neutrophils production by the bone marrow [17]. This has continued to affect the ability of clinicians to predict the presence of bacterial infections from leukocyte counts in sickle cell anemia patients [18]. Significant difference in platelet count between study and control groups was encountered. The finding in agreement with previous study reported that, platelet count is higher in SCA than in healthy control, because of absent of splenic platelet pool in adult sickle cell patients [19].

When compared HbSS to HbAS subjects, we observed significant lower levels of hemoglobin, hematocrit and red cell counts and significant high values of total leukocyte and platelet counts (P value $\leqslant 0.05$), has been attributed to some factors intrinsic to the HbSS genotype such as excess hemolysis, frequent infections or immune mediated responses of granulocytes to various pathogens [20]. The results obtained in the present study correlated significantly with those earlier reported study [21].

Conclusion:

We conclude, low hemoglobin and lower red blood cell counts indicate occurrence of moderate to severe anemia, while high white blood cell count result from inflammatory stimulus of sickle cell crisis, Further large sample size studies are needed to determine the association clinical manifestation of the disease and its effect on the hematological parameters.

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