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Hematological Parameters in Sudanese Child and Adolescents with Sickle Cell Anemia (Hb SS Pattern) during Crisis

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Abstract

Background and Objectives: *One of the most important clinical symptoms of Sickle Cell Anemia (SCA) is severe anemia (hemolytic and a plastic). Hematological parameters, on the other hand, will be affected. Thus we try to assess hematological parameters in Sickle Cell Anemia (SCA) patients with Hb SS pattern during crisis.*

Methodology: *A cross sectional hospital based study, included 340 child and adolescents clinically and laboratory diagnosed as sickle cell anemia homozygous (SS pattern). Their age ranged 1–18 years. Patients younger than six months and older than 18 years of age, were excluded also patients with other haemoglobinopathies and sickle cell trait. A 2,5 ml of venous blood was collected in ethylenediamine- tetraacetic acid (EDTA) anticoagulated tube from each patient. The blood mixed well with an anticoagulant then analyzed immediately for full blood count was analyzed immediately using sysmex autoanalyzer Kobe, Japan. Data analyzed using IBM SPSS advanced statistics version 22 (SPSS Inc., Chicago, IL).*

Results: *The study observed low RBCs count (2.7 X 1012 /L ±0.51) and HCT (21.1 ± 3.1) %. Elevation in the total white blood cells (leuckocytosis) with the mean 14.9 X 109 /L±6.3. Platelets had insignificant correlation with crisis p, value 0.458. In conclusion, the above findings have highlighted the urgent need for Sickle Cell Anemia center in this area and could be the first step towards addressing effective control.*

Keywords: Sickle Cell Anemia (SCA). SS Pattern. Crisis. Sudanese Child. Hb F. Platelets count, White Blood Cells count, leuckocytosis, RBCs count, Kosti

INTRODUCTION:

Sickle cell disease (SCD) described at 1910 when a patients with severe anaemia was noted to have elongated and sickle shaped red blood cells (RBCs). Many years later, Linus Pauling and his colleagues found the sicklling phenomenon is caused by hemoglobin with abnormal characteristics then, subsequently Vernon Ingram with his colleagues reported the causative amino acid in the ß- chain of hemoglobin. [(1)] SCA is a

hemolytic anemia characterized by structural changes in the ß-globin chain, leads to synthesis of an abnormal hemoglobin (Hb) in homozygous (Hb SS).[2] It is an inherited autosomal recessive genetic hemoglobinopathy disorders due to the substitution of an Adenine (A) for a Thymine (T) in the sixth codon of the beta globin gene, leading to the substitution of glutamic acid for valine and then production of Hemoglobin S (HbS), which cause deoxygenated sickle hemoglobin to form polymers that destroy RBCs. [3]

This mutation appears to have originated independently in different parts of the world. It is one of the most common single gene mutations in man and has a wide geographical distribution. It is found across most of Africa, the Middle East, India, and parts of the Mediterranean. SCD globally affects more than 20 million people. [4] Sickle cell gene is known to be prevalent in Sudan since 1950. [5] In central Sudan Khartoum which is a multiethnic area due to migrations, 632 patients attending Khartoum Teaching Hospital, 5.1% of them had Hb AS and 0.8% had Hb SS. [6] This rate is highest in Sudanese from Western ethnic groups particularly Messeryia tribes. [7]

The pathophysiology of sickle cell anemia depends on the degree of polymerization of deoxygenated sickle hemoglobin, thus the clinical symptoms of patients with HbSS disease are varies considerably from a symptomatic in some patients, to death in infancy in the others. One of the most important clinical symptoms is severe anemia (hemolytic and a plastic) . [8]

Hemolytic anemia is characterized by reduced red blood cells (RBCs), hemoglobin, and hematocrit in patients with homozygous SS and heterozygous S/ßo mutations. [9] White blood cell (WBC) and platelet counts (PLT) on the other hand, are increased and vary. The degree of anemia generated by the cells' hemolysis, sequestration, and bone marrow response to anemia. In SCA patients using Hydroxyurea, the mean corpuscular volume (MCV) is frequently higher. Because of the distinct subpopulations of RBCs, SCA patients have an increased red cell distribution width (RDW), CBC is commonly used to characterize hematological parameters as useful information, however it is insufficient to provide a comprehensive picture of a patient's diagnosis. [9] The complete blood count (CBC) is the most common test used to distinguish between different kinds of anemia. Hematological parameters, on the other hand, will be affected by the hemoglobin mutation, with a varied alteration. [9] Thus hematological assessment of Sickle cell anemia (SCA) patients (Hb SS pattern) is very important to guide early diagnosis.

METHODOLOGY:

A cross sectional hospital based study, included 340 child and adolescents clinically and laboratory diagnosed as sickle cell anemia homozygous (SS pattern). All patients attended in SCA crises and admitted to Kosti Teaching Hospital, Sudan, during 2018 – 2023. Their age ranged 1–18 years. Patients younger than six months and older than 18 years of age, were excluded also patients with other haemoglobinopathies and sickle cell trait. The study approved by research committee of Faculty of Medical Laboratory Sciences, University of Gezira. The informed consent form written in Arabic was given and explained to the parents in local language. Taken the local cultural context into account, a verbal response was sufficient to be included in the study. Using simple random sampling method and sample size calculation formula. [10] A 340 children and adolescents with SCA who satisfied the inclusion criteria were included in this study.

$$N = \frac{Z^2 \times P \times Q}{d^2}$$

(N= Sample size. Z= 1.96. Q= 1-P. P= Expected prevalence rate (33%). d= Desired absolute precision=0.05)

$$N = \frac{1.96^2 \times 0.33 \times (1 - 0.33)}{0{,}05^2} = 339.7$$

Demographic and clinical data collected by structured questionnaire filled by the researcher through translation to local language. A 2,5 ml of venous blood was collected in ethylenediamine- tetraacetic acid (EDTA) anticoagulated tube from each patient. The blood mixed well with an anticoagulant then analyzed immediately for full blood count was analyzed immediately using sysmex autoanalyzer Kobe, Japan. The following parameters were determined; haemoglobin concentration (Hb), haematocrit (Hct), red blood cell count (RBCs), mean corpuscular haemoglobin (MCH), mean cell volume (MCV), mean corpuscular haemoglobin concentration (MCHC), total white cell count (TWBCs), and platelets count (Plt ct).Data analyzed using IBM SPSS advanced statistics version 22 (SPSS Inc., Chicago, IL). Numerical data expressed as mean and standard deviation or median and range as appropriate. Qualitative data expressed as frequency and percentage. Chi-square test was used to examine the relation between qualitative variables. For not normally distributed quantitative data comparison between three groups were done using nonparametric ANOVA. *P-value* was considered significant at 0.05.

RESULTS:

Table 1: Study population according to sex:

Sex	Frequency	Percent (%)
Male	160	47.1
Female	180	52.9
Total	340	100

Table 2: Distribution of study population according to their age.

Age group	Frequency	Percent (%)
1-5 yesrs	140	41.2
6-10 years	100	29.4
> 10 years	100	29.4
Total	340	100.0

Table 3: Hemoglobin concentrations g/dl among study population:

Age group	Mean ± SD	Minimum	Maximum	Total
1-5 yesrs	6.9 ± 1.0	4.7	8.1	140
6-10 years	7.2 ± 0.64	6.4	8.0	100
> 10 years	6.8 ± 0.70	5.5	7.9	100
Total	6.9 ± 0.85	4.7	8.1	340

Table 4: Hemoglobin concentrations g/dl according to sex:

Sex	Minimum	Maximum	Mean ± SD	Total
Male	4.7	8.1	6.8 ± 0.83	160
Female	4.7	8.1	6.9 ± 0.86	180
Total	4.7	8.1	6.8 ± 0.85	340

P. value 0.073

Table 5: Correlation of hematological parameters in study population:

Parameters/ unit	Normal Values	Minimum	Maximum	Mean ± SD	*P. value*
Hb g/dl	11 – 16	4.7	8.1	6.8 ±0.85	0.000
RBCs X 10^{12} /L	3.50 - 5.50	1.88	4.48	2.7 ±0.51	0.000
HCT %	35 – 54	14.4	30.0	21.1 ± 3.1	0.000
MCV fl	80 – 100	58.0	94.4	78.9 ± 8.9	0.000
MCH pg	27 – 34	17.6	31.0	25.6 ± 3.1	0.000
MCHC g/dl	32 – 36	28.6	36.8	32.5 ± 1.8	0.000
RDW-CV %	11 – 16	21.00	28.5	28.1 ± 44.5	0.000
TWBCs X 10^9 /L	4.0 -11.0	3.080	28.800	14.9 ± 6.3	0.000
Platelet X 10^9 /L	150 – 450	91.00	943.00	378.5± 155.8	0.458

DISCUSSION:

Sickle cell crisis refers to the devolop of acute symptoms usually due to sudden sickling of red blood cells in a patient of SCA. There are four main types of crisis namely vaso-occlusive crisis, haemolytic crisis, sequestration syndrome and aplastic crisis. As a consequence, a red blood cell becomes less pliable and some become deformed into the characteristic sickle shape.

The current study included 340 child and adolescents, clinically and laboratory diagnosed as sickle cell anemia homozygous (SS pattern). All patients attended in SCA crisis and admitted to Kosti Teaching Hospital, Sudan, during 2018 – 2023. A 180 (52.9%) were females whereas 160 (47.1%) were males (Figure 1), (male to female ratio was 0.9:1), Similar results reported by Gloire Mbayabo, *et al*. 2023. [11]

Participants age ranged from 1- 18 years and the mean age was (7.8 ± 4.7). They classified into three group 1-5 years 140 (41.2%), group (2) was 6-10 years included 100 (29.4%) and group (3) was > 10 years included 100 (29.4%). The age group of 1-5 years representing 41.2%, this result supported by Jain *et al* [12] who reported that the highest incidence of acute events may be due to cross-infection and 56% of them were younger than three years old.

Generally hematological parameters in patients with SCA (SS) at steady state in comparison to normal HbA as controls, the Hb and Hct of patients are significantly less than normal however the white cells and platelet counts are higher. [13] In this study we assessed hematological parameters of SCA patients during crisis. In the present study hemoglobin concentration was low in contrast to normal values, it ranged from 4.7 to 8.1 with mean 6.8 ±0.85. A significant correlation between low Hb level and crisis was observed, this result due to autosplenectomy, hemolysis and recurrent infections associated with SCA, this result agree with Rajeev *et al* 2021. [14] No statistical differences between male and female Hb level, *P. value* (0.073). Differences between male and female accepted at puberty due to hormonal effect. The majority of female in this study were before puberty moreover socioeconomic factors and nutritional status influence the Hb level.

The study observed low RBCs count (2.7 X 1012 /L ±0.51) and HCT (21.1 ± 3.1) %. This result supported by Fasola1 F.A. and Adekanmi A.J 2019 [13] and these changes have been generally attributed to autosplenectomy, irrespective to the reduction degree in spleen size. Mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were low in present study. Above results were in accordance with Chavda J, *et al*, 2015. [15] RDW-CV % ranged from 21% to 28.5% with the mean 28.1 ± 44.5 this result reflects the marked poikiloanisocytosis due to Hb SS polymerization resulting in crisis. This result supported by Imoudu A, *et al* 2021. [16]

The present study reported elevation in the total white blood cells (leuckocytosis) with the mean 14.9 x 109 /L ± 6.3 in SCA patients during crisis, this elevation significantly correlated with crisis p, value 0.000. This result in accordance with Chukwurah Ejike Felix *et al*, 2019 [17] who reported that the severity of SCA is highly correlated with the number of neutrophils in the blood.

Tagwa Yousif Elsayed Yousif [18] reported that an elevated leukocyte count is responsible for worse clinical manifestations in SCD, eg, clinical stroke, acute chest syndrome, end organ damage, and infarction pain. Leukocytes attach to erythrocytes and vascular endothelium to cause vasoocclusion, responsible for these effects. They also elaborate inflammatory mediators to aid the process. The higher the leukocyte count, the worse the effects.

The study observed that platelets had insignificant correlation with crisis p, value 0.458. The platelets count ranged from 91.00 X 10^9 /L to 943.00 X 10^9 /L with mean 378.5± 155.8, this result agree with Phelipe G *et al* 2017. [21]

While in Sudan Alam Eldin Musa Mustafa, *et al*, [19] reported marked elevated platelets count, above 600,000. This differences attributed to variation in sample size as their study include 75 child only. However Shome DK *et al* 2018 [20] documented that thrombocytopenia was significantly more common in patients with SCA than thrombocytosis. Many factors affecting platelets count such as malaria and infection especially in the study area (Kosti) which is considered endemic area also blood transfusion and drugs such as Hydroxyurea may affect results. In conclusion, the above findings have highlighted the urgent need for Sickle Cell Anemia center, in this area could be the first step towards addressing effective control activities and management.

Limitations:

One of the most important limitation of this study is that, blood transfusion history and variations in spleen size of patients with sickle cell were not assessed, other study should be done to determine these relationship during crisis and steady state.

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