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Pediatric Sickle Cell Disease Patients' Hematological Changes during Vaso-Occlusive Crises (VOCS) Versus Steady State

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Abstract

***Background*:** The primary acute outcome of sickle cell disease (SCD) is a vaso-occlusive crisis (VOC) with extreme pain. More than three vaso-occlusive crisis (VOC) hospitalizations in a year increase the risk of early death. The objective of the study was to evaluate the hematological alterations in complete blood count (hemoglobin, red blood cell indices, white blood cell count, and platelets) and C-reactive protein levels during vaso-occlusive crises in patients with sickle cell anemia (HbSS) compared to a stable symptomatic state. ***Methodology*:** This study is a prospective descriptive study conducted in a hospital setting. During the period from February to June 2015, a Sudan Sickle Cell Anemia Center (SSCAC) in North Kordofan State, Sudan, treated a total of 100 patients with sickle cell anemia. Out of these patients, 74 had a vaso-occlusive crisis and 26 had a steady-state condition. All patients had measurements of their complete blood count (CBC) and C-reactive protein (CRP) levels. We calculated the average values of CBC and CRP level counts during vaso-occlusive crises and compared them to the values during steady state using independent t-tests. We analyzed the collected data using the Statistical Tool for Social Sciences (SPSS) software tool, specifically version 13. ***Results*:** The statistical analysis of the patient sample during vaso-occlusive crisis and steady state revealed that the concentration of hemoglobin (Hb) was 6.55 g/dl ± 1.3 and 9.8 g/dl ± 2.4, respectively, with a p-value of 0.000. The packed cell volume (PCV) was 20.4% ± 3.9 and 30.7% ± 7.1, respectively, with a p-value of 0.000. The red blood cell (RBC) count was 2.5×106/µl ± 0.57 and 3.9×106/µl ± 1.1, respectively, with a p-value of 0.000. A lot more white blood cells (WBC) were present in vasoocclusive than in steady state, with numbers 19.36 x 109/l ± 10.645 and 76.76 x 109/l ± 20.19, respectively, and a P-value of ≤0.000. There was a notable statistical disparity in the platelet count, with values of (357.108109/l ± 162.838) and (290.4610×9/l ± 124.40), with a P value of 0.05. In vaso-occlusive crises, the amounts of hemoglobin, packed cell volume (PCV), and red blood cells (RBCs) are lower than they are in the steady-state phase. Conversely, white blood cell (WBC) and platelet levels are much greater in patients experiencing vaso-occlusive crises compared to those in a steady state. The levels of C-reactive protein (CRP) were significantly different between patients experiencing vaso-occlusive crises and those in a stable condition.

Keywords: Sickle cell disease, vaso-occlusive crisis, hematological parameters, children.

INTRODUCTION

Sickle cell disease (SCD), the most common genetic blood disease, is more widespread in sub-Saharan Africa. The disorder is caused by a recessive autosomal mutation in the β-globin gene on chromosome 11, which replaces glutamic acid with valine at the sixth position. The structure and dynamics of hemoglobin

change, making deoxygenation and acidosis predisposed to polymerization. This causes erythrocytes to become distorted and stiff, causing intravascular inflammation and tiny blood vessel blockages [1].

In Africa, SCA kills 5% of under-5s, and only half survive [2]. Most SCD symptoms and problems are caused by clinical and subclinical crises. Activation and destruction of endothelial cells and adhesion molecules cause inflammation, CRP release, and ischemia [3, 4].

In 95% of SCD cases, acute pain episodes, also known as sickle cell pain crises or vaso-occlusive crises (VOCs), are the main presenting morbidity and the reason for hospitalization. VOCs and ACS are the most common predictors of death in SCD patients [5].

A prior investigation found that SCD patients have raised WBC counts, activated granulocytes, monocytes, and endothelial cells, increased endothelial cell adhesion molecules, cytokine levels, and acute-phase reactants [6].

An acute-phase reactant, the liver produces C-reactive protein (CRP) and releases it into the blood within hours of tissue injury, infection, or inflammation [7]. The CRP test can monitor flare-ups and treatment efficacy in chronic inflammatory disorders. While the CRP test cannot diagnose a specific disease, it does indicate infection and inflammation, leading doctors to additional testing and therapy. Doctors may perform additional tests to determine the cause of the inflammation [8].

This study aims to investigate the significance of hematological findings and C-reactive protein levels in vaso-occlusive crises among patients with sickle cell anemia at Alkuwaity Pediatrics Hospital in Northern Kordofan State, Sudan.

MATERIAL AND METHODS

This study is a prospective descriptive investigation that took place at the Sudan Sickle Cell Anemia Center (SSCAC) in Alkuwaity Pediatrics Hospital, located in Northern Kordofan State, Western Sudan. The study was done from February to June 2015. The study period saw patients with sickle cell anemia seeking treatment at the Sudan Sickle Cell Anemia Center (SSCAC). The study comprised a total of 100 individuals, with 74 experiencing vaso-occlusive crises and 26 in a stable condition. This study included all male and female patients with sickle cell anemia who were receiving treatment at the hospitals. We excluded patients on hydroxyurea or any other treatment that could influence the outcome.

We used a questionnaire to collect data on demographics, family history, and symptoms. A 2.5-ml blood sample was obtained from each participant and distributed into ethylene diamine tetraacetic acid (EDTA) for complete blood count (CBC) measurement, followed by plasma separation into plain tubes for CRP calculation. The blood cell count was determined using a Sysmex automated hematological analyzer. Sysmex analyzers primarily use electronic resistance (impedance) detection to count and size leukocytes, erythrocytes, and platelets. Using three preliminary hydraulic systems for WBCs, RBCs, platelets, and hemoglobin, the blood count data were displayed on a liquid crystal display (LCD) with a histogram and printed on thermal paper. The amount of CRP was determined using commercially available CRP kits and icromaTM CRP. The test employs a sandwich immunodetection approach, in which the detector antibody in buffer binds to CRP in the sample, and the antigen-antibody combination is collected by another CRP antibody immobilized on the test strip when the sample mixture migrates across the nitrocellulose matrix. As a result, the higher the concentration of CRP antigen in the sample, the greater the accumulation of the antigen-antibody complex on the test strip. CRP concentrations greater than 5 mg/l may indicate an acute-phase response to viral infections or disorders marked by acute inflammation. The data was analyzed using the Statistical Package for Social Sciences (SPSS) software package version 13 (using T tests).

Ethical Consideration

Ethical Clearance The ethical clearance was obtained from both the hospital administration and the ethical committee at Alkuwaity Pediatrics Hospital. All patients involved in the research provided their consent.

RESULTS

The age range between 8 months and 15- years, with a high frequency of 65/100 (65%), seen in the age group of patients spanned between 1 and 5 years (Figure 1). The sex claims that the data revealed a higher frequency of male patients (58/100, 58%), than female patients (42/100, 42%). Eighty-percent of the patients had a known family history of 80/100. Following Niger-Congo 48/100 (48%), most of the patients are Afro-Asiatic tribes 52/100 (52%), (Figure 2).

Patients presented with a variety of clinical features, but pallor was the predominant one in 76/100 (76%) of the cases [Table 1]. Vaso-occlusive crises were observed in 74 out of the 100 patients with sickle cell anemia, while the remaining 26 patients (26%) were in a continuous state.

The statistical examination of the patient samples during vaso-occlusive crisis and steady state revealed that the Hb concentration was 6.55 g/dl ± 1.3 and 9.8 g/dl ± 2.4, respectively, with a P-value of less than 0.000. The PCV levels were measured to be 20.4% ±3.9 and 30.7% ±7.1, respectively, with a statistically significant difference ($P < 0.000$). The RBC counts were measured to be 2.5×106/µl ± o.57 and 3.9×106/µl ± 1.1, respectively, with a statistically significant difference (P

< 0.000). The red cell indices in vaso-occlusive crisis and steady state were as follows: mean corpuscular volume (MCV) of 78.7 fl ± 9.6 and 75.5 fl ± 7.7, respectively, with a p-value of less than 0.135; mean corpuscular hemoglobin (MCH) of 26.1 pg ± 3.8 and 25.5 pg ± 4.6, respectively, with a p-value of less than 0.48; mean corpuscular hemoglobin concentration (MCHC) of 32.2 g/dl ± 3.3 and 32.6 g/dl ± 3.3, respectively, with a p-value of 0.66 (Table 2).

The white blood cell count (WBC) was measured to be 19.36 x 109/l ± 10.645 and 76.76 x 109/l ± 20.19, with a statistically significant difference (P < 0.000). The platelet count was measured to be 357.108109/l ± 162.838 and 290.4610×9/l ± 124.40, with a statistically significant difference (P < 0.045). The statistical analysis of C-reactive protein revealed considerable disparities between patients experiencing vaso-occlusive crises and those in a stable condition. The levels of CRP were found to be 16.43 mg/l±12.35 in vaso-occlusive crisis patients and 4.56 mg/l ± 1.45 in steady-state patients, respectively. This difference was highly significant, with a p-value of less than 0.000 (Table 3).

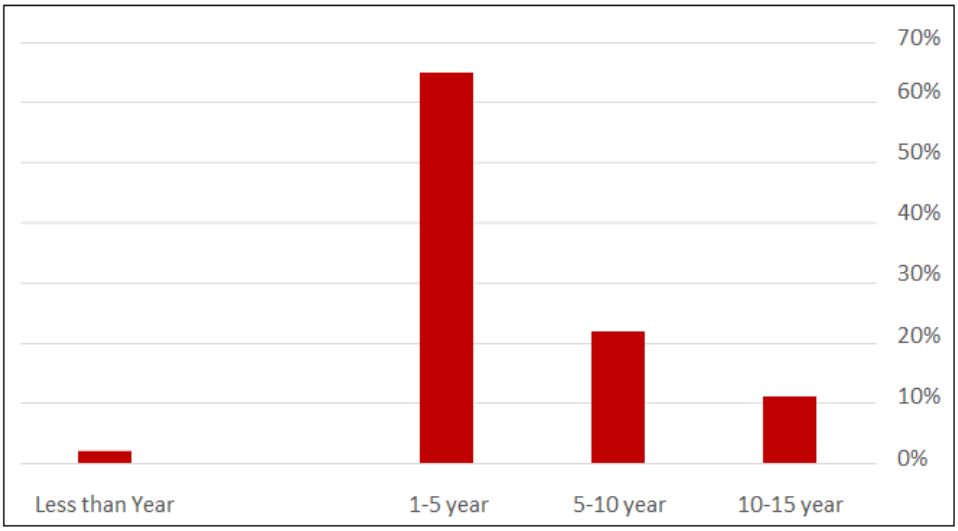

Figure 1: Distribution of the study population according to the age

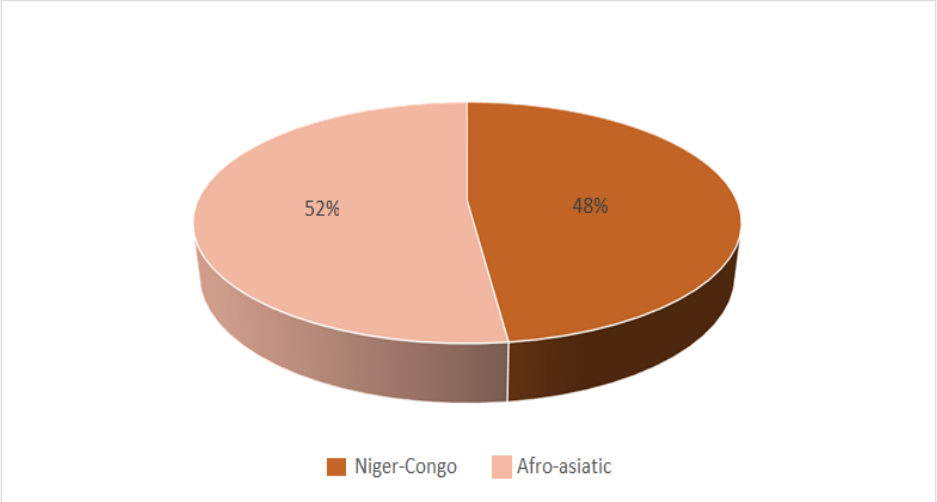

Figure 2: Tribal origins in the patients with sickle cell anemia

Table 1: Clinical Feature of the Study patients

Clinical Feature	Frequency	Percentage
Pale	76	76%
Abdominal Pain	21	21%
Jaundice	51	51%
Swollen joints	46	46%

Table 2: Hematological picture of the study patients

Hematological variable	Patient state	Mean	±SD	P. value
Hb g/dl	Vaso-occlusive	6.55	1.30	0.000
	Steady state	9.80	2.40	
PCV%	Vaso-occlusive	20.40	3.96	0.000
	Steady state	30.69	7.14	
RBCs×10^6/µl	Vaso-occlusive	2.48	.57	0.000
	Steady state	3.88	1.13	
MCV fl	Vaso-occlusive	78.68 FL	9.60	0.135
	Steady state	75.53 fl	7.70	
MCH pg	Vaso-occlusive	26.16 pg.	3.85	0.477
	Steady state	25.50 pg.	4.63	
MCHC g/dl	Vaso-occlusive	32.21 g/dl	3.35	0.659
	Steady state	32.56 g/dl	3.34	
TWBC×10^9/l	Vaso-occlusive	19.36	10.64	0.000
	Steady state	76.76	20.19	
Platelts×10^9/l	Vaso-occlusive	357.10	162.83	0.045
	Steady state	290.46	124.40	

Table 3: Comparison of C. Reactive Protein between Vaso-occlusive crisis and steady state

Patients state	Mean of CRP	±SD	P. value
Vaso-occlusive crises	16.43 mg/l	12.35	0.000
Steady state	4.56 mg/l	1.45	

DISCUSSION

During this study period, a cohort of 100 individuals diagnosed with sickle cell anemia were registered at the sickle cell center. Out of the total, 74 individuals experienced vaso-occlusive crises, while the remaining 26 were in a stable condition. All participants in the study were children and adolescents, with a higher prevalence observed in children compared to adolescents. The male population exhibited a higher frequency compared to the female population, with a ratio of 1.38:1. This finding is consistent with previous observations from Saudi Arabia, where a male-to-female ratio of 1.6 was seen [9]. The majority of the study population has a familial predisposition to sudden cardiac death (SCD). This study demonstrates that the predominant ethnic groups among the patients are from Afro-Asiatic tribes, with Niger-Congo tribes being the second largest.

In vaso-occlusive crises, the mean hemoglobin and RBC count values were lower compared to a steady state. This finding aligns with a study conducted in Nigeria [10], which demonstrated a decrease in Hb, RBCs, and PCV during both steady-state and vaso-occlusive crises. Although there was no variation in MCV and MCHC between steady-state and vaso-occlusive crises, it is worth noting that [10] observed a significant difference in MCV and MCHC. Due to the nature of SCA, patients experience ongoing hemolysis of their red blood cells, resulting in a shorter lifespan of these cells, typically between 12 and 14 days. As a result, individuals with SCA often have lower hemoglobin and PCV values compared to those without the condition. This is demonstrated in a study where the levels of hemoglobin and PCV during vaso-occlusive crises were noticeably lower compared to the control group.

In a vaso-occlusive crisis, we observed a higher total white blood cell count (WBCs) compared to the steady state. This is similar to a report conducted in India [11], which found a strong association between the inflammatory markers CRP and WBC and the clinical outcome of hospitalization for pain events in the HbSS group. This is not surprising given the underlying processes that lead to a higher concentration of neutrophils in the venous blood of patients with SCA. These processes involve the movement of neutrophils from the blood vessels, their release from the bone marrow, and a decrease in the rate at which they exit the bloodstream [12]. According to Darbari DS, it has been observed that higher neutrophil counts are associated with more severe disease, such as earlier death, increased incidence of silent brain infarcts, hemorrhagic stroke, and acute chest syndrome (ACS).

In addition, there is a notable increase in the total platelet count during a vasoocclusive crisis compared to the steady state. However, it has been reported that platelet counts do not consistently show a connection with the frequency or severity of VOCs. Nonetheless, it has been observed that platelet hyperactivity tends to increase during VOC. Additionally, a study conducted in Saudi Arabia revealed that in VOC, there is a correlation between higher hemoglobin concentration, higher white blood cell and neutrophil counts, and lower platelet counts, indicating a higher frequency of painful crises. The hemostasis and coagulation processes in SCA were greatly improved as a result of the ongoing destruction of sickle red blood

cells, both within and outside of blood vessels. This destruction leads to chronic and acute hemolytic anemia, which is often accompanied by a high occurrence of thrombotic events in clinical settings [13].

Our study revealed a notable increase in CRP during crises as compared to the steady state. This finding aligns with the research conducted in Nigeria by [14]. It was observed that CRP levels are noticeably higher during a crisis in individuals with HbSS compared to when they are in a stable state. Additionally, individuals with HbSS have higher CRP levels compared to those with HbAS and HbAA. This is because CRP production is a component of a general acute-phase response to inflammation and tissue necrosis. It is believed that the repeated blockage of blood vessels and subsequent restoration of dead tissue result in the creation of harmful oxygen radicals. These radicals cause damage to the tissues and trigger a persistent state of inflammation [4].

CONCLUSION

Results showed more male than female patients. The majority have sickle cell anemia in their families. Afro-Asiatic tribes dominate the patients, followed by Niger-Congo. A crisis lowers hemoglobin, PCV, and RBCs more than a steady state. WBC, platelets, and CRP were considerably greater in vaso-occlusive crises than in steady states. MCV, MCH, and MCHC were low in all patients, with no significant differences between vaso-occlusive crises and steady-state individuals.

All follow-up patients should have a CBC with differential count and CRP measured. To clarify the function of a chronic inflammatory state with vaso-occlusive crises and specific disease consequences, adequately controlled research using more inflammatory markers is needed. Active sickle cell disease education by medical professionals and the public. Pre-marital counseling should reduce sickle cell disorders.

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