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Assessment of some Hematological Parameters in Sickle Cell Disease during Steady State and in Vaso-Occlusive Crisis

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ORIGINAL STUDY

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Assessment of some Hematological Parameters in Sickle Cell Disease during Steady State and in Vaso-Occlusive Crisis

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Abstract

Background: Sickle cell disease is a monogenetic disorder resulting in early mortality and widespread organ damage, including pulmonary, cardiac, and splenic dysfunction, as well as cerebral infarcts and avascular osteonecrosis. It results from a single point mutation causing the replacement of the amino acid glutamic acid by valine. Chronic hemolysis can affect sickled red cells, chronic inflammation, and oxidative stress, which contribute to the occurrences of vasoocclusion.

Objectives: To measure hematological parameters and their relationship to the development of vasoocclusion.

Materials and Methods: This case-control study was conducted on 80 Iraqi subjects, including 40 cases with sickle cell disease diagnosed previously by hemoglobin electrophoresis. They were collected from Babylon Teaching Hospital for Maternity and Children when they attended the Hereditary Blood Disease Center in that hospital. Another 40 subject consider as controls. Three milliliters of venous blood were drawn in EDTA tubes, and investigations were made immediately at the laboratory of this Hospital by use of hematology analyzer.

Results: Mean leukocytes in SCD were (10.10 ± 4.70) and (7.53 ± 1.80) for controls, showing a significant difference (P value 0.002). The mean RBC (3.22 ± 0.97), (4.59 ± 0.58) for patients and control respectively. Mean platelets count was (358.68 ± 135.82), (286.52 ± 72.95) for patient and control respectively. The mean PCV (26.48 ± 5.71) for patients and (37.48 ± 5.72) for controls.

Conclusions: There were significant alterations in RBC, WBC, and platelets between SCD patients and controls. Hematocrit and hemoglobin were lower in patients than in controls, and even lower during crises than in steady states.

Keywords: Sickle cell disease, Steady state, Vasoocclusive crisis, Inflammation

1. Introduction

In the twenty-first century, people frequently disregard sickle cell illness, a chronic, non-contagious congenital blood ailment. It includes a set of clinical disorders related to aberrant polymerized deoxygenated hemoglobin inside red blood cells. The children inherited this defective hemoglobin from their parents, which causes red blood cells to deform in shape. When two mutant sickle β-globin subunits join, they make erythrocytes that look like sickles or crescents. This is where the name “sickle cell disease" (SCD) comes from [1, 2].

In their erythrocytes, sickle cell disease patients have variable levels of hemoglobin S, an aberrant form of hemoglobin. Sickle cell anemia is caused by adenine instead of thymine in the glutamic DNA codon, which results in valine instead of glutamic acid at position six of the beta globin chain [3].

Sickle-shaped red blood cells (RBCs) lack the flexibility and deformability of normal RBCs due to their inability to bend and fit into small blood channels.

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This can cause blockages and decrease blood flow. Usually, SCD is characterized by painful crises that can appear in any part of the body and have a significant impact on patients. Both chronic pain, with or without a nerve injury, and acute, repeated, painful crises are possible presentations of pain. The four phases of the painful crises are prodromal, beginning, established, and resolving. It is the primary reason for hospitalization and emergency care for SCD [4, 5].

More than 300,000 newborns with SCD are diagnosed each year. Sub-Saharan Africa, the Middle East, and India account for the bulk of cases. The high level of defense to malaria that the sickle cell trait confers helps to explain some of this distribution. People of Mediterranean, Middle Eastern, Caucasian, Indian, Hispanic, Native American, and other ancestries currently have a higher prevalence of SCD, which could be explained by migration [6].

According to epidemiological research, sickle cell disease patients are concentrated in two regions of Iraq: among the Arab population in the extreme south and among the Kurdish population in the extreme north. These regions account for the majority of sickle cell disease cases, which pose serious health issues [7].

The pathophysiology of SCD frequently includes vaso-occlusion and chronic hemolytic anemia, which are often defined by significant inflammation, leukocytosis, leukocyte activation, and possibly enhanced leukocyte adherence to the vascular endothelium [8, 9].

Earlier studies involving SCD patients observed an increase in total white cell count due to fundamental mechanisms that result in an elevated number of neutrophils in the venous blood of SCD patients. These events include demargination of intravascular neutrophils, increased release from the bone marrow, and a decrease in the rate at which neutrophils escape the blood [10, 11].

Additional research also revealed the possibility of creating an invisible inflammatory response that results in the release of cytokine mediators, some of which have the primary purpose of stimulating the bone marrow's production of neutrophils [12, 13].

Studies have shown that individuals with SCD in a steady state have greater platelet counts than people in the general non-SCD population. This is because SCD is characterized by persistent hemolysis and vasoocclusion, which cause anatomical and physiological adaptations [14]. The high difference in platelet count due to loss of splenic function in adult patients or due to splenectomy. And also could also be the result of a negative feedback effect on high-level erythropoietin release in response to anemia, as it has structural homology with thrombopoietin [15, 16].

The aim of this study is to measure hematological markers and their role in the pathophysiology of SCD during steady state and in painful crisis and compare them to controls.

2. Materials and methods

This was a case-control study conducted in the Department of Pathology and Forensic Medicine, College of Medicine, Babylon University. The study involved 80 Iraqi participants, 40 of whom had been previously diagnosed with SCD by hemoglobin electrophoresis. They attended the Hereditary Blood Disease Center in this Hospital for follow-up and to receive therapy in a period from September 2023 to February 2024. The patients were divided into two subgroups, 20 cases in steady state and 20 in VOC. Patients on antiplatelets, anticoagulants, and antibiotics, those with chronic liver disease, pregnant women, and women taking oral contraceptive pills were excluded from the study as these may interfere with the actual count of red cells, white blood cells, and platelets.

The other 40 individuals were disease-free and had a negative family history of SCD, being considered as age and sex-matched controls.

Three milliliters of venous blood were drawn from all participants after obtaining their consent and placed in EDTA tubes.

The test performed immediately in the laboratory unit of Babylon teaching hospital by using a hematology analyzer (STEL3 automated analyzer/3diamentional/Spain/2013)

2.1. Ethical approval

The study was conducted in compliance with the ethical guidelines outlined in the Helsinki Declaration. Before drawing a sample, verbal and written consent was taken. The study protocol and the individual data, and consent forms were reviewed and approved by a local ethics committee according to document number 6–7 on June 25-06-2023 to obtain this approval.

2.1.1. Statistical analysis

The statistical analysis was conducted using the Statistical Package for social sciences SPSS version 27. Categorical variables presented as frequencies and percentages while continuous variables were expressed as (Means ± SD). Pearson's Chi-square test and Fisher's Exact test were utilized to find the relationship between categorical variables. The Student's t-test was used to compare means between two groups, Mann-Whitney test was used to compare two

Table 1. Age comparison between patients and controls.

	SCD patients				
Age (years)	Steady state	VOC	Total (N = 40)	Controls	P-value
10–20 years	11 (55.0)	14 (70.0)	25 (62.5)	22 (55.0)	0.786
20–30 years	6 (30.0)	2 (10.0)	8 (20.0)	10 (25.0)	
30–40 years	1 (5.0)	3 (20.0)	4 (10.0)	5 (12.5)	
40–50 years	1 (5.0)	1 (5.0)	2 (5.0)	2 (5.0)	
50–60 years	1 (5.0)	0 (0.0)	1 (2.5)	1 (2.5)	
Total	20 (100.0)	20 (100.0)	40 (100.0)	40 (100.0)	

groups when variable was not normally distributed variables. A p-value of < 0.05 was considered statistically significant.

3. Results

The mean age of patients with SCD was (20.20 ± 9.82) years, with the youngest patient being 10 years old and older patient was 53 years old. The majority of patients presented with an age group of 10–20 years (N = 25, 62.5%) while the mean age of the control group was (20.97 ± 9.77) years (Table 1).

The mean differences of complete blood count RBC (10^9/L), WBC (10^9/L), Hb (g/dl), PCV (%), MCH (pg), MCV (fL), Platelet count (10^9/L), Granulocyte (10^9/L) and Lymphocyte (10^9/L) are presented in (Table 2). According to study group including (sickle cell disease and control group). There was significant mean differences of study variables (RBC (10^9/L), WBC (10^9/L), Hb (g/dl), PCV (%), Platelet count (10^9/L), Granulocyte (10^9/L) and Lymphocyte (10^9/L).

The mean differences of RBC (10^9/L), WBC (10^9/L), Hb (g/dl), PCV (%), MCH (pg), MCV (fL), Platelet count (10^9/L), Granulocyte (10^9/L) and Lymphocyte (10^9/L) between two patient groups including (VOC and steady state) were presented in (Table 3). There were significant mean differences of RBC (10^9/L), Hb (g/dl), PCV (%) and Granulocyte (10^9/L) between patients during steady state and VOC.

4. Discussion

In the current study, the mean differences of PCV and Hb according to the study group were (26.48 ± 5.71), (8.83 ± 1.70) in SCD patients and (37.48 ± 5.72), (13.26 ± 1.78) in the control group, respectively, with significant differences between them (p value < 0.001) for both variables (Fig. 4). The results were compatible with the study of Iwalokun *et al*. [17] in which the mean differences of PCV and Hb were lower in SCD patients compared to the control group, with a statistically significant difference between them [17] and study of Omoti in Nigeria [18]. The low PCV and Hb in SCD explained by excessive red cell hemolysis.

Table 2. The mean differences of complete blood count according to study group (N = 80).

Complete blood count	Study group	N	Mean ± SD	P-value
RBC (10^9/L)	Sickle cell disease	40	3.22 ± 0.97	<0.001*
	Control group	40	4.59 ± 0.58	
WBC (10^9/L)	Sickle cell disease	40	10.10 ± 4.70	0.002*
	Control group	40	7.53 ± 1.80	
Hb (g/dl)	Sickle cell disease	40	8.83 ± 1.70	<0.001*
	Control group	40	13.26 ± 1.78	
PCV (%)	Sickle cell disease	40	26.48 ± 5.71	<0.001*
	Control group	40	37.48 ± 5.72	
MCH (pg)	Sickle cell disease	40	28.08 ± 4.16	0.103
	Control group	40	29.30 ± 2.09	
MCV (fL)	Sickle cell disease	40	85.32 ± 15.17	0.34
	Control group	40	82.86 ± 5.65	
Platelet count (10^9/L)	Sickle cell disease	40	358.68 ± 135.82	0.004*
	Control group	40	286.52 ± 72.95	
Granulocyte (10^9/L)	Sickle cell disease	40	6.03 ± 3.14	0.004*
	Control group	40	4.39 ± 1.42	
Lymphocyte (10^9/L)	Sickle cell disease	40	3.17 ± 1.64	0.013*
	Control group	40	2.43 ± 0.79	

Table 3. The mean differences of complete blood count between two patient groups (N = 40).

Complete blood count	Patient group	N	Mean ± SD	P-value
RBC (10^9/L)	VOC	20	2.80 ± 0.70	0.005*
	Steady state	20	3.63 ± 1.04	
WBC (10^9/L)	VOC	20	11.34 ± 4.87	0.094
	Steady state	20	8.85 ± 4.28	
Hb (g/dl)	VOC	20	8.09 ± 1.45	0.004*
	Steady state	20	9.57 ± 1.64	
PCV (%)	VOC	20	23.82 ± 4.10	0.002*
	Steady state	20	29.13 ± 5.93	
MCH (pg)	VOC	20	28.78 ± 4.06	0.298
	Steady state	20	27.39 ± 4.25	
MCV (fL)	VOC	20	85.58 ± 9.83	0.915
	Steady state	20	85.06 ± 19.38	
Platelet count (10^9/L)	VOC	20	322.70 ± 107.70	0.097
	Steady state	20	394.65 ± 153.43	
Granulocyte (10^9/L)	VOC	20	7.05 ± 3.56	0.04*
	Steady state	20	5.02 ± 2.33	
Lymphocyte (10^9/L)	VOC	20	3.55 ± 1.71	0.14
	Steady state	20	2.78 ± 1.50	

While the mean differences of PCV and Hb in steady state (29.13 ± 5.93), (23.82 ± 4.10) and in VOC (9.57 ± 1.64), (8.09 ± 1.45) respectively with significant differences p-value (0.002) for PCV and (0.004) for Hb. This result was incompatible with the findings of Omoti in Nigeria who found that there were no significant differences between steady state and VOC [18] may be due to variation in study design or differences in disease genotypes.

The mean differences of platelets in our study were (358.68 ± 135.82) in the patient group and (286.52 ± 72.95) in the control group with a significant mean difference between them p-value (0.004) (Fig. 2). This finding was similar to the finding of *Maha K. Al-Mishrey* (2023) in Iraq found that platelet counts were higher in patients than the control group, indicating the activation of platelets as a significant factor in the pathogenesis and outcome of SCD patients [19]. The increase in platelet count may be attributed to the loss of splenic sequestration as a result of functional asplenia and the effect of pro-inflammatory mediators [20].

While the mean platelet count in steady state (394.65 ± 153.43) and in VOC (322.70 ± 107.70) with the P value was not significant (0.097). There was some reduction in platelet count in VOC because of increased consumption at the site of vaso-occlusion, but this change was not significant. This finding was similar to the findings of Demagny *et al*. [21] and the finding of Omoti [18] but it was incompatible with the study of Al-Mishrey who found that the platelet count was higher in VOC [19].

In the present study, the mean RBC count in the patient group was (3.22 ± 0.97), which was lower than the mean of the control (4.59 ± 0.58) with a

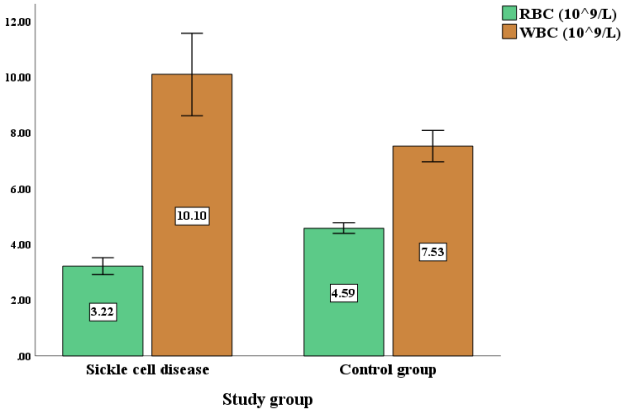

Fig. 1. The mean differences in RBC (10^9/L) and WBC (10^9/L) based on the study group (N = 80).

significant difference between them p value (<0.001) (Fig. 1). This result was compatible with the study conducted by Iwalokun *et al*. [17], and the study of Antwi-Boasiako *et al*. [8]. The best explanation is that hemoglobin S causes abnormal red cell shape and rheology and hemolytic anemia associated with a significantly shortened red cell half-life (10–20 days instead of 120 days) [22].

Additionally, the mean difference in RBC count was higher in the steady state (3.63 ± 1.04) than in VOC (2.80 ± 0.70) with significant differences between them p value (0.005). These findings were incompatible with the study done by Feugray *et al*. [23] who found that the RBC count was higher in the steady state with significant differences in p-value [23]. The best explanation for this finding is that Vaso-occlusive crisis is characterized by accelerated

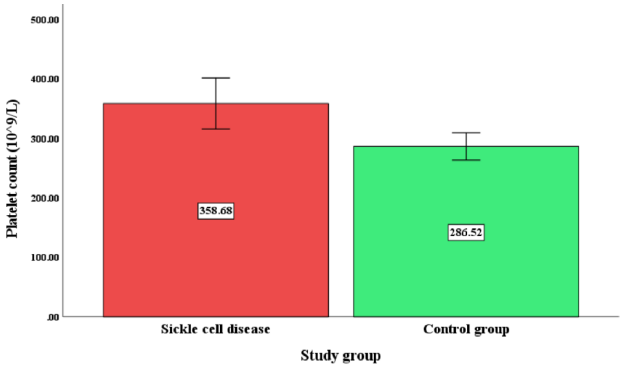

Fig. 2. The mean difference of Platelet count (10^9/L) based on the study group (N = 80).

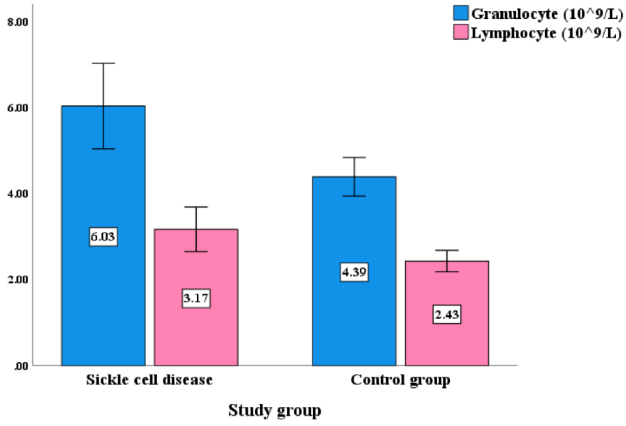

Fig. 3. The mean differences in Granulocyte (10^9/L) and Lymphocyte (10^9/L) based on the the study group (N = 80).

hemolysis, endothelial damage, and potentially life-threatening complications [24].

The mean difference in total leukocyte count was higher in patients (10.10 ± 4.70) than in controls (7.53 ± 1.80) with statistically significant relationships (p value 0.002) (Fig. 1). This finding was consistent with the findings of Akinsegun Akinbami *et al*. [25] in Nigeria, who found the mean differences of WBC in SCD patients was (10.27 ± 3.94) and (5.67 ± 1.59) for controls [25]. The redistribution of the white cells between the marginal and circulating pools, pain, nausea, vomiting, and anxiety have been reported to cause leukocytosis in the absence of infection and may be due to autosplenectomy or subclinical infection [25].

While the WBC count was higher in VOC than in steady state, a statistically significant relationship could not be established in this study (p value 0.094). This result was consistent with Qari *et al*. in Saudi Arabia [26]. Leukocytes have been shown to play visible roles in the production of thrombi, in addition to being mediators of inflammation, according to growing data. This is not unexpected given the close relationship between inflammation and thrombosis and their evolutionary preservation as host defense mechanisms against infections [27].

In our study, the granulocytes count was higher in SCD patients than the control group, with statistically significant differences between them (p value 0.004). In addition, granulocytes count was more elevated in VOC than in the steady state, with a significant difference (p value 0.04) (Fig. 3). This result was consistent with the findings of Gollamudi *et al*., because of a state of chronic inflammation in SCD. Neutrophils also exhibit higher adhesion molecules, which are heightened during vaso-occlusion and increase the risk of VOC. NETs are released by neutrophils and serve as a framework for platelets, RBCs, and fibrin deposition adherence [28].

In the current study, the lymphocytes count was significantly elevated in SCD as compared to controlss (3.17 ± 1.64 for SCD, 2.43 ± 0.79 for control) (Fig. 3) but there was no statistically significant difference between patients in the steady state and in VOC. These findings were compatible with the study conducted by Omoti in Nigeria [18], and Iwalokun *et al*. [17]. The result indicated lymphocytes as a marker of chronic inflammation in SCD. But in contrast to the findings of Emokpae *et al*. [29] who found that lymphocytes did not significantly differ in SCD and controls [29].

In this study, there were no significant differences in red cell indices (MCV, MCH) between patients and controls (p values 0.34, 0.103) for MCV and MCH respectively. Similarly, there was no statistically significant relationship between patients in the steady state and in VOC p-values (0.915, 0.298) for MCV and MCH respectively.

These findings closely similar to finding of Antwi-Boasiako *et al*. [8] who also found no significant

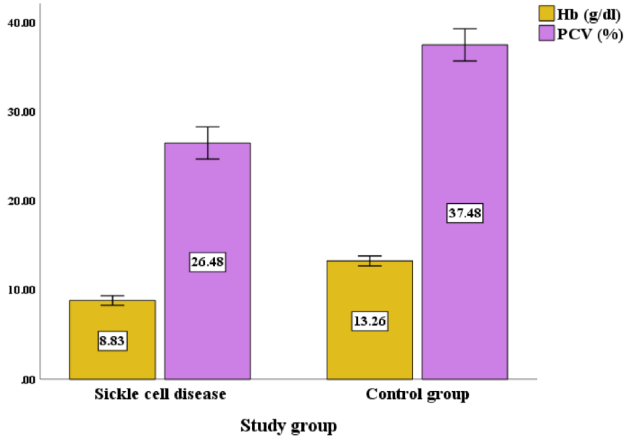

Fig. 4. The mean differences of Hb (g/dl) and PCV (%) based on the the study group (N = 80).

differences among steady state, VOC and controls. Meshay *et al.* in Iraq found normal MCV and MCH in SCD. These findings reflect the normal iron status, which is the result of accelerated red cell turnover and frequent blood transfusion in patients with sickle cell disease [30].

5. Conclusion

The levels of red cell count, Hb, and PCV were lower in SCD patients compared to controls and additionally lower in VOC than in patients in a steady state. The platelet count was significantly higher in SCD patients compared to controls with no significant change during VOC. The white cell count was significantly increased in SCD patients with higher elevations occurring during a crisis. Red cell indices showed no difference between patients and controls or between patient subgroups. The high level of leukocytes particularly granulocytes was significantly linked to thrombosis in SCD.

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