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Hematological Characteristics of a Sample of Iraqi Patients with Sickle Cell Anemia and Their Correlation with Age and Gender

Hassan Dede Meshay (FIBMS)[1], Mohammed Haseeb Khamees (FIBMS)[2], Hussein Abdalzehra Wadaha (FIBMS)[3]

[1,3]Aldiwanyah Teaching Hospital, Ministry of Health-Aldiwanyah, Aldiwanyah, Iraq

[2]Baghdad Medical Office-Al-Imamein Al-Kadhimaein Medical City, Ministry of Health, Baghdad, Iraq

Abstract

Background: Characterization of hematological parameters in patients with sickle cell anemia can direct treatment goals toward strategies reducing morbidity and mortality rate.
Objective: To evaluate the hematological parameters in a subset of Iraqi patients with sickle cell anemia in relation to age and gender.
Patients and Methods: This cross-sectional study was included 30 patients with sickle cell anemia who were known to be at a steady clinical state with no vaso-occlusive crises. About 5 ml of venous blood was collected in EDTA tube from each participant. The complete blood count was conducted according to standard protocol.
Results: The mean age was 7.93 ±2.43 years and the age range was 4 to 12 years. The study included 17 males and 13 females. 29 (96.7 %) were anemic and there was no significant difference in mean hemoglobin levels between males and females (p = 0.838). Males demonstrated higher frequency of low mean cell volume (MCV) and mean cell hemoglobin (MCH) (64.7% and 58.8%, respectively) than females (7.7% and 7.7%, respectively) with highly significant differences.
Conclusion: Some hematological parameters in patients with sickle disease are affected by gender but show no significant correlation to age.
Keywords: Hematological characteristics, Sickle cell anemia, Iraq

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Correspondence Address: Mohammed Haseeb Khamees
Baghdad Medical Office-Al-Imamein Al-Kadhimaein Medical City, Ministry of Health, Baghdad, Iraq

Email: mohamed.haseb1975@yahoo.com

Website:https://djm.uodiyala.edu.iq/index.php/djm

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Introduction

Sickle cell anemia is caused by a point mutation affecting the beta globin gene in which thymine (T) replaces Adenine (A) at codon 6 of the beta globin gene, thus resulting in a protein having valine amino acid instead of glutamic acid rendering the red blood corpuscle to sickle when exposed to low oxygen. This type of hemoglobin is called hemoglobin S (Hb S) [5].

The prevalence of sickle cell trait is higher among people whose ancestors come from Africa, subtropical and tropical world areas. In the United States, the prevalence is higher in African Americans than in Caucasians, 9 % versus 0.2 %, respectively [6]. Globally, there are at least 300 million individuals suffering from the trait and the disease in prevalent in areas in which malaria is

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endemic [7]. Figures as high as 25 % have been reported in Africa and rates as high as 60 % have been reported in some regions of Saudi Arabia [6]. Western countries have reported an increasing prevalence of the trait due to people migration from Africa and Middle East toward European and American countries [8].

According to Kadhim *et al*, there were about 5,124 patients with sickle cell anemia in Iraq in 2015. The prevalence of this disease significantly increased from 13.1 per 100,000 in 2010 to 13.9 per 100,000 in 2015. On the other hand, the incidence had dropped from 19.7 per 100,000 in 2010 to 13.2 per100,000 in 2015. Basra province (the most southern province) had the higher prevalence rate (124/100,000), while Sulaymaniyah and Salahaldin had the lowest rate (0.3 per 100,000).

The main clinical concern regarding sickle cell disease is the development of vaso-occlusive disease due to exposure to conditions that favor sickling, such as increased sympathetic outflow, dehydration, hypoxia and hypothermia. Repeated episodes are associated with ischemia and organ damage in various body anatomical parts [10].

Hematological parameters assessment in recent years concerning Iraqi patients with sickle cell anemia is lacking. The association of significant morbidity and mortality of sickles cell patients with leukocyte count and severity of anemia in previous reports [11] justify the characterization of such hematological parameters in our patients in order to direct treatment goals toward strategies reducing such morbidity and mortality rate, thus the current study aim was at evaluating the hematological parameters in a subset of Iraqi patients with sickle cell anemia living in Baghdad province.

Patients and Methods

Study design

This cross sectional study was carried out at Al-Imamein Al-Kadhimaein Medical City, Baghdad, Iraq. The beginning of the study is dated back to April the 15th 2020, and the study continued through March the 20th 2021. The study included 30 patients with sickle cell anemia who were known to be at a steady clinical state with no vaso-occlusive crises. Those patients were randomly selected out of the pool of patients visiting the hematology unit at the Medical City during the period of the study. The principal inclusion criterion for patients to be enrolled is an established diagnosis of sickle cell disease. Patients with conditions that may interfere with hematological parameters, such as recent blood transfusion or renal failure, were excluded from the study. The definition of a steady state was based on at least 2 weeks history of no active crises and being clinically well.

Sample collection: From each eligible patient, 5 ml of venous blood was withdrawn and transferred into an EDTA tube. A complete blood count was performed using "Abbott Cell Dyn 3700" Hematology analyzer/Germany.

Statistical analysis

The statistical package for social sciences (SPSS) version 16.0 (IBM, Chicago, USA) was employed for data analysis. Binomial variables were presented as number and percentages and analyzed with Chi square/exact Fisher test. Numerical variables were expressed as mean and standard deviation (SD) and analyzed with a student's t-test was used to compare mean

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values between study and control groups. A p-value of ≤ 0.05 was considered statistically significant.

Results

The present study included 30 patients with sickle cell anemia with a mean age of 7.93 ±2.43 years and an age range of 4 to 12 years. The study included 17 males and 13 females, and their corresponding mean of age was 7.53 ±2.24 years and 8.46 ±2.67 years, respectively; there was no significant difference in mean age between males and females (p = 0.307), as demonstrated in Table (1).

Comparison of hematological characteristics between males and females with sickle cell disease is shown in Table (2). The mean hemoglobin level of all patients was 9.37 ±1.13 g/dl and 29 (96.7 %) were anemic. There was no significant difference in mean hemoglobin level between males and females (p = 0.838). In addition, there was no significant difference in mean RBC count between males and females (p = 0.099) and the mean RBC count in all patients was 3.68 ±0.69 X1012/L. Low RBC count was seen 19 (63.3 %) patients. In addition, there was no significant difference in mean hematocrit level between males and females (p = 0.879) and all patients had low hematocrit level.

There was a highly significant difference in mean MCV between males and females (p = 0.004) and the level was higher in females in comparison with males, 79.58 ±5.45 fl versus 71.11 ±8.35 fl, respectively. Moreover, low MCV level were more frequently seen in males in comparison with females, 11 (64.7 %) versus 1 (7.7 %), respectively, in a highly significant manner (p = 0.002).

Regarding mean MCH, the level was higher in females in comparison with males, 28.17 ±2.34 versus 24.63 ±3.33, respectively, and the difference was highly significant (p = 0.003). Added to that, low MCH level was more frequently encountered in males in comparison with females, 10 (58.8 %) versus 1 (7.7 %), respectively in a highly significant manner (p = 0.013).

The mean WBC count in all enrolled patients was 8.59 ±3.55 X109/L and there was no significant difference in mean WBC count between males and females (p = 0.224); however, leukopenia was more frequently seen in males in comparison with females, 5 (38.5 %) versus 1 (5.9 %), respectively and leukocytosis was seen in only 2 cases out of all enrolled sickle cell disease patients.

Regarding platelet count, the mean of all included cases was 308.83 ±142.36X109/L and there was no significant difference in mean count between males and females (p = 0.829); however, thrombocytosis was more frequently observed in males in comparison with females, 4 (23.5 %) versus 1 (7.7 %).

Correlations of hematological characteristics to age of patients with sickle cell disease are shown in table 3. The age of patients was not correlated significantly to any of the enrolled hematological characteristics (p > 0.05).

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Table (1): Mean and age range in male and female patients with sickle cell disease

Age (years)	Total *n* = 30	Male *n* = 17	Female *n* = 13	*p*
Mean ±SD	7.93 ±2.43	7.53 ±2.24	8.46 ±2.67	0.307 I NS
Range	4 -12	4 -11	4 -12	

*n: number of cases; SD: standard deviation; I: independent samples t-test; NS: not significant at p > 0.05

Table (2): Hematological characteristics of male and female patients with sickle cell disease

Characteristic	Total *n* = 30	Male *n* = 17	Female *n* = 13	*p*
Hb				
Mean ±SD	9.37 ±1.13	9.34 ±1.02	9.42 ±1.30	0.838 I NS
Range	7.6 -11.8	7.6 -11.4	8 -11.8	
Anemia, *n* (%)	29 (96.7 %)	17 (100.0 %)	12 (92.3 %)	0.433 F NS
Normal, *n* (%)	1 (3.3 %)	0 (0.0 %)	1 (7.7 %)	
RBC				
Mean ±SD	3.68 ±0.69	3.86 ±0.69	3.44 ±0.65	0.099 I NS
Range	2.6 -5.65	2.81 -5.65	2.6 -4.57	
Low, *n* (%)	19 (63.3 %)	10 (58.8 %)	9 (69.2 %)	0.838 Y NS
Normal, *n* (%)	11 (36.7 %)	7 (41.2 %)	4 (30.8 %)	
HCT				
Mean ±SD	26.85 ±3.19	26.93 ±2.80	26.75 ±3.76	0.879 I NS
Range	22.1 -32.9	23 -32.2	22.1 -32.9	
Low, *n* (%)	30 (100.0 %)	17 (100.0 %)	13 (100.0 %)	---
Normal, *n* (%)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
MCV				
Mean ±SD	74.78 ±8.31	71.11 ±8.35	79.58 ±5.45	0.004 I HS
Range	49.4 -85.4	49.4 -81.9	66.1 -85.4	
Low, *n* (%)	12 (40.0 %)	11 (64.7 %)	1 (7.7 %)	0.002 C HS
Normal, *n* (%)	18 (60.0 %)	6 (35.3 %)	12 (92.3 %)	
MCH				
Mean ±SD	26.16 ±3.40	24.63 ±3.33	28.17 ±2.34	0.003 I HS
Range	15.6 -31.2	15.6 -29.3	22.1 -31.2	
Low, *n* (%)	11 (36.7 %)	10 (58.8 %)	1 (7.7 %)	0.013 Y S
Normal, *n* (%)	19 (63.3 %)	7 (41.2 %)	12 (92.3 %)	
WBC				
Mean ±SD	8.59 ±3.55	9.29 ±3.62	7.68 ±3.36	0.224 I NS
Range	4.02 -15.57	4.52 -15.57	4.02 -15.2	
Leukopenia, *n* (%)	6 (20.0 %)	1 (5.9 %)	5 (38.5 %)	---
Normal, *n* (%)	22 (73.3 %)	15 (88.2 %)	7 (53.8 %)	
Leukocytosis, n (%)	2 (6.7 %)	1 (5.9 %)	1 (7.7 %)	

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Platelet				
Mean ±SD	308.83 ±142.36	313.88 ±169.00	302.23 ±103.99	0.829 I NS
Range	50 -647	50 -647	151 -459	
Thrombocytopenia, *n* (%)	2 (6.7 %)	2 (11.8 %)	0 (0.0 %)	---
Normal, *n* (%)	23 (76.7 %)	11 (64.7 %)	12 (92.3 %)	
Thrombocytosis, *n* (%)	5 (16.7 %)	4 (23.5 %)	1 (7.7 %)	

*n: number of cases; SD: standard deviation; I: independent samples t-test; F: Fischer exact test; Y: Yates correction for continuity; C: Chi-square test; NS: not significant at $p > 0.05$; S: significant at $p \leq 0.05$; HS: highly significant at $p \leq 0.01$

Table (3): Correlations of hematological characteristics to age of patients with sickle cell disease

Characteristic	***r***	***p***
Hb	-0.052	0.785 NS
RBC	0.024	0.898 NS
HCT	-0.055	0.774 NS
MCV	-0.067	0.726 NS
MCH	-0.014	0.943 NS
WBC	0.121	0.525 NS
Platelet	0.039	0.837 NS

*r: correlation coefficient; NS: not significant at $p > 0.05$

Discussion

The current study was carried out on a subset of Iraqi children with sickle cell disease to figure out the main hematological characteristics in patients with steady state from a clinical perspective. Nearly all patients enrolled in this study had hemoglobin levels that were lower than normal, therefore the mean hemoglobin level was 9.37 g/dl which is lower than normal. Indeed, it is recommended to have a hemoglobin level that is more than 9 to 10 g/dl [12, 13]; thus the mean hemoglobin of 9.37 reflects well-controlled and effectively treated patients. Actually, the low hemoglobin levels of nearly all patients enrolled in this study are in line with the observation of previous studies [14-17]. The reasons for low hemoglobin in patients with sickle cell disease are attributed to nutritional insufficiency, low erythropoietin response and the most important "reduced life span of RBC" [14-17].

There was no significant difference in mean hemoglobin level between male and female patients participating in the current study. In addition, age of patients did not affect hemoglobin levels significantly. These findings are inconsistent with the observation of previous authors [14] who described low hemoglobin levels in young children and in male patients. Low hemoglobin levels in young children have been also reported by Iheanacho *et al* [18] and low hemoglobin levels in males have been reported by

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Abubakar *et al* [19]. However, and in line with our observation, previous authors have reported no significant difference in mean hemoglobin between males and females [18, 20]. In the current study, there was no significant difference RBC count and hematocrit between males and females. Furthermore, the RBC count and hematocrit were not significantly affected by age.

In this study, there was highly significant difference in mean MCV and mean MCH between males and females and low MCV and MCH levels were significantly more frequently seen in males in comparison with females. However, it should be mentioned that the majority of enrolled patients had normal MCV and MCH values. This observation is indeed supported by the observation of previous authors who found that most of patients with sickle cell disease had normal MCV, MCH and even MCHC values [19, 21, 22]. These indices reflect normal iron status, which is the result of increased red cell turn-over and blood transfusion in patients with sickle cell disease. Moreover, the low MCV and MCH in males in our study is similar to the observation of some previous authors [14].

In the current study, the mean WBC count of patients was within normal and most patients had normal WBC counts; however, leukopenia was more frequently seen in females than in males and leukocytosis was reported in 2 cases only. Actually, these findings disagree with the findings of previous authors [14, 18, 19] who found significant leukocytosis in patients with sickle cell anemia. It has been suggested that steady state of inflammation in patients with sickle cell anemia could explain the rise in WBC count associated with cytokine production [24]. In addition, the higher count in males in the current study in comparison with females is in line with several previous reports [14, 18, 19].

In the current study, mean platelet count was within normal and no significant difference was seen between males and females, but, thrombocytosis was observed in a significant proportion of patients and it was more frequent in males than in females. This high rate of thrombocytosis is in line with several previous reports [14, 19]. The high platelet count can be attributed to two important reasons, the first is functional and or structural asplenia and the second is the high erythropoietin production and erythropoietin has homology to thrombopoietin and may induce higher platelet production [14].

Conclusions

Some hematological parameters in patients with sickle disease are affected by gender but show no significant correlation to age in patients with sickle cell disease.

Recommendations

The study recommends full investigation of hematological indices, especially for males, in order to properly mange those patients.

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Ethical clearance: The study was approved by Al-Karkh health board of directors, the formal demonstrative of Iraqi ministry of health. A verbal consent was obtained from every contributor after full illustration of the aim and the processes of the study.

Conflict of interest: Nill

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الخصائص الدموية لعينة من مرضى فقر الدم المنجلي في العراق وعلاقتهم بالعمر والجنس

د.حسن ديدي مشاي[١]، د.محمد حسيب خميس[٢] ، د.حسين عبدالزهرة وداعة[٣]

الملخص

خلفية الدراسة: توصيف المعلمات الدموية في المرضى الذين يعانون من فقر الدم المنجلي يمكن أن يوجه أهداف العلاج نحو استراتيجيات الحد من معدل الاصابة والوفيات.

اهداف الدراسة: لتقييم المعايير الدموية في مجموعة من المرضى العراقيين المصابين بفقر الدم المنجلي وعلاقتها بالعمر والجنس.

المرضى والطرائق: شملت هذه الدراسة المقطعية ٣٠ مريضًا يعانون من فقر الدم المنجلي والذين عُرفوا بأنهم في حالة سريرية مستقرة دون أزمات انسداد الأوعية الدموية. تم جمع حوالي ٥ مل من الدم الوريدي في أنبوب مانع تخثر من كل مشارك. اجري تعداد الدم الكامل وفقًا للبروتوكول القياسي.

النتائج: كان متوسط العمر ٧,٩٣ ± ٢,٤٣ سنة والمدى العمري كان من ٤ إلى ١٢ سنة. شملت الدراسة ١٧ ذكراً و ١٣ أنثى. ٢٩ (٩٦,٧%) يعانون من فقر الدم ولم يكن هناك فرق معنوي في متوسط مستوى الهيموجلوبين بين الذكور والإناث (p = 0.838) أظهر الذكور معدل أعلى من حجم الخلية المتوسط المنخفض وهيموجلوبين الخلية المتوسط (٦٤,٧ % و ٥٨,٨% على التوالي) من الإناث (٧,٧% و ٧,٧% على التوالي) مع وجود فروق معنوية.

الاستنتاجات: تتأثر بعض المتغيرات الدموية في مرضى الداء المنجلي بالجنس ولكنها لا تظهر ارتباطًا معنويًا بالعمر

الكلمات المفتاحية: الخصائص الدموية، فقر الدم المنجلي، العراق

البريد الالكتروني: mohamed.haseb1975@yahoo.com

تاريخ استلام البحث: ٢٢ آب ٢٠٢١

تاريخ قبول البحث: ١ تشرين الثاني ٢٠٢١

[١،٣] مستشفى الديوانية التعليمي - وزارة الصحة - الديوانية - الديوانية - العراق

[٢] مكتب بغداد الطبي - مدينة الإمامين الكاظمين الطبية - وزارة الصحة - بغداد - العراق