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Sickle Cell Disease in Karbala and Efficacy of Hydroxyurea in Management

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ABSTRACT

Background Sickle cell disease (SCD) is the most common hemoglobinopathy worldwide. The abnormal hemoglobin's inherited as autosomal recessive (AR) disorders, where carrier parents transmit the abnormal genes to the offspring. Objective: To study the epidemiology of sickle cell disease in Karbala & To study efficacy of hydroxyurea in sickle cell disease treatment. Patients and Methods: This is a retrospective study conducted at our inherited hematological center in Karbala Teaching Hospital for children in the period from first April, 2019 to July, 31, 2019. The inclusion criteria: all patients who were registered & diagnosed sickle cell anemia and other types of sickle cell disease. Exclusion criteria: Twenty patients were excluded from this study due to incomplete data in the recorded files. The remaining 405 patients were distributed in this study according to origins, gender, consanguinity, types of sickle cell anemia, level of HbF and their complications. Results**:** The result of the study included 405 patients 189 females (46.7%) & and 216 males (53.3%), 149 patients living in Karbala, the youngest age 1 year and the oldest one 65 year. The age group > 10-20 years was the most prevalent group in this study. The types of sickle cell disease reported with the study according to the result of Hb electrophoresis and sickle cell anemia (HbSS) was the most prevalent type 60.5%. The distribution of the patient according to HbF among 245 patients with HbSS was more than 50% of them had HbF more than 20% and The patients who had sickle cell anemia with HbSS(245) and a higher level of HbF >20 were less need to blood transfusion (P value 0.008), but there is no significant relationship regarding the painful crisis and splenic sequestration with level of HbF. All patients were treated with hydroxyurea got improvement in their quality of life by decreasing the severity and complications which noticed by decreasing of the frequency of painful crisis and a decrease the need of blood transfusions after one year of treatment (**P** value<0.001). Conclusion: 1- the most common complications in patients who had SCA are acute painful crisis, anemia, splenic sequestration and gall stone.2-The patients with HbF more than 20% have less complication.3- Hydroxyurea improved the quality of life by decreasing admission to hospital and decreasing the need for blood transfusions.

INTRODUCTION

Sickle cell disease (SCD) is the most common haemoglobinopathy worldwide(1).The abnormal hemoglobin's inherited as autosomal recessive (AR) disorders, result a point mutation in amino acid substitution in abnormal gene resulting glutamic acid replaced by valine at the position sixth where carrier parents transmit the abnormal genes to the offspring. If both parents are heterozygotes for HbS, there is a 25 percent chance of having a homozygous HbSS (Sickle cell anemia, SCA) child.

It results in an abnormality in the oxygen-carrying protein hemoglobin found in red blood cells. This leads to a rigid, sickle-like shape red blood cell under certain circumstances (hypoxia, dehydration, fever, cold, stress). Long-term pain may develop as people get older. The average Life expectancy in the developed world is 40 to 60 years.(3) If one parent is a carrier for HbS and the other is a carrier for other hemoglobinopathy variants, it results in a double heterozygote state. Heterozygotes are generally asymptomatic carriers (traits), while the SCD is expressed in the homozygotes and the double heterozygotes for two abnormal hemoglobin genes like HbS and the thalassaemias are usually symptomatic(1,2,3).

Clinical presentation of SCD

The major symptoms of SCD are mild to severe anemia, painful crises, frequent infections, hand and foot syndrome, and stroke. Some patients require frequent blood transfusions, while others may never need a single transfusion during their lifetime.

In the severe form of SCD, the patients may have retarded growth, bone defects, multiple organ dysfunction and other complications due to frequent transfusion requirements, while patients with a mild disease may reach average height and have no multiple organ abnormalities.

The SCD in different Middle Eastern Arab countries shows a significant variation in its clinical presentation (1).

Aim of the study

- To study the epidemiology of sickle cell disease in Karbala.
- To study the efficacy of hydroxyurea in sickle cell disease treatment.

PATIENTS & METHODS

Study design

This study was a retrospective conducted on inherited hematological center diseases in Karbala Teaching Hospital for children.

Patients

Four hundred twenty five patients participated in the study, their median age was 23 years (range: 1 to 65), data collected from first April, 2019 to July, 31, 2019.

The inclusion criteria: all patients who were registered & and diagnosed as sickle cell anemia and other types of sickle cell disease.

The exclusion criteria: Twenty patients were excluded from this study due to incomplete data in the recorded files.

The remaining 405 patients were distributed in this study according to origins, gender, consanguinity, types of sickle cell anemia, level of HbF and their complications.

Sixty-two out of four hundred-five patients were received hydroxyurea; they were taken hydroxyurea in special indications (severe vasooclusive crisis, acute chest syndrome, pulmonary hypertension, stroke, and priapism).

All of the patients signed informed consent statement before started treatment with hydroxyurea, the dose of it 20 mg/kg/day ±5.5 mg/kg/day.

Three out of 62 patients stopped hydroxyurea due to side effects (thrombocytopenia, GIT upset and infertility), the remaining 59 patients were distributed according to gender, and age and we were monitoring them one year before and one year after treatment with hydroxyurea, especially their painful crisis and blood transfusion, depending on the clinical data that available in their medical records.

HbF quantification

The HbF percentage was determined using the HPLC technique (Variant Express, Bio-Rad laboratories, Inc, Hercules, CA, USA) and the beta-thalassemia short program (Variant™, Bio-Rad Laboratories, Inc, Hercules, CA, USA).

Classify of HbF according to the level of it's between less than 10%, & (10&20%) or more than 20%.

Results:

The studied patients were 405 out of 189 females (46.7%) and 216 males (53.3%), 149 of them, they lived in karbala-Ein AL tamer, 85 patients lived in Karbala center, 12 patients lived in Karbala- Hindia, 7 patients lived in Karbala –Hussainia, 133 patients lived in Karbala but their original from Basra , and 19 patients lived in Karbala but their originals from other cities as shown in figure 1.

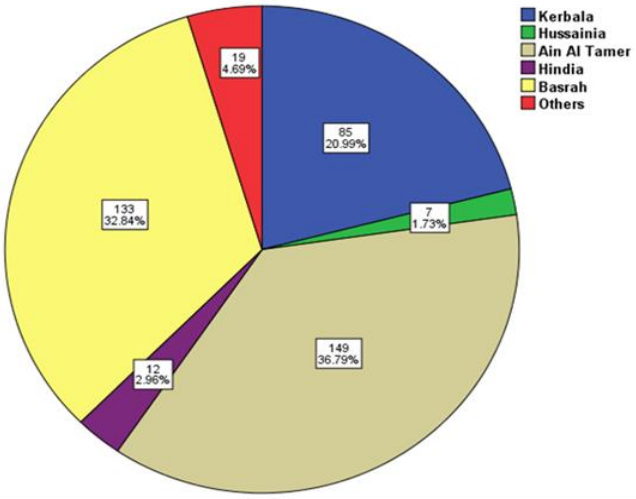

Figure 1 Distribution of patients according to origin.

Figure 2 Shows the distribution of patient according to age groups from youngest age was 1 year to oldest age was 65 years. The age >10-20year was the most prevalence group in this. Study

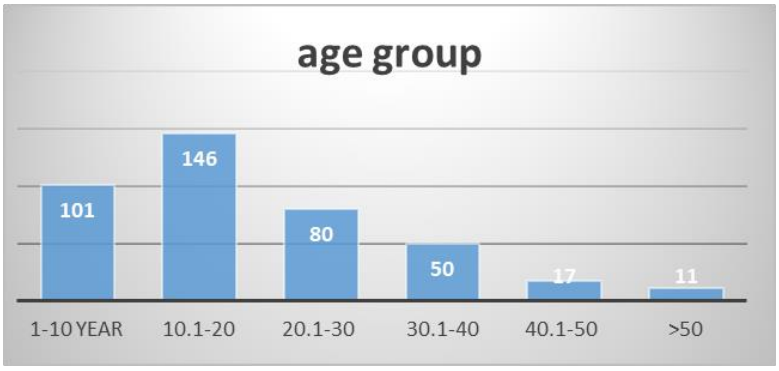

Figure 2: The distribution of the patients according to the age.

Table 1: The types of SCD in studied group

Sickle cell variant	***Frequency***	***percent***
Sickle cell anemia (HbSS)	*245*	*60.5*
S-Thalassemia anemia (HbST)	*119*	*29.4*
D sickle cell anemia (HbSD)	*23*	*5.7*
Sickle cell trait (HbSA)	*11*	*2.7*
C-sickle cell anemia (HbSC)	*7*	*1.7*
Total	*405*	*100.0*

Table 1 shows types of sickle cell disease recorded according to the results of Hb electrophoresis in which sickle cell anemia (HbSS) was the most common type 60.5%. Figure 3 shows the distribution of patients according to HbF level between 245 patients with HbSS more than 50% of them had HbF more than 20%.

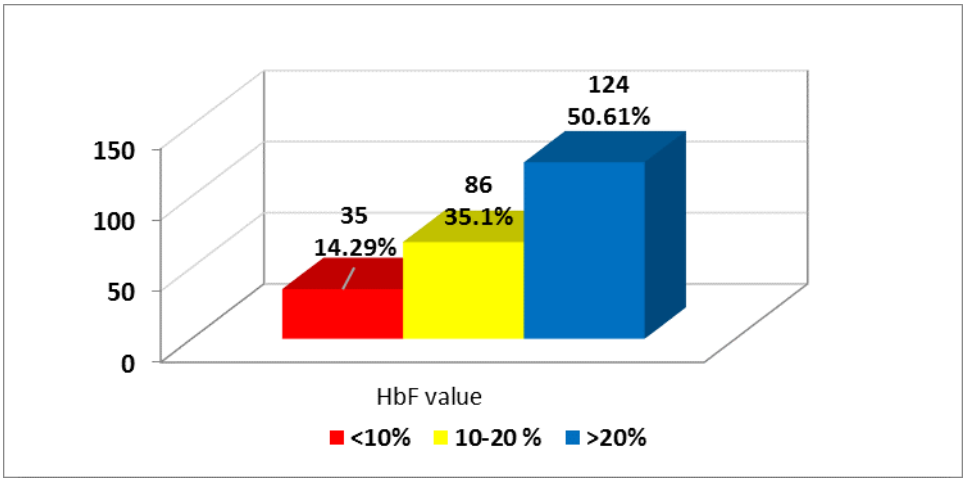

Figure 3 Classification of HbSS patients according to HbF levels.

Table1 shows the relationship between the level of HbFand the need for blood transfusion, splenic sequestration and painful crises in HbSS, we found that the higher level of HbF(>20%) the less need for blood transfusion(P value0.008), but no significant relationship regarding painful crises and splenic sequestration with level of HbF.

Table 2 relationship between levels of HbF and the need for blood transfusion, painful crises and splenic sequeatration in HbSS patients.

	HbF value			**P value**
	<10% Total no.(35)	10-20% Total no.(86)	>20% Total no.(124)	
Blood transfusion	15 42.9%	41 47.7%	34 27.4%	0.008
Painful crises	16 45.7%	58 68.4%	73 58.9%	0.081
Splenic sequestration	10 28.6%	34 38.3%	40 32.3%	0.409

All patients treated with hydroxyurea get improvement in their quality of life by minimizing the severity of complications which was noticed by minimizing frequency of painful crises and decreasing the need of blood transfusion within one year of treatment.

Table 3 Effect of hydroxyurea on need of blood transfusion.

NO/year	No.	Min	Max	Mean	P
Before 1 year	59	0	15	2.31	0.001
After 1 year	59	0	7	0.6	

Table 4 Effect of hydroxyurea on painful crises.

NO/year	No.	Min	Max	Mean	P
Before 1 year	59	3	16	6.6	0.001
After 1 year	59	0	7	2	

DISCUSSION

In the current study, we tested 405 patients who had sickle cell disease included 189 females(46.7%)& 216 males (53%) all lived in Karbala but had different origins, the

distribution of age for them between one year and 65 years, most of them had +ve consanguinity (295, 72.8%) , and the patients in our center divided according the type of SCD to HbSS(245, 60.5%), HbST(119, 29.4%), HbSD(23, 5.7%), HbSA(11, 2.7%) &HbSC(7, 1.7%). These findings are in line with two Iraqi studies and a Uganda study, in Basra, south Iraq (by Dr. Mead K. Hassan et.al) [4]& in Dohuk, Northern Iraq (by Dr. Nasir A.S. Al-Allawi et al) [5] except in consanguinity our study differ from study done by DR. Nasir (no significant of consanguinity in his study) & in line with Uganda study (by Peter Olupot-Olupot et al)[6] according to distribution of the age, gender and consanguinity.

We noticed that patients who had higher Hb F levels more than 20% had fewer clinical complications of the disease (regarding frequency of blood transfusion). Therefore, patients with low Hb F need close follow-up and monitoring since early age to detect complications as early as possible and consider use of disease-modifying agents. These findings are similar to the study Dr. Mead K. Hassan et al[7]& Nimer, et al[8] study in Sudan.

In those studies, we found that the most common and severe complications of SCA that necessitate hospitalization are acute painful crises then ACS, 245 patients had acute painful crisis 245 (60.5%) & 10 patients had ACS (2.5%), which is similar to Saudi study done by AbeerA.Abd Elmoneim, MD et al[9].

Fifty nine patients put on hydroxyurea 32(54.2%) males &27(45.8%) females, 33 patients had HbSS(56%), 25 patients had HbST(42.4%) & only one had HbSD(1.7%). We had 41 patients they received blood transfusion before treatment with hydroxyurea(1-15 times/year)mean 3 time/year and after treatment with hydroxyurea the frequency of blood transfusion decreased to (0-7 times/year) (mean 1time/year). The same thing to painful crises, we had 46 patients who had painful crises and put on hydroxyurea , we observed the frequency of attacks of painful crises were (3-17 attack/year)before treatment to(0-6 attacks/year)after treatment with hydroxyurea , our study similar to Nigerian study done by Akinyemi O.D.et al[10] & Saudi study done by Fauzia R. Azmet et al[11].

CONCLUSION

1- the most common complications in patients had SCA are acute painful crisis, anemia, splenic sequestration and gall stones.

2-The patients with HbF more than 20% have less complication.

3- Hydroxyurea improved the quality of life by decreasing admission to the hospital and decreasing the need for blood transfusions.

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