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Original Research Article

Lifespan and pattern of sickle cell disease in Saudi elderly patients

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Abstract

Sickle cell disease (SCD) is one of the most common inherited blood disorders in Saudi Arabia and its severity is widely variable even among patients sharing the same HBB haplotype. And since there are no data in Saudi Arabia about the life span of SCD patients or pattern of complications in elderly patients. we have studied the severity of SCD among patients older than 50 years of age. Patients with SCD (HbSS. or. HbSB0) who are followed in King Khalid University hospital in Riyadh and older than 50 years of age were enrolled. Each patient underwent a detailed medical history and physical examination in addition to reviewing medical charts to obtain specific information. Laboratory workups performed during steady state, and data analysis cut off was March 30, 2014. We identified five patients only from our SCD cohort (n=261). HbF level is higher among older patients compared to younger patients(P=0.001). It is clear that the number of patients in our study decline pass the age of 35 years, which could be an indication of higher rate of mortality among Saudi SCD patients as they approached their 40s. There was no difference in the clinical complications pattern in older patients compared to younger patients, however, HbF level was clearly higher among older patients. We identified only few patients ≥ 50 years (n=5), which might be an indirect indicator of the age of death among Saudi SCD patients as none of our patients is older than 60 years of age. Number of elderly patients with SCD per single institution is very small to draw any specific conclusion. Larger multi-institutional study is needed to determine the mortality pattern in SCD and define ameliorating factors that are associated with prolonged survival.

Keywords: Elderly, Lifespan, Saudi Arabia, SCD, Sickle Cell Diseas

INTRODUCTION

Sickle cell disease (SCD) is one of the most common inherited blood disorders in Saudi Arabia and its severity is widely variable even among patients sharing the same HBB haplotype (Alsultan et al., 2012; Alsultan et al., 2014). SCD related complications such osteonecrosis, gallstones, renal impairment, pulmonary hypertension,

and cardiac dysfunction are seen more frequently in adults and contribute to the increased mortality among SCD patients limiting their average predicted age at death in the US to 39 years with few patients surviving beyond 60 years of age (Hassell, 2010). SCD manifestations are inconstant. The leading features are linked to vasoocclusion and hemolytic anemia, which may cause pain either acute or chronic, and infarction or ischemia to the tissue. The risk of infection is increased due to functional hyposplenism which is a result of splenic infarction in the early time of the life. The mortality and morbidity are impacted directly by these complications (http://www.uptodate.com/contents/overview-of-the-clinic al-manifestations-of-sickle-cell-disease?source=search_result&search=Sickle+Cell+Disease+in+Saudi+Elderly+Patients&selectedTitle=5%7E150). One of the most important reasons of mortality and morbidity in SCD patients are the long standing outcomes of vasoocclusive crisis which cannot be reversed. Some medications like Hydroxyurea have been used to lower the vasooclusive episodes and limit the irreversible SCD complications (http://www.uptodate.com/contents/hydroxyurea-and-othe r-disease-modifying-therapies-in-sickle-cell-disease? source=search_result&search=Sickle+Cell+Disease+in+Saudi+Elderly+Patients&selectedTitle=2%7E150). There are no data in Saudi Arabia about the life span of SCD patients or pattern of complications in elderly patients. In this report, we studied the severity of SCD among patients older than 50 years of age from both the southwestern (SW) province with African origin HBB haplotypes and the eastern province with AI haplotype. Our hypothesis is that SCD patients older than 50 years will have higher fetal hemoglobin (HbF) and lower rate of organ dysfunctions compared to other SCD patients in our cohort.

MATERIALS AND METHODS

Patients

Patients with SCD (HbSS or HbSB 0) who are followed in King Khalid University Hospital in Riyadh and older than 50 years of age were enrolled in our study either during their clinic visit or inpatient stay, after obtaining informed consent. Our institutional review board approved the study. In addition, complete list of all patients with SCD who are followed at King Khalid University Hospital were obtained from the medical records department to ensure that no patients will be missed. Saudi patients with both African origin HBB haplotypes (e.g. Benin, Bantu, and Senegal) and the AI haplotype were included in our study. Each patient underwent a detailed medical history and physical examination in addition to reviewing medical charts to obtain the following information: age, gender, use of hydroxyurea, splenomegaly, and SCD complications such as acute painful episodes, osteonecrosis, acute chest syndrome, overt stroke, gallstones, splenic sequestration, serious infections, priapism, and leg ulcers.

Laboratory evaluation

Laboratory workup was performed during steady state. DNA was extracted from peripheral blood of all patients using Gentra Puregene blood kit (Qiagen, Valencia, CA). Laboratory workup included CBC, reticulocytes, liver function tests, G6PD level, and hemoglobin electrophoresis. HBB gene cluster haplotype was determined using restriction fragment length polymorphism (RFLP) technique as previously described (Muralitharan et al., 2003) and molecular diagnosis of common -thalassemia deletions (3.7, 4.2, 20.5, and --MED) was performed by multiplex polymerase chain reaction assay (Tan et al., 2001). The presence of the non deletional poly A signal mutation (TSaudi) was determined as previously described (Viprakasit et al., 2002).

Statistical analysis

Data analysis cut off was March 30th, 2014. Descriptive analyses involved calculation of mean values (± one standard deviation) and ranges for continuous data and frequencies for categorical data. Distribution of continuous variables was compared between groups using student t test for categorical predictors and simple linear regression for continuous predictors. SCD complications frequency was compared between different age groups via chi-squared testing for categorical predictors and simple logistic regression for continuous predictors. All variables with a P-value ≤ 0.05 on univariate analysis were included in the multivariate analysis. P-value and lt; 0.05 was considered statistically significant. Stata Statistical Software: Release 12 was used for all analyses (College Station, TX: StataCorp LP).

Table 1. Clinical characteristics of sickle cell disease patients based on age

	Patients ≥ 50 years (n=5) mean±SD or %	Patients < 50 years (n=256) mean±SD or %	P value
Gender (Female%)	60%	47%	0.66
Hydroxyurea use	60%	48%	0.67
Pain episodes/year	3.0±4.0	5.9±6.6	0.33
Osteonecrosis	40%	18%	0.22
Gall stones	40%	36%	1.00
Splenic sequestration	40%	30%	0.63
Acute chest syndrome	40%	39%	1.00
Overt Stroke	20%	9%	0.44

Table 2. Laboratory characteristics of sickle cell disease patients based on age

	Patients ≥ 50 years (n=5) mean±SD or %	Patients < 50 years (n=256) mean±SD or %	P value
Hb (g/dL)	9.2±1.4	9.1±6.1	0.96
MCV (fl)	85.5±9.1	80.7±12.1	0.38
Alpha thalassemia	0% (n=4)	35% (n=118)	0.29
G6PD deficiency	25% (n=4)	6% (n=160)	0.24
HbF	20.2±4.6	11.3±6.2	**0.002**

RESULTS

Patient characteristics

We identified five patients only from our SCD cohort (n=261) who were older than 50 years of age. We also reviewed the list of 300 SCD patients from our medical records department and found only five patients who were already included in our SCD cohort. The median age was 51 (range, 50-55 years). There were three females and two males. Two patients had hypothyroidism, one patient had chronic hepatitis C, one patient with history of pulmonary embolism and also stroke. All five patients had normal renal functions. The HBB gene cluster haplotype was Arab-Indian in 2 patients, Senegal in 1 patient, Benin in 1 patient, and not determined in 1 patient. Additional clinical characteristics and laboratory observations are shown in Table 1 and 2.

Variability in Clinical and Laboratory Characteristics based on Age

The right group to serve as control will be SCD patients who died prior to the age of 50 years, however, such data is not available. Instead we used the data from our SCD cohort for patients younger than 50 years of age. There is no statistical significant difference between the patterns of complications seen in both groups as shown in Table 1. HbF level is higher among older patients compared to younger patients (P=0.001). No other difference in laboratory values, Table 2.

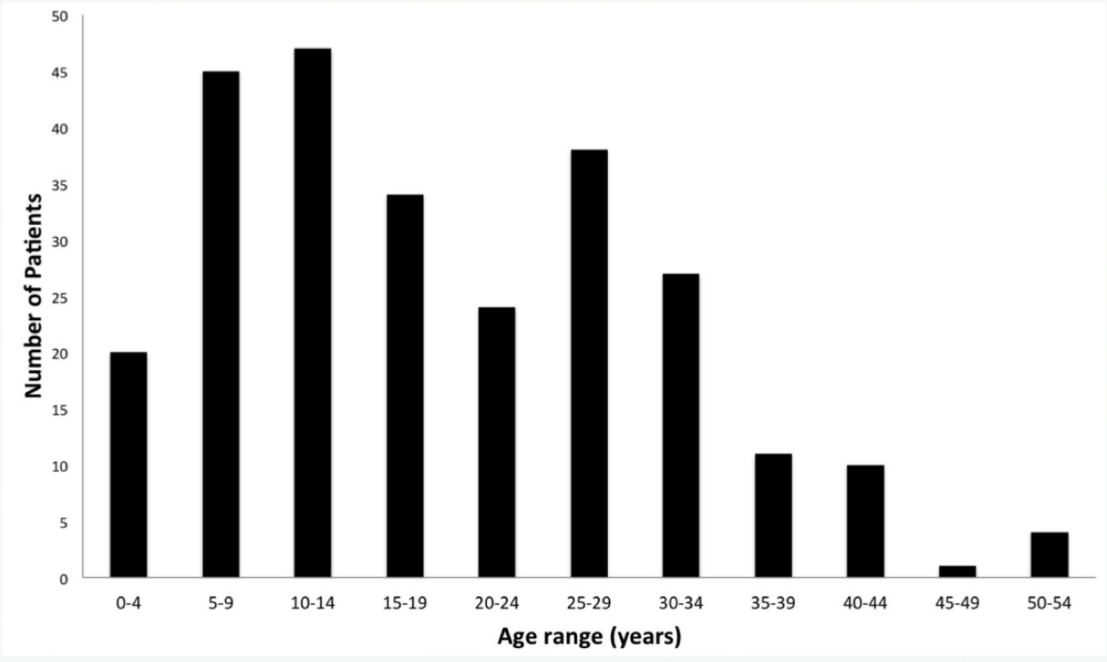

Figure 1. Distribution of age among all patients

Distribution of Age among all patients included in our SCD cohort

Figure 1 shows the distribution of age at enrollment among all SCD patients enrolled in our study. It is clear that the number of patients in our study decline pass the age of 35 years, which could be an indication of higher rate of mortality among Saudi SCD patients as they approached their 40s. However, the exact age or cause of death among deceased SCD patients followed in our hospital is not available.

In our study we have two groups. First group is in our study is the control which are the patients who have SCD and below 50 years of age (n=256) of which 47% were female and we compare it with the second group which are the patients who have SCD and above 50 years of age (n=5) of which 60% are female.

The incidence of clinical characteristics of sickle cell disease were higher and more evident in the second group (patients >50), 60% were using hydroxyurea compared to 48% in the controlled group (p value 0.67). 40% of them had osteonecrosis, gallstones, splenic sequestration and acute chest syndrome compared to 18%, 36%, 30%, 39% respectively in the controlled group (p value 0.22, 1.00, 0,63, 1.00 in row) .20% of them had overt stroke in comparison to 9% only in controlled group (p value 0.44) . Whereas pain episode recurrence per year were lower than the controlled group; 3-4 times a year compared to 5.9-6.6 times a year in the controlled group (p value 0.33). Moreover, our data did not show a significant difference in alpha-thalassemia and G6PD deficiency between these two groups. However, HbF level was significantly higher among elderly patients (≥ 50 years).

DISCUSSION

One Jamaican study that described SCD phenotype in patients older than 60 years. A total of 102 patients (64.7% women) older than 60 years of age (range 60.2-85.6). Only 40 still alive at the time of the analysis. None were on hydroxyurea. Mostly Benin haplotype with possible familial clustering. Pain crisis was observed in 82%, leg ulcers in 58%, renal impairment increased with age, alpha thalassemia was detected in 54%, HbF on average was 4.9% higher than Jamaican cohort and hemoglobin continued to decline with age (Serjeant et al., 2007). We noticed a similar observation in term of higher HbF level

among ≥ 50 years old patients. There are very limited data on the causes of death among Saudi patients. One study from the EasterIn our current study, we characterized the clinical phenotype of SCD patients older than 50 years of age. There was no difference in the clinical complications pattern in older patients compared to younger patients, however, HbF level was clearly higher among older patients. We identified only few patients ≥ 50 years (n=5), which might be an indirect indicator of the age of death among Saudi SCD patients as none of our patients is older than 60 years of age. The average age of death in the US is 39 years with fewer patients living past the age of 60 years possibly similar to our population (Hassell, 2010). There was no province reported acute chest syndrome to be the leading cause of death followed by sepsis among patients with the Arab Indian haplotype (Al-Suliman et al., 2006). No data is available from other regions. Understanding the mortality pattern can help in improving preventive care among SCD patients as they get older.

Life expectancy of female sicklers is consistently higher than male which is showed in our study and in a similar study done in 1994 ((Platt et al., 1994). The level of fetal hemoglobin seems to be a key player in determining the survival of sicklers which has been also shown in our study and the previous studies (Platt et al., 1994; Perronne et al., 2002). Both our study and similar study (Platt et al., 1994) illustrated that the existence of concurrence alpha thalassemia has no statistically significant impact on the prognosis or mortality of sicklers. In a study done in 2014 it showed that the low level of Hemoglobin was associated with decreased survival but in our study there's no statistical significant difference in the level of hemoglobin in those who lived beyond the age of 50 in comparison to those in younger age and in the same study the presence of one attack of stroke was also associated with decreased survival but our data did not suggest that as the older patients (>50) have more stroke (20%) while the younger patient (<50) have only 9% and the same study suggests that the use of hydroxyurea has no rule in survival although in our data the use of hydroxyurea in the older population 60% is more than the younger one 48% (Elmariah et al., 2014).

CONCLUSION

Number of elderly patients with SCD per single institution is very small to draw any specific conclusion. Larger multi-institutional study in needed to determine the mortality pattern in SCD and define ameliorating factors that are associated with prolonged survival.

Conflict of Interest

All authors declare no conflict of interest.

Authors' Contributions

All authors contributed in all the aspects of this research from reviewing existing literature, conception and design of this study, acquisition of the data, analyzing and interpreting the data, drafting the article to a developed final version.

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