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Original Research Article

Inpatient Hospitalized Sickle Cell Disease for Adults in Al-Ahsa Saudi Arabia Chart Review Study, 2015-2017

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Abstract

Background: Sickle cell disease (SCD) is an autosomal recessive disease characterized by production of abnormal hemoglobin S. The aim of this study is to review the history of SCD adults patients who were admitted to inpatient ward in Al-Ahsa, Saudi Arabia. ***Method:*** A retrospective cross sectional study was conducted through medical records chart review in King Fahad Hospital (KFH) in Al Ahsa to detect all SCD adults patients who were admitted to inpatient ward during 2013 to 2015. A structured Self designed questionnaire was reviewed and used during data collection from patients files. ***Results:*** A total of 130 patients were admitted to inpatient ward, consanguinity reported in 96.2 %. In the last visit, 64.3 % had diagnosed with vaso-occlusive crises, 10.1 % had sequestration crises, 13/2 % had acute chest syndrome, and 12.4% had gall stone. Complications of SCD included spleen removed (46.4%), infection (93%), anemia (93%) and acute chest syndrome (40.6%). ***Conclusion:*** SCD is considered as a load in the secondary health care services. Further studies need to be conducted in this subject.

Keywords: Sickle cell anemia, Saudi Arabia.

INTRODUCTION

Sickle cell disease (SCD) according to WHO is a genetic blood disorder that affects the hemoglobin within the red blood cells [1]. It is a common problem and major public health concern worldwide and the most common inherited hematologic disorder in the United States (Central and South America) affecting 70 000 to 80 000 Americans, 1 in 500 African Americans and 1 in 1,000 to 1,400 Hispanic Americans [2, 3]. It is also common in Mediterranean, some Caribbean countries, Sub -Saharan Africa, Central India, Turkey and Middle East [2, 4].

In Saudi Arabia, It is a common disease especially in Eastern (Al-Ahsa) and Southwestern Provinces (Jazzan) [5]. Clinical picture of inpatient admitted cases of SCD includes chronic hemolytic anemia and vaso-occlusive crisis. Diagnosis is confirmed by Electrophoresis by presence of homozygous HbS and can also document other hemoglobinopathies (eg, HbSC, HbS-beta+ thalassemia) [6]. Signs and symptoms include fatigue, yellowish discoloration of the skin (*jaundice)*, whites of the eyes (*icterus*) and painful swelling of the hands and feet (*dactylitis)*. Major Complications of SCD include acute pain *(vaso-occlusive) cris*es [5], splenic sequestration crisis and aplastic crisis which is caused by a parvovirus B19 infection. The sequestration crisis and aplastic crisis most commonly occur in infants and children with SCD [7]. Other complications of SCD include Kidney, Gallstone, Liver, Joints, *intrahepatic cholestasis*, hemochromatosis, *avascular necrosis*, *d*elayed growth and puberty [7].

The aim of the Management is to avoid crises, relieve pain, prevent complications and improve the ability of the patient to live with the disease. Folic acid supplements are recommended for the aim of producing red blood cells. To relieve pain during a sickle crisis, give pain medications and increasing fluid intake. Hydroxyurea may reduce the frequency of painful crises and of acute chest syndrome for adults. Antibiotics are recommended routinely to prevent infections in children. Children and adults should also receive all recommended vaccinations, including influenza vaccine and pneumococcal vaccine. Bone marrow transplants can cure sickle cell disease [8].

Information about the prevalence of SCD in Saudi Arabia is patchy and underestimated, but studies

have reported that SCD is a common genetic disorder in Saudi Arabia [9, 3]. The highest prevalence in the Eastern region (17% for sickle-cell trait and 1.2% for SCD) [3]. The fifth major haplotype is the ′Arab-Indian′ haplotype (also called the Asian or Saudi haplotype) is found in India and Saudi Arabia [9]. The common disease pattern of sickle cell hemoglobin in Saudi Arabia is benign severe with HbS (%) < 1-17.0 [10]. SCD is an autosomal recessive disease but are common in this part of the world as consanguineous marriage rates exceed 50% [9]. Hemoglobin SS Disease is the most common type of SCD. It occurs when the hemoglobin S gene inherited from both parents. Hemoglobin SC Disease is the second most common type of SC [11].

Hb- F called fetal hemoglobin, is the main hemoglobin present during the fetal life which counting approximately 60 to 80% of total hemoglobin in the full-term newborn. It is replaced by adult hemoglobin (hemoglobin A, Hb - A) by approximately 6 to 12 months of age. Its amounts in the normal adult is less than 1% of total hemoglobin [4]. To decrease the prevalence of SCD in Saudi Arabia, All Saudi couples planning for marriage are required to perform the screening test as recommended by the Ministry of Health (MOH) [12]. This study aims to review the history of SCD adults patients who were admitted to inpatient ward.

LITERATURE REVIEW

Lervolino G. estimated the prevalence of SCD and sickle cell trait in national neonatal screening studies in Brazil 2011. He concluded that the best screening coverage area is consistent with and the lowest rates for sickle cell trait and sickle cell disease [13].

Brousseau DC Study estimated the number of people with sickle-cell disease in the United States in 2009 and showed that the states with the highest estimated number of people with sickle-cell disease were New York with 8308; Florida with 7539; Texas with 6765; California with 6474; then Georgia with 5890. These five states comprised more than 43% of the total sickle-cell population [14].

Mvundura M Study estimated the Health Care Utilization and Expenditures for Privately and Publicly Insured Children with Sickle Cell Disease in the United State in 2009. It is Cross sectional study shows, that The percentage of children with SCD registered in Medicaid with an inpatient admission was higher compared to those privately covered (43% vs. 38%) [15].

Ahmed AE Study estimated the Health-related quality of life in patients with sickle cell disease in Saudi Arabia in Nov 2015. It is a Cross sectional study shows, that SCD patients who hold a university degree reported positive impacts on the following domains of SF-36: physical role function, vitality, emotional well-being, social function, pain reduction, and general health (P = .002, P = .001, P = .001, P = .003, P = .004, and P = .001, respectively)" [16].

Wang WC conducted a retrospective cohort study at New York on August, 2013 about Hydroxyurea is associated with lower costs of care of young children with sickle cell anemia. Study shows that the extent of hospital stay was similar in the 2 groups (hydroxyurea and placebo). Annual cost of the hydroxyurea ($11 072) was 21% less than the cost of the placebo ($13 962; P = .038) [17].

Sabahelzain MM Study estimated the ethnic distribution of sickle cell disease in Sudan in 2014. It is a theoretical subject not a field, shows that the most common haplotypes associated with the S gene in Sudan are Cameroon, Benin, Bantu and Senegal haplotypes rather than Saudi-Asian haplotype [18].

Jastaniah W study Studied the Epidemiology of sickle cell disease in Saudi Arabia in Riyadh on 2011. It reported that the prevalence of the sickle cell gene in the adult population at 4.2% for sickle-cell trait and 0.26% for SCD, with the highest prevalence in the Eastern province (17% for sickle-cell trait and 1.2% for SCD) [9].

Al Qurashi conducted a cross sectional study at king Saud University in Riyadh on 2004-2005 about the prevalence of sickle cell disease in Saudi children and adolescent and showed that high prevalence of SCD in eastern and southern region of the country [19].

Alsultan A. study conducted a hospital-based study to assess the pattern of SCD complications in adults in 2010. 96% of patients had a history of acute painful crises within 1 year back. 47% had at least one episode of acute chest syndrome but only 15% had two or more episodes. 66% had gallstones. All cases of osteonecrosis were in the hip, and only two cases in the shoulder. Osteomyelitis or septic arthritis was observed in 8 patients and 13 patients had bacteremia [20].

Al Hamdan N.A. assessed results of premarital screening program in Saudi Arabia in 2007. It is a population-based study for 488,315 individuals screened on 1425-26. It reported that 4.20% had sickle cell trait, 0.26% had sickle cell disease, 3.22% had thalassemia trait, and 0.07% had thalassemia disease. Both the diseases were focused mainly in the eastern, western, and southwestern parts of the country [21].

Alabdulaali MK study found that SCD patients in eastern province of Saudi Arabia suffer less severe acute chest syndrome than patients with African haplotypes.it is a retrospective study done in Hofuf 2007. It noticed that acute chest syndrome in SCD patients in Hofuf area causes significant morbidity and mortality. Although the prevalence of SCD recurrence and

mortality were low compared to patients with African haplotypes [22].

METHODS

A retrospective cross sectional study was conducted through medical records chart review. This study was conducted at King Fahad Hospital (KFH), in Al-Ahsa, Saudi Arabia on November 2017. KFH was established in 1986 and considered as a secondary governmental health care hospital that includes 700 beds.

Study subjects include all sickle cell adult patients (21-38 years) who were admitted to inpatient ward of KFH due to SCD crises during the 2015 to 2017. SCD cases who have other chronic diseases were included. All cases were diagnosed by Internal Medicine specialist or consultant. Cases of age group less than 21 years old, Non admitted cases of SCD and other blood diseases cases were excluded.

Inpatient admission books of the Internal Medicine ward in 2015 to 2017 were reviewed to detect all SCD admitted cases and take their medical record number (MRN). It included the personal data, admission information and diagnosis of all admitted cases. A structured questionnaire was designed to detect the general personal information, family and genetic history of SCD, clinical picture during admission, hemoglobin level during admission and discharge, management and complications of the last admission in addition to percentage of hemoglobin S, F, A, Weight and height during the last visit.

Data were extracted through collection of the required information from the patient file from the medical record department. Study questionnaire was revised by two family physicians. Pilot study was done in KFH through reviewing the Inpatient admission book of the Internal Medicine ward in 2012 and medical files of 20 SCD admitted cases.

Study questionnaire was two parts; general information and history of last admission of with SCD during the study period. General information included MRN, date of birth, gender, consanguinity, date of diagnosis with SCD, Percentage of hemoglobin types, number of admissions, history of chronic diseases and SCD in family. Second part included date of admission, clinical picture, diagnosis, management, complications and length of stay. Age, weight, height, number of admissions, length of stay and hemoglobin level were collected as continuous variables and other variables were categorical.

Collected data was computerized and analyzed using (SPSS) software version 22.0. Frequency table was drawn with percentages, measures of central tendency and dispersion to explore study findings. Chi-square tests and t-test to determine the association between predictors and sickle cell variables were used. Significance level is equal to or more than 95% ($p = \leq 0.05$).

RESULTS

Characteristics of the patients are presented in Table 1. Of 130 SCD patients included in the study, 40.4 % were males. A total of 130 patients, consanguinity was reported in (96.2 %), percentage of positive family history of SCD in both parents (F+M+) was 33.1%, 43.1% had a father with SCD and 23.8 % had a mother with SCD only. SCD patients who had other chronic diseases were 118 (90.8%) and percentage of obesity was 11.5%. Regarding Hg level for SCD admitted patients, 70% had HgF level between (10-14.9) and 79.2% had HgA level between (11-20). Percentage of more than 4 days length of stay in inpatient ward for SCD was 53.1% compared to 46.9% who had less than 4 days.

Table 2 Presents the distribution of hemoglobin level during admission, discharge and difference in the last visit. The mean Hg level was 7.4 during admission and 10.3 during discharge (Difference= 2.9). The mean Hg levels in the last admission were HgS=82, HgF =13.3 and HgA =11.5.

During last admission, 64.3% of SCD patients were diagnosis with vaso-occlusive crises, 10.1% with sequestration crises, 13.2% with acute chest syndrome, and 12.4% with gall stone (Graph 1). Management plan and complications of admitted SCD patients were illustrated in graphs 2 and 3. All SCD admitted patients had received I.V fluids, 98.5% received blood transfusion, 99.2% had analgesia, 24.6% received Antibiotics. Of 130 SCD patients, 46.4% had spleen removal, 93% complicated by infection, 93% anemia, 40.6% acute chest syndrome.

Table 3 Presents the results of a bivariate analysis of SCD cases. There was no significant difference between males and females SCD patients in age, consanguinity, family history of SCA, body mass index, level of Hemoglobin (S-A-F), diagnosis of last visit and length of stay at hospital. The majority of age group in males SCD patients was 25-31 years which was 54.7% compared to 35.1% in females. Consanguinity rate was 3.8% in males and almost same (3.9%) in females. Regarding family history of SCD, Father positive /Mother negative (F+ M-) was found in 41.5% of males and 44.2% in females. For body mass index level of SCD patients, overweight percentage was high in SCD patients which was 73.6% in males and 63.6% in females.

Other results indicated that Hemoglobin types S, F and A levels have some small differences between SCD males and females without statistical significant results. Most common SCD cases were admitted to inpatient ward due to Vaso-occlusive crises which was 67.3% in males and 62.3% in females. Length of stay at

hospital for 2-4 days had higher in female 48.1% than male 45.3%, and for >4 days had higher in male 54.7% than female 51.9% without any statistical difference.

Table 1: Distribution SCA patients characteristics

Item	Categories	Number (130)	Percent (%)
Age	18-24	37	28.5%
	25-31	56	43.1%
	32-38	37	28.5%
Gender	Male	53	40.8%
	Female	77	59.2%
Consanguinity	Yes	125	96.2%
	No	5	3.8%
Family history of SCA	F- M+	31	23.8%
	F+ M-	56	43.1%
	F+ M+	43	33.1%
Other Chronic diseases	Yes	118	90.8%
	No	12	9.2%
BMI	<18.5	27	20.8%
	18.5-24.9	88	67.7%
	25-29.9	15	11.5%
HgF	<10	7	5.4%
	10-14.9	91	70%
	15+	32	24.6%
HgA	1-10	27	20.8%
	11-20	103	79.2%
Length of stay in the	2-4 days	61	46.9%
	>4 days	69	53.1%

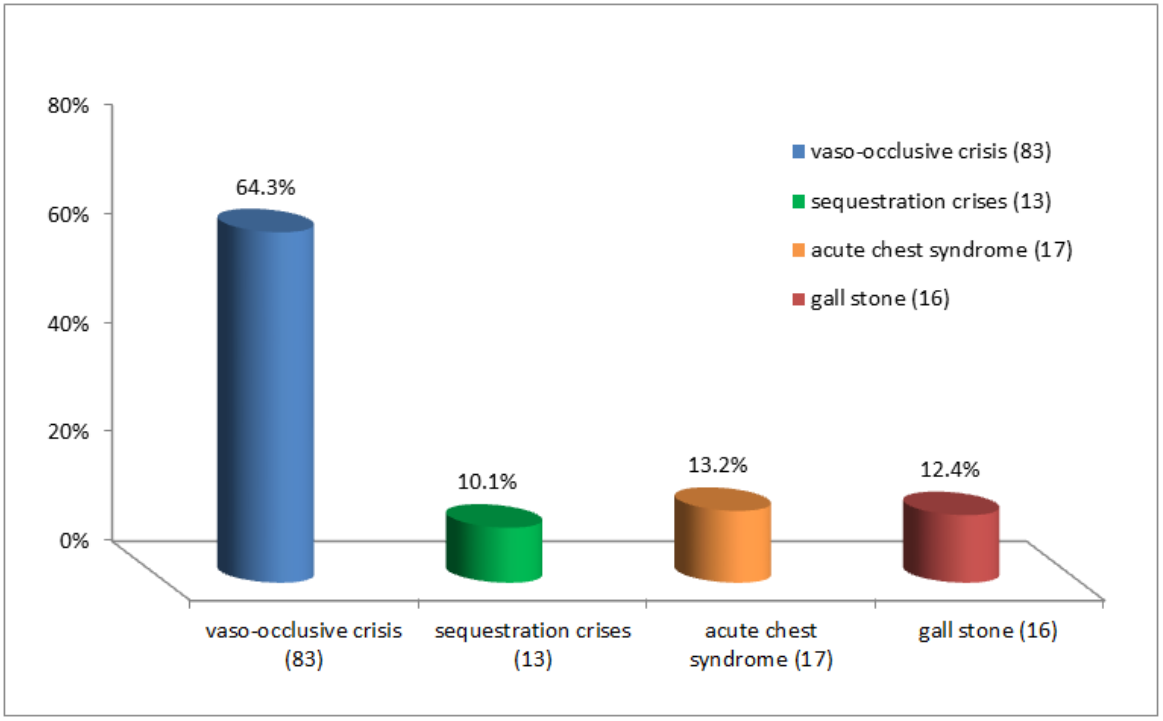
Table 2: Distribution of Hemoglobin level during admission, discharge and difference in the last visit (n=130)

Item	Mean	Median	SD
Hg level during admission (Missed=1)	7.4	7.1	1.3
Hg level during discharge	10.3	10.2	1.2
Hg (Difference) (Missed=1)	2.9	3	1.04
HgS	82	82	8.7
HgF	13.3	13.5	2.7
HgA	11.5	12	3.8

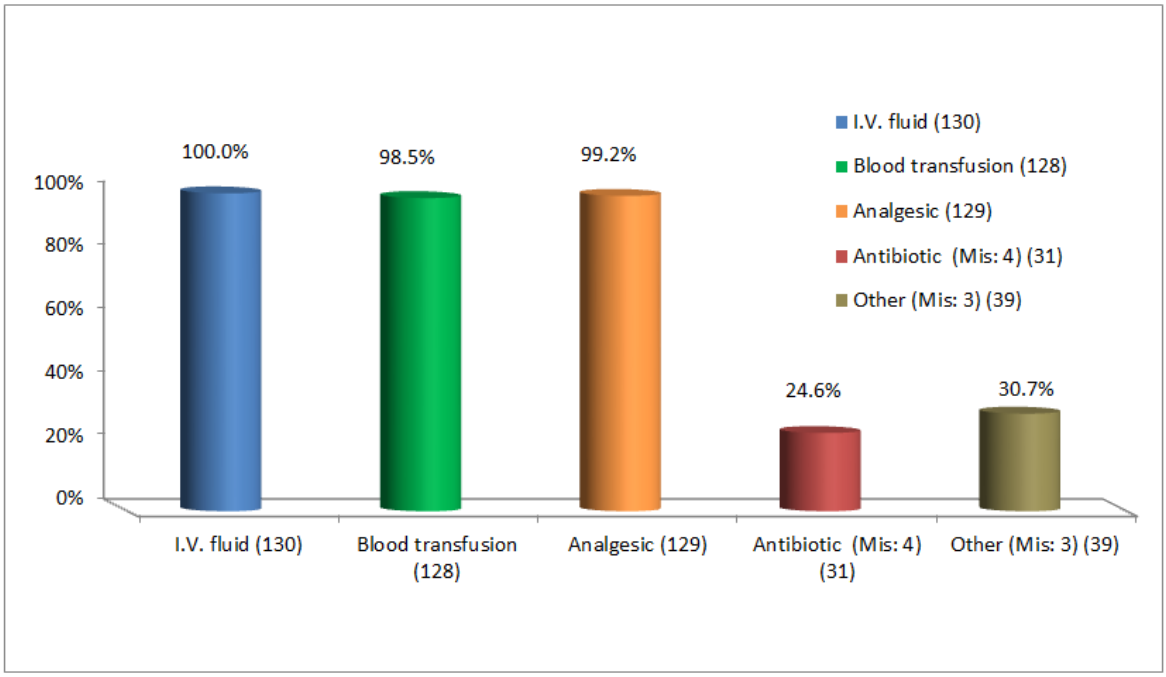
Table 3: Bi- variate analysis

Item	Categories	Male		Female		P value
		Number (53)	Percent (%)	Number (77)	Percent (%)	
Age	18-24	13	24.5%	24	31.2%	0.075
	25-31	29	54.7%	27	35.1%	
	32-38	11	20.8%	26	33.8%	
Consanguinity	No	2	3.8%	3	3.9%	1
	Yes	51	96.2%	74	96.1%	
Family history of SCA	F- M+	15	28.3%	16	20.8%	0.6
	F+ M-	22	41.5%	34	44.2%	
	F+ M+	16	30.2%	27	35.1%	
BMI	<18.5	9	17%	18	23.4%	0.5
	18.5-24.9	39	73.6%	49	63.6%	
	25-29.9	5	9.4%	10	13%	
HgS	60-80	24	45.3%	32	41.6%	0.7
	81-100	29	54.7%	45	58.4%	
HgF	<10	3	5.7%	4	5.2%	0.1
	10-14.9	32	60.4%	59	76.6%	
	15+	18	34%	14	18.2%	

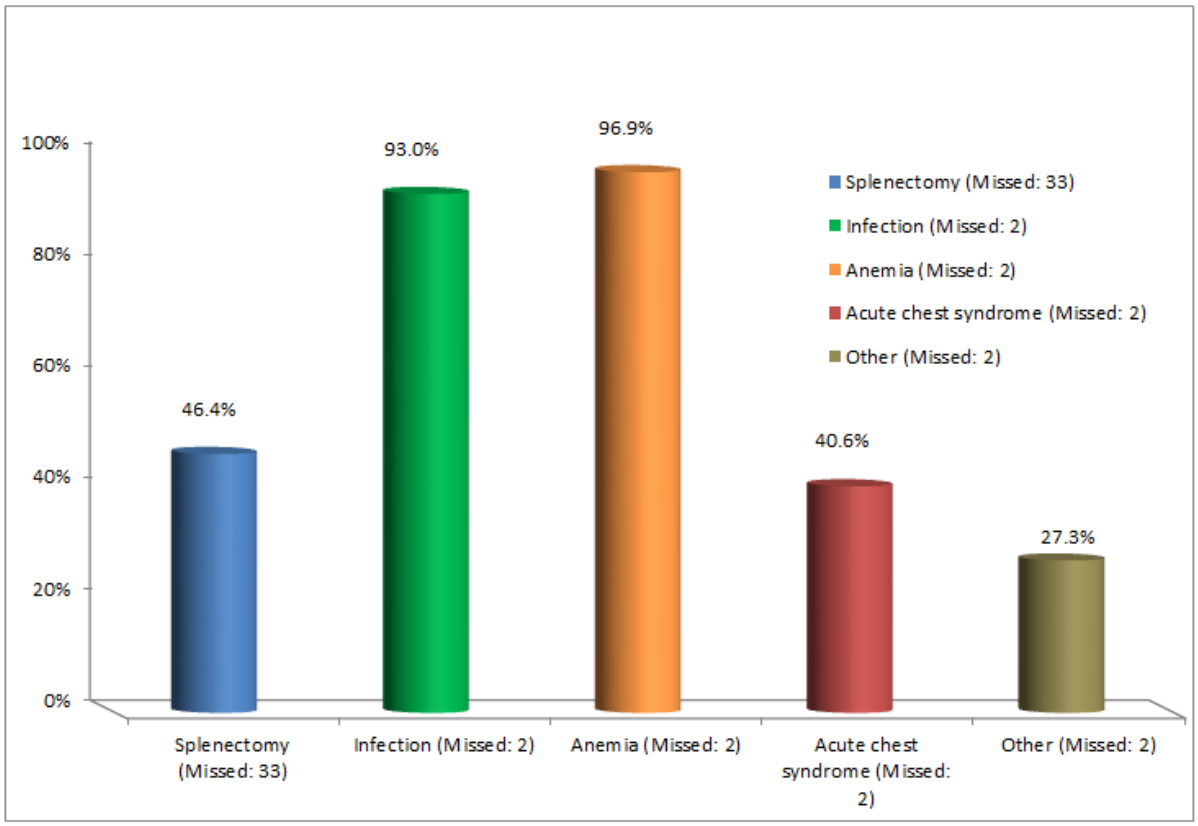
HgA	1-10	9	17%	18	23.4%	0.5
	11-20	44	83%	59	76.6%	
Diagnosis of last visit (Missed: 1)	vaso-occlusive	35	67.3%	48	62.3%	0.8
	sequestration	6	11.5%	7	9.1%	
	acute chest S.	6	11.5%	11	14.3%	
	gall stone	5	9.6%	11	14.3%	
Length of stay in the	2-4 days	24	45.3%	37	48.1%	0.9
	>4 days	29	54.7%	40	51.9%	



Graph 1: Diagnosis of SCD patients (n=129)



Graph 2: Mamagement of SCA patients.....



Graph 3: Complication of SCA patients (n=130)

DISCUSSION

Prevalence of SCD in Saudi Arabia was estimated in some previous studies [23, 24]. Of course it is one of the major health problems in Saudi Arabia, especially in Eastern region, where the consanguinity is common, and the gene frequency of this disease is quite prevalent. In our study consanguineous marriage seen in 96.2% of SCD patients and this high rate is linked to the social traditional habits in this area. Zaini R [23] and Al Otaibi M [24] estimated the consanguinity rate in Saudi Arabia which was more than 50% with the rate of marriage between first cousins ranging from 40% to 50% [23]. However, it was 57.7% in Al Otaibi study which was published recently in 2017 [24]. Saudi Arabia implemented a mandatory premarital screening for the common hematologic diseases in 2003. High risk couples who have a positive test for sickle cell disease or/ and Thalassemia can't receive the marriage certificate and will be referred to genetic counseling clinic. But, they have the decision to marry regardless of the results. However, after implementation of Premarital Screening Program, Jastaniah W (2011) found that about 90% of Saudis couples ignored the advice in counseling clinic about high risk of SCD after premarital screening and continue the process of marriage [9]. SCD patients have occupied many beds in Internal Medicine inpatient ward and utilized the medical resources in Saudi Arabia. In this study, length of stay for less than 4 days was more in Females (48.1%) than males (45.3%). On the other side, length of stay for more than 4 days was more in males (54.7%) than females (51.9%). Length of stay (for how many days??) in previous research is higher than the rate of 49% estimated by Danny A *et al.*, (2015) in Atlanta [25]. ((Not clear)) This study found that most hospitalized SCD patients in Eastern region has mild avascular necrosis of femoral head and splenic complications. It is attributed to high prevalence of Asian haplotype among SCD patients in this area. Also, we found that about 90.8% with history of other chronic diseases and Vaso-occlusive crises more in males (67.3%) than females (62.3%). Lionnet F *et al.*, in 2012 reported that the most common chronic complications were retinopathy and ear disease in 70% and 29% of SCD patients. Actually, complications reported in homozygous SS disease such as nephropathy, pulmonary hypertension, strokes and leg ulcers was less (13%, 4% and 1%, respectively). The difference between our study and Lionnet F may be due to differences of study place and population. For management of inpatient hospitalized SCD patients, most of them received blood transfusion and hemoglobin level was increasing. Management plan was consistent with the National Institute of Health guidelines for management of SCD (R). This study found that most SCD patients were within normal range of BMI, according to WHO classification. On the other side, Ballas S (2017) reported that the prevalence of obesity increased in patients with SCD especially in women.

Limitations of study:

1. Our study did not calculate the prevalence of inpatient hospitalized SCD exactly. Some SCD

cases came to the ER for receiving a strong analgesic drugs and discharge under their personal responsibility and against the medical advice. It was difficult for us to include these cases in our study.

2. Diagnosis date and medication used were not included in our study.
3. Death of SCD patient was not documented. SCD patients who have chronic diseases and severe complications, such as recurrent acute chest syndrome, renal failure or pulmonary hypertension are at higher risk of early death [22].
4. Completeness of data in SCD patients files. It was an old filing system and some files had unclear hand writing.

CONCLUSION

Our results lead us to conclude that SCD is considered as a load in the secondary health care services. Further educational and awareness programs can help increase compliance with results of counseling and further decrease the risk of SCD in Al-Ahsa.

RECOMMENDATION

Further studies are needed to establish sensitive interventions to manage SCD symptoms in KSA. Primary data collection method is recommended to avoid incompleteness of data. There is a need to initiate epidemiological studies to assess the prevalence rates of SCD in different regions in Saudi Arabia. Also, health education for couples about the possible complication and to give him chance to make decision when they are both carriers of the gene. Genetic counseling and screening of a carrier to prevent additional transmission of the disease are essential steps for controlling SCD. Carrier screening should be offered through prenatal and neonatal investigations for hemoglobin abnormalities. In addition, awareness and education about SCD among general public and the health care providers are essential approaches. These can be accomplished by making lectures in the school, workshops, symposium organization, and activating a special day for SCD.

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Appendix

Assessment of inpatient hospitalized Sickle cell cases during 2013 to 2015, Al Ahsa / Chart review

1- General information
◆File no. : _____kljknl___o
◆Code no.: hb_____bjh,j
◆Gender: ☐Male ☐Female
◆Date of birth: / /
◆Consanguinity: ☐Yes ☐No ☐Not reported
◆Date of diagnosis with SCD: / /
◆Hg S:_____% ◆ Hg F:_____% ◆Hg A:_____%
◆No. of admission with SCD:_____ times
◆Family history of SCD: ☐**F-M-** ☐**F**-m+ ☐f+**M-** ☐f+m+
◆Chronic diseases of patient : _____kljknl___o_____kljknl___o_____k kljknl___o
2- History of last admission with SCD
◆Date of last admission: / /
◆ Weight:_____KG ◆height: _____Cm
◆Symptoms during last admission:__ one one one one book
◆Diagnosis (crisis):_____1 1
◆Hg level during admission:_____g/dl
◆Hg level during discharge:_____g/dl
◆Management plan: ☐IV fluid ☐Blood transfusion ☐Analgesic ☐Antibiotic Other: kljknl o one o kljknl
◆Length of stay:_____Days
◆Complication: ☐Splenectomy ☐Infection ☐Anemia ☐Acute chest syndrome
◆Other: _____1

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