Measuring the Percentage of Consanguinity in Sickle Cell Patients and Its Effect on the Prognosis of the Disease

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ABSTRACT

SCD is one of the major health problems in Saudi Arabia, specially in Southern, Western and Eastern areas where the gene frequency of this disease is quite prevalent. Many studies were carried out in these areas. There is a lack of studies of the effect of consanguinity on disease outcome and prognosis. we did this study in western area in Almadinah Almunawarah. We determined the effect of consanguinity on the disease by three factors. These factors are (Blood Transfusion, First complain, and complications). In this study, we carried out a retrograde analysis of patients' files, and found that 44% of the patients were products of consanguineous marriages. But the research concluded that there was no clear increase in complications caused by the state of consanguinity of the patient's parents, although patients on consanguineous parents have had slightly more incidences of vaso-oclusive crisis.

1.INTRODUCTION

Sickle cell disease (SCD) and its variants are genetic disorders resulting from the presence of a mutated form of hemoglobin, hemoglobin S (HbS). The most common form of SCD found in North America is homozygous HbS disease (HbSS), an autosomal recessive disorder first described by Herrick in 1910. SCD causes significant morbidity and mortality, particularly in people of African and Mediterranean ancestry.

Sickle cell disease (SCD) usually manifests early in childhood. Complaints may include, Acute and chronic pain in any body part: The most common clinical manifestation of SCD is vaso-occlusive crisis. Anemia: Universally present, chronic, and hemolytic in nature Aplastic crisis:

Serious complication due to infection with B19V. Splenic sequestration: Characterized by the onset of life-threatening anemia with rapid enlargement of the spleen and high reticulocyte count. Infection: Organisms that pose the greatest danger include encapsulated respiratory bacteria, particularly Streptococcus pneumonia; adult infections are predominately with gram-negative organisms, especially Salmonella. Growth retardation, delayed sexual maturation, being underweight. Hand-foot syndrome: This is a dactylitis presenting as bilateral painful and swollen hands and/or feet in children. Acute chest syndrome: Young children present with chest pain, fever, cough, tachypnea, leukocytosis, and pulmonary infiltrates in the upper lobes; adults are usually afebrile, dyspneic with severe chest pain, with multilobar/lower lobe disease.

Pulmonary hypertension: Increasingly recognized as a serious complication of SCD. Avascular necrosis of the femoral or humeral head: This is due to vascular occlusion. CNS involvement: Most severe manifestation is stroke Ophthalmologic involvement: Ptosis, retinal vascular changes, proliferative retinitis. Cardiac involvement: Dilation of both ventricles and the left atrium. GI involvement: Cholelithiasis is common in children; liver may become involved. GU involvement: Kidneys lose concentrating capacity; priapism is a well-recognized complication of SCD. Dermatologic involvement: Leg ulcers are a chronic painful problem. [1]

1.1 Litreature Review

Sickle cell disease (SCD) is one of the most important single gene disorders of human beings. In the United States, SCD affects about 72 000 people and 2 million are carriers.[2]

In Africa, more than 200 000 infants are born yearly with SCD. [3] In the United States, mortality has decreased dramatically with newborn screening and better comprehensive care. The median age of death in patients with SCD in the United States is now 53 years for men and 58 years for women. However, SCD patients are still hospitalized frequently and by the fifth decade of life, 48% of surviving patients have documented irreversible organ damage.

SCD in Saudi Arabia was first reported in the Eastern province in the 1960s.[4] This led to the initiation of multiple regional and national screening studies to determine the clinical characteristics and frequency of SCD genes in different regions of Saudi Arabia. Sickle cell disease was detected in 108 of 45,682 children and adolescents with a prevalence of 24 per 10,000. The regional distribution of sickle cell disease showed eastern region dominance with a prevalence of 145 per 10,000, followed by the southern region with a prevalence of 24 per 10,000, western region 12 per 10,000, and central region with 6 per 10,000. No cases were found in the northern regions. The male to female ratio was approximately 1:1.[5] Of a total of 488,315 individuals screened, 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. Among the 207,333 couples who were issued certificates for matching, 2.14% were declared high risk. Among the 2,375 high-risk couples contacted by telephone, 89.6% married each other, despite the known high-risk status.[6]

Comprehensive national survey of the distribution of the sickle-cell (Hb S) gene and thalassemia genes was initiated in 1982, with more than 30,055 blood samples collected. The Hb S, alpha- and beta-thalassemia gene frequency range was 0.005-0.145, 0.01-0.40 and 0.01-0.15 respectively in various areas of Saudi Arabia. We present here an appraisal of sickle-cell and thalassemia gene occurrence in the Saudi population, based on our studies conducted over 10 years in different regions of Saudi Arabia.[7] During the two-year study period (2004-2005), 11 554 of 11 874 (97%) mothers answered the question on consanguinity, and 6470 of 11 554 (56%) were consanguineous. there was no significant association with either sickle cell disease (P=.97) or glucose-6-phosphate dehydrogenase deficiency (P=.67) for first-cousin consanguinity.[8]

2. Methodology

The study was conducted in Maternity and Children Hospital, Madinah, Saudi Arabia. Data was obtained from the medical records by data collection sheets. The data collection sheet was built partially on previous studies on clinical presentations of sickle cell disease. The data collection sheet included the following variables: socio-demographic variables (Age, sex, residency, nationality,...), first clinical presentation of the disease (Main complain , clinical sign and investigations), , age at diagnosis, duration of illness , type of Sickle Cell anemia, electrophoresis,

number and causes of following admissions(acute infections, fever, Splenic Sequestration, painful crisis, stroke, priapism…), blood transfusions, surgical procedures, use of hydroxyurea medication, presence of Dactylitis, vaccination, family pedigree, age and cause of death (if deceased) and other complications that are attributed to the disease. Coding of the data was be carried out by the investigators. A total of 120 samples were collected, varying in age from 6 months to 18 years. There was no documentation of mortality due to the lack of a system that shares medical records across all hospitals.

2.1 Data Management and Analysis

Data was analyzed through the Statistical Package for the Social Sciences (SPSS). Descriptive analysis have been used for categorical variables and chi-square test were applied to identify the main factors under study by using the statistical significance. Backward logistic regression was also used to find the association between related factors.

3. RESULTS

During the period of this study, Which was conducted on a sample size of 120 patients, we have found out that The incidence of sickle cell disease in children of Almadinah Almunawarah city is 1.2:100000. The prevalence of sickle cell disease in children of Almadinah Almunawarah city is 38:100000. We also found out that 44% of the patients were products of consanguineous relationships. Although both consanguineous & non- consanguineous groups suffered from complications, however, consanguineous group were more likely to suffer from more serious complications like vaso-occlusive crisis, and they were more likely to undergo splenectomy because of complications from SCD.

3.1 The study participant's Demographic analysis

Table 1. Shows Age Group Distribution

Variable		Frequency	Percent
Age	Younger than 5	29	24.2
	Older than 5 and younger than 10	52	43.3
	Older than 10	39	32.5
	Total	120	100.0

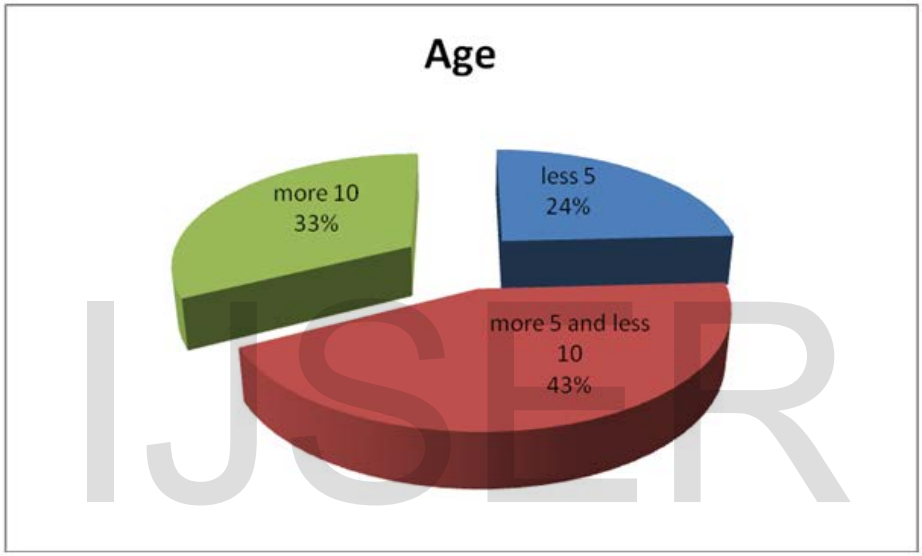

Figure 1. showing age distribution

Table 2. Shows Gender Distribution

Variable		Frequency	Percent
Gender	Male	69	57.5
	Female	51	42.5
	Total	120	100.0

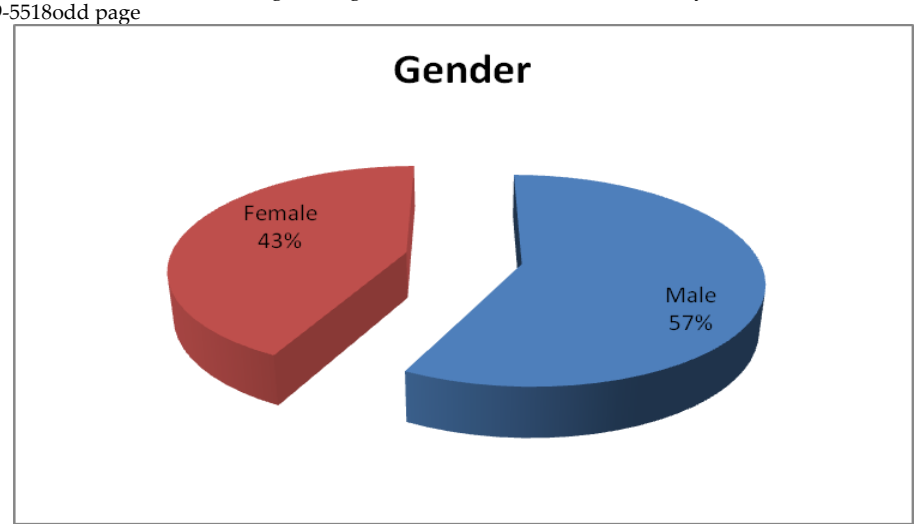

Figure 2. showing gender distribution

Table 3. shows Nationalities

Variable		Frequency	Percent
Nationality	Saudi	88	73.3
	Non-Saudi	32	26.7
	Total	120	100.0

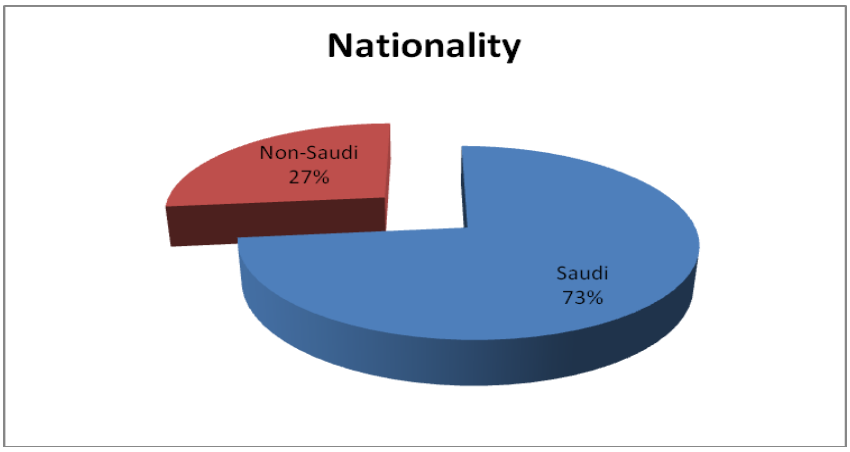

Figure 3. showing nationality distribution

Table 4. shows Consanguinity

Variable		Frequency	Percent
Consanguinity	Yes	53	44

	No	67	56
	Total	120	100.0

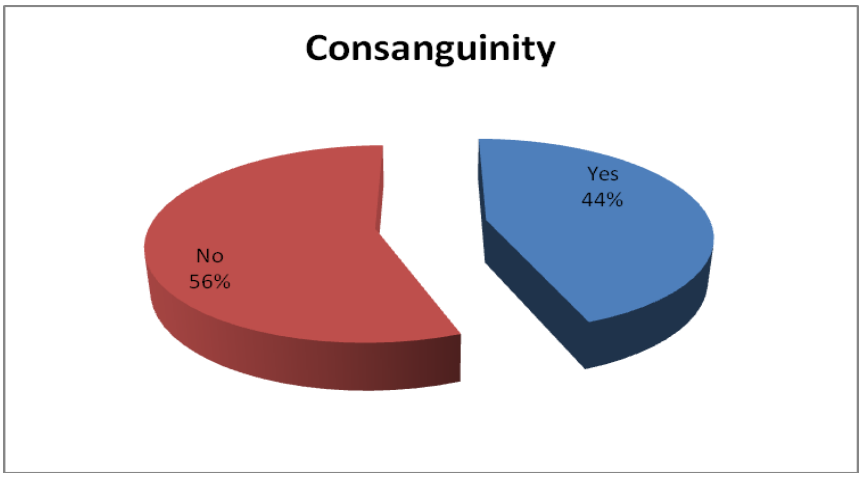

Figure 4. showing rate of consanguinity

Table 5. shows the Time of Diagnosis

	Variable	Frequency	Percent
Date of Diagnosis	2001-2010	25	21
	2011-2012	52	43
	2013-2016	43	36
	Total	120	100.0

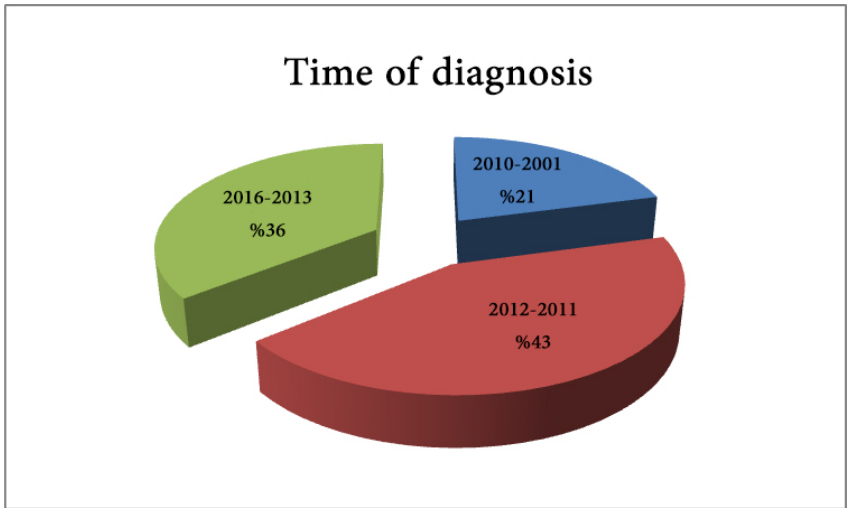

Figure 5. show Distribution of the participants by date of diagnosis.

3.2 Significance of the relation between the incidence of SCD and Consanguinity

Table (6)

	Correlation	Chi test	df	Sig
Pearson Chi-Square	.043	12.136	5	.033
N of Valid Cases	120			

From Table (6) we can say that there is no Sig of consanguinity in sickle cell anemia incidence.

3.3 The effect of consanguinity on disease outcome and prognosis by (Blood Transfusion, First complain, and complications)

Table 7. Distribution and Rate of Complications

Complications	Consanguinity		Total
	Yes	No	
Vaso-oclussive crisis	6	3	9
Infection	3	5	8
Stroke	2	3	5
Anemia	1	0	1
Hand foot syndrome	0	2	2
Hepatitis	6	1	7
Acute chest syndrome	15	24	39
Splenomegaly	10	14	24
Pain crisis	10	15	25

First Complain (8) Table

First Complain	Consanguinity	Total

	yes	No	yes
Pain crisis	12	19	31
anemia	7	11	18
infection	2	5	7
others	32	32	64
Total	53	67	120

Table (9) Surgical Procedures

Surgical procedure	Consanguinity		Total
	yes	No	yes
splenctomy	15	4	19
cholecystectomy	4	4	8
others	1	5	6
No	33	54	87
Total	53	67	120

Table 10. Significance of Data

		Correlation	Chi test	df	Sig
Blood transfusion	Pearson Chi-Square	.085	.862	1	.353
	N of Valid Cases	120			
First complain	Pearson Chi-Square	-.104	2.15	3	.542
	N of Valid Cases	120			
complications	Pearson Chi-Square	.158	17.333	9	.044

	N of Valid Cases	120			

Table (10) shows that all chi tests are not significant and that there is no correlation of the mentioned variables to consanguinity.

4. DISCUSSION

SCD is one of the major health problems in Saudi Arabia, specially in Southern, Western and Eastern areas where the gene frequency of this disease is quite prevalent. Many studies were carried out in these areas. There is lack of study in effect of consanguinity on disease outcome and prognosis. We inducted this study in western area in Almadinah Almunawarah. We determined the effect of consanguinity on disease by three factors according to pediatric hematological physician. These factor are (Blood Transfusion, First complain, and complications). There was lack of mortality data ,due to this we didn't put in in the study.

We also determine the percent of consanguinity in compared to non- consanguinity. Consanguinity was 44% and non-consanguinity 56%. This high percent of consanguinity is due to our tribal culture and lack of community education about this disease. We will educate our community by publishing our study in form of posters. In consanguinity group the percent of blood transfusion was 68%. In non-consanguinity group the percent of blood transfusion was 59%. The first presenting complaint presented in this table.

5. CONCLUSION

We have found in our study that the non-consanguineous patients suffer from more complications (this may due to decreased awareness in less educated families and noncompliance to medication). However, the consanguineous group are more likely to develop more serious complication (vaso-oculusive criss), and they are more likely to undergo surgical procedures

(splenectomy and cholecystectomy). We would like to conduct further research in the future with a larger sample size to improve the significance and have a clearer results and correlations.

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