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Prevalence Of Sickle Cell Disease And Sickle Cell Trait In Al-Madinah Region Of Kingdom Of Saudi Arabia: A Descriptive Retrospective Study

Khalid D Aljohani[1], Mohammad Ishag[2], Sultan Fareed[3], Abdulmajed Alrasheidi[4], Dolyem Alrasheidi[4], Mohammad Alobaidi[4], Rakan Alenzi[4], Dawod Almoairfi[4], Abdulaziz Alhafdhi[4], Abdullah Abass[4]
[1]MSc, Medical Laboratory Science Department, Prince Sultan Armed Forces Hospital, Madinah.
[2]MSc, Medical Laboratory Science Department, Prince Sultan Armed Forces Hospital, Madinah.
[3]BSc, Medical Laboratory Science Department, Prince Sultan Armed Forces Hospital, Madinah.
[4]MLT, Medical Laboratory Science Department, Prince Sultan Armed Forces Hospital, Madinah.
Corresponding Author E-mail: kjohani1711@gmail.com.

Abstract

Introduction: *The high prevalence rate of Sickle Cell Disease can cause health and social problems among populations. The knowledge on the prevalence of SCD and SCT is a pre-requisite for reducing the affected individuals in different regions of the city. Therefore, in this study, the aim was to determine the prevalence of SCD & SCT in Al-Madinah City in KSA between 2015 and 2020 and compare hematological parameters between healthy subjects and SCD.*

Method: *A retrospective study was employed using a hospital-based population screening of 3211 patients for of SCD and SCT in King Fahd Hospital at Al Madinah between 2015 and 2020. Statistical analysis of the data was performed by SPSS.*

Results: *The findings indicated that the prevalence rates of SCT and SCD in Al Madinah City between 2015 and 2020 was 6.23% and 7.44% respectively. Also, females had a greater prevalence of SCT, and males showed a greater prevalence of SCD. The findings indicated a strong prevalence of SCT and SCD in the age group of 10 to 19 years. Moreover, the study found variations in hematological parameters between healthy and SCT and SCD subjects.*

Conclusion: *There was a high prevalence of SCD compared to SCT in Al-Madinah City with age groups 10-19 years being affected more. The findings yield important aspects in SCD for decision makers in enabling prioritization of new programs and implementation of policy changes.*

INTRODUCTION

Sickle Cell Disease (SCD) is a condition related to abnormal hemoglobin contributing to the imbalance of health systems and the Kingdom of Saudi Arabia (KSA) in particular.

SCD affects the RBCs' structure in which genetic mutation results in substitution of glutamic acid by valine at position 6 of the globin chain resulting in abnormal sickle hemoglobin (HbS) [1,2]. In deoxygenated or dehydrated states, HbS causes RBC polymerization, causing intracellular tactoids that cause RBC deformation into sickle cell shape associated with microvascular obstruction, hypercoagulation, and abnormal adhesion of white blood cells and platelets. These pathogenetic mechanisms are linked to the complications that sickle cell disease patients experience including vaso-occlusive crises, enhanced susceptibility to infections, and chronic organ damage [3,4].

Saudi Arabia has been studied and a high prevalence of inherited hematological conditions been noted. A study by Alhamdan et al. (2007) indicated that 4.2 percent of participants had SCT, and 0.26% percent had SCD [5]. There are several cultural reasons contributing to the high prevalence of SCD in KSA including the great numbers of consanguineous marriages, increasing maternal & paternal ages, and large family sizes [6,7]. Because of the healthcare burden and effect on the quality of life in these patients, Saudi Ministry of Health mandated for premarital genetic screening in 2004 [8]. Moreover, fewer studies on the attitudes, knowledge, and practices linked to SCD are scarce in different regions in KSA, necessitating for the need for subsequent research on the prevalence of SCD in different parts of KSA and the nation as a whole [9].

The detection of SCD depends on the diagnosis of Hemoglobin S with regards to Hemoglobin A and Hemoglobin F. The available methods for the diagnosis and screening of SCD include gel & capillary-based electrophoresis, isoelectric focusing, and molecular approaches such as high-pressure liquid chromatography, and PCR [10]. However, successful

diagnosis by these techniques requires reasonable laboratory facilities, well-trained staff, special equipment, and systems for storage of the reagents. Houwing et al. (2019) reported that more than eight percent of the population susceptible to SCD reside in nations with middle and low income because of diagnostic facilities for SCD being in poor conditions in these countries [11]. Although, recently, promising new methods have been developed for
rapid and reliable point of care for diagnosis of hemoglobin fractions in low resource settings such as Sickle SCAN™ and HemoTypeSC™ [12,13].
Treatment of SCD involves a combination of essential preclinical (prevention) and clinical interventions aimed in reducing morbidity and mortality of the disease and improve quality of life of these patients. Preclinical interventions include education, prophylactic
antibiotics, and immunization [14, 15, 16]. Clinical interventions comprise of blood
transfusions, hydroxyurea therapy, bone marrow transplantation, gene therapy, analgesics, and folic acid supplementation [17, 18, 19, 20]. Royal Highness Crown Prince Mohammed bin Salman bin Abdulaziz initiated the Saudi Genome Program (SGP) as part of the Vision 2030 aimed at the reduction of the incidence of genetic conditions utilizing advanced
genomic technologies via the creation of a database to document the first genetic map of the Saudi society, create an individualized medicine practice, decrease cost of healthcare, and improve life quality [21]. The aim of this study was to showcase the prevalence of SCD and SCT at Al-Madinah-Monawarah City in KSA, evaluating the recent time trends of SCD and SCT prevalence and its distribution by demographic characteristics in the city between 2015 and 2020.

METHODOLOGY

Study Design

The retrospective descriptive study was conducted to determine the frequency of SCD and SCT among patients of AL Madinah in KSA. The study was conducted in the Clinical
Laboratory Department in collaboration with the King Fahd Hospital Hematology Department, a key hospital in Madinah region.

Study Population and Sample

The population of the study was the people of Al Madinah Al Munawwarah which is the second Islamic City and Capital of Medina Province in the western region of KSA. The
population of Medina is 1,488,782, with the city regarded as the fourth-most populated city in KSA. A sample of 3211 patients who were referred to King Fahd Hospital at Al Madinah in KSA were included in the study.

Data Collection

Data was collected from the Clinical Laboratory department in collaboration with the Hematology Department of King Fahd Hospital. The 3211 sample patients were subjected to various tests to identify any existing haemoglobinopathies. The outcomes measurements of SCD included complete blood cell count, sickling test, and high-performance liquid
chromatography [14,15, 16].

Statistical Analysis

The collected data was analyzed using the SPSS version 21. Descriptive statistics including
percentages and frequencies, were utilized to examine the distribution of categorical variables and offer an overview of the participants' responses. Furthermore, standard deviations and means were calculated for continuous variables, enabling the examination of central
tendencies and variations in the data. Via the examination of the means, insights were gained into the average level of the hematological parameters and on the other hand, standard
deviations offered information on the dispersion or spread of data.

RESULTS

Demographic Analysis

The data of 3211 patients was analyzed according to the gender, age, and year.

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Table 1.1: Sample Characteristics according to Demographic Variables

Variables		Frequency	Percentage
Gender	Female	1722	53.6%
	Male	1489	46.4%
	Total	**3211**	**100.0%**
Age Group	Less than 10 years	294	9.2%
	From 10 to 19 years	65	2.0%
	From 20 to 29 years	882	27.5%
	From 30 to 39 years	1025	31.9%
	From 40 to 49 years	576	17.9%
	From 50 to 59 years	359	11.2%
	60 years and more	10	0.3%
	Total	**3211**	**100.0%**
Year	2015	383	11.9%
	2016	428	13.3%
	2017	467	14.5%
	2018	518	16.1%
	2019	723	22.5%
	2020	692	21.6%
	Total	**3211**	**100.0%**

As shown in table 1.1 there were more females than males in the total sample population (53.6% vs 46.4%).

The distribution of sample according to the age classified into seven groups. Figure 1.1 shows the majority of the sample subjects fall within the age group of 30 -39 years accounting for 31.9%, followed by age group 20-29 years accounting for 27.5%. Smaller proportions of patients were found in the age groups of less than 10 years (9.2%), 10-19 years (2.0%), and 60 years and above (0.3%). The figure below shows the distribution of the sample according to the age group variable.

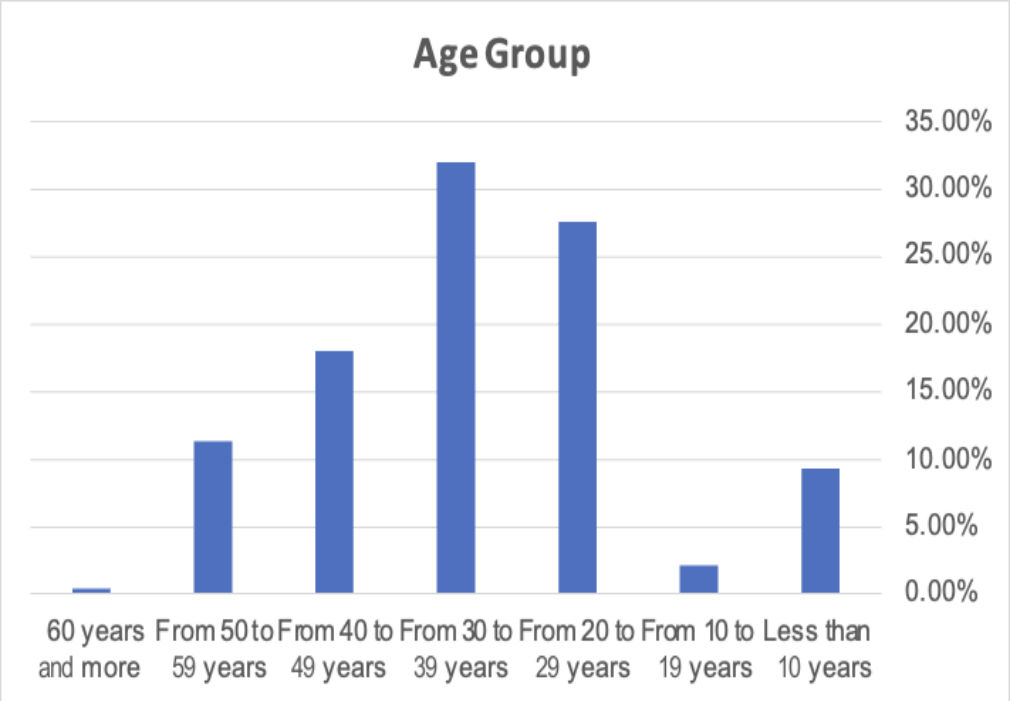

Figure 1.1: Distribution of sample according to the age group variable

For the distribution of the sample according to the year, the data was gathered over six years between 2015 and 2020. Figure 1.2 demonstrates that majority of the sample subjects was in the year 2019 (22.5%), followed by year 2020 (21.6%). Years 2018, 2017, 2016, and 2015 accounted for 16.1%, 14.5%, 13.3%, and 11.9% respectively.

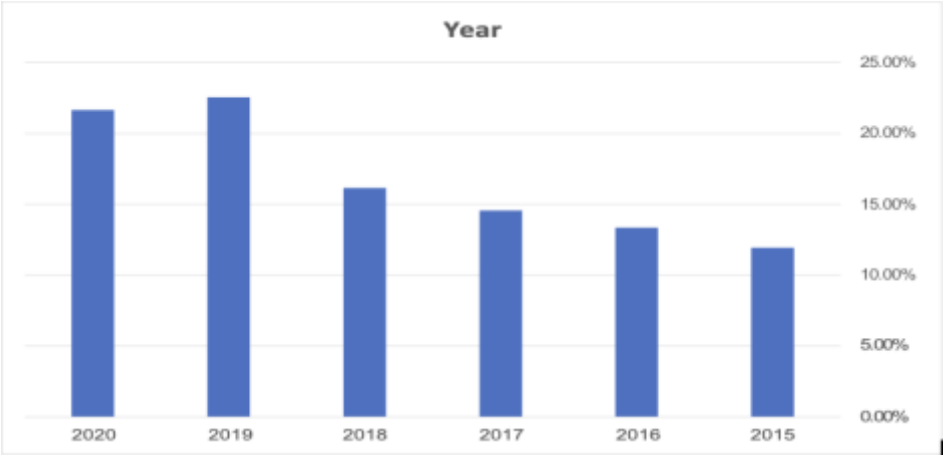

Figure 1.2: Distribution of Sample according to year Variable

Descriptive Analysis

Differences of SCT & SCD Prevalence Between 2015 and 2020

Table 1.2 shows the overall rate of SCT prevalence in Al-Madinal City, KSA between 2015 and 2020 which was 6.23%. Prevalence of SCT fluctuated over the years but overall remained relatively stable. The highest prevalence was observed in 2016 (9.1%) and the lowest in 2019 (5.3%).

Table 1.2: Prevalence of SCT between 2015 and 2020 in Al-Madinah City in KSA

		SCT				
		Negative		Positive		Total
		N	%	N	%	N
Year	2015	361	94.3%	22	5.7%	383
	2016	389	90.9%	39	9.1%	428
	2017	441	94.4%	26	5.6%	467
	2018	482	93.1%	36	6.9%	518
	2019	685	94.7%	38	5.3%	723
	2020	653	94.4%	39	5.6%	692
Total		**3011**	**93.77%**	**200**	**6.23%**	**3211**

Table 1.3 shows that the prevalence of SCD varied over the years between 2015 and 2002, with the highest levels of prevalence being in 2015, 2019, and 2016 (9.7%, 9.3%, and 9.1%) respectively. The lowest level of prevalence was observed in 2017 and 2020 (4.7% and 5.2%) respectively.

Table 1.3: Prevalence of SCD between 2015 and 2020 in Al-Madinah City in KSA

		SCD				
		Negative		Positive		Total
		N	%`	N	%	N
Year	2015	346	90.3%	37	9.7%	383
	2016	389	90.9%	39	9.1%	428
	2017	445	95.3%	22	4.7%	467
	2018	480	92.7%	38	7.3%	518
	2019	656	90.7%	67	9.3%	723
	2020	656	94.8%	36	5.2%	692
Total		**2972**	**92.56%**	**239**	**7.44%**	**3211**

Differences of SCD & SCT Prevalence According to Gender

Table 1.4 indicates that the positive cases of both SCT and SCD had slight differences in SCT and SCD between male and female subjects, in which females had a higher percentage. For the prevalence of SCT, a higher prevalence was observed in females (6.6%), than males
(5.8%). For SCD, the prevalence was lower for females (7.3%) compared to 7.6% for male patients.

Table 1.4: Differences in the Prevalence of SCD & SCD According to Gender

		SCT				SCD			
		Neg tive		Positive		Negative		Positive	
		N	%	N	%	N	%	N	%
Gender	Female	1609	93.4%	113	6.6%	1596	92.7%	126	7.3%
	Male	1402	94.2%	87	5.8%	1376	92.4%	113	7.6%
Total		**3011**	**93.77%**	**200**	**6.23%**	**2972**	**92.56%**	**239**	**7.44%**

Differences of SCD & SCT Prevalence According to Age Group

Table 1.5 shows the difference in SCD & SCT prevalence according to age group with varied patterns. For SCT, higher percentage of positive cases was seen in age groups of 10 to 19
years (10.8%) and age group of less than 10 years had the lowest prevalence at 2.4%. On the other hand, SCD had slightly different results with age group 10 to 19 years with the highest percentage of positive cases (33.8%), and zero SCD positive cases in age group of 60 years and more (0.0%).

Table 1.5: Differences in the Prevalence of SCT & SCT According to Age Group

		SCT				SCD			
		Negative		Positive		Negative		Positive	
		N	%	N	%	N	%	N	%
Age Group	Less than 10 years	287	97.6%	7	2.4%	291	99.0%	3	1.0%
	From 10 to 19 years	58	89.2%	7	10.8%	43	66.2%	22	33.8%
	From 20 to 29 years	828	93.9%	54	6.1%	777	88.1%	105	11.9%
	From 30 to 39 years	952	92.9%	73	7.1%	955	93.2%	70	6.8%
	From 40 to 49 years	541	93.9%	35	6.1%	554	96.2%	22	3.8%
	From 50 to 59 years	336	93.6%	23	6.4%	342	95.3%	17	4.7%
	60 years and more	9	90.0%	1	10.0%	10	100.0%	0	0.0%
Total		**3011**	**93.77%**	**200**	**6.23%**	**2972**	**92.56%**	**239**	**7.44%**

3.3. Comparison of Hematological Parameters Between Healthy and SCD & SCT Subjects

Table 1.6 shows comparison of the hematological parameters by mean and standard deviation (SD) for SCD &SCT positive and negative cases. For SCT, individuals with a positive result showed lower mean values compared to those with a negative result in terms of Hb (10.889 verses 11.807), RBC (10^12/L) (4.119 vs. 4.558), MCV (fL) (80.98 vs. 82.20), Hb F (%) (2.65 vs. 4.76), and HbA (%) (60.70 vs. 91.78). However, the positive group of SCT had a higher mean value for MCH (pg) (26.87 vs. 26.77), MCHC (g/dL) (33.01 vs. 32.40), Hb A2 (%) (2.96 vs. 2.58), and Hb S (%) (34.97 vs. 0.00). Moreover, the mean result of Sickling test for SCT positive cases was (positive) and it was (negative) for SCT negative cases.

In the case of Sickle Cell Disease (SCD), individuals with a positive result showed lower mean values compared to those with a negative result in terms of Hb (g/dL) (9.302 vs. 12.089), RBC (10^12/L) (3.130 vs. 4.726), Hb F (%) (10.45 vs. 4.76), and Hb A (%) (13.23 vs. 94.44). However, the positive group of SCD had a higher mean value for MCV (fL) (89.68 vs. 80.99), MCH (pg) (30.97 vs. 26.16), MCHC (g/dL) (34.44 vs. 32.16), Hb A2 (%) (3.21 vs. 2.55), and Hb S (%) (78.59 vs. 0.00). Moreover, the mean result of Sickling test for SCD positive cases was (positive) and it was (negative) for SCD negative cases.

Table 1.6: Comparison of Hematological Parameters between SCT & SCD Positive and Negative Cases

Parameters	SCT				SCD			
	Negative		Positive		Negative		Positive	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Hb (g/dL)	11.807	2.840	10.889	3.135	12.089	2.832	9.302	1.792
RBC (10^12/L)	4.558	3.025	4.119	1.257	4.726	3.058	3.130	.936
MCV (fL)	82.20	11.22	80.98	11.63	80.99	10.08	89.68	15.24
MCH (pg)	26.77	4.88	26.87	4.77	26.16	4.35	30.97	6.04
MCHC (g/dL)	32.40	2.32	33.01	2.03	32.16	2.20	34.44	1.95
Sickling Test	Negative		Positive		Negative		Positive	
Hb A (%)	91.78	21.04	60.70	8.91	94.44	10.72	13.23	15.14
Hb A_2 (%)	2.58	.66	2.96	.60	2.55	.59	3.21	1.10
Hb F (%)	4.76	7.99	2.65	3.95	1.65	4.63	10.45	8.96
Hb S (%)	0.00	0.00	34.97	7.35	0.00	0.00	78.59	11.95

DISCUSSION

The study aimed to determine the prevalence of SCD and SCT in Al-Madinah City, KSA based on retrospective clinical data gathered from population screening of 3211 patients including 1489 (46.4%) males and 1722 (53.6%) females who attended screening at King Fahd Hospital at Al Madinah in KSA between 1st January 2015 to 30th December 2020. The findings from the current study indicated that the prevalence rate of SCT and SCD in Al- Madinah City, KSA between 2015 and 2020 was 6.23% and 7.44% respectively. The findings are higher in prevalence rate of SCT and SCD compared to findings by Alhamdan et al. (2007), Memish et al. (2011), and Alsaeed et al. (2018) who reported lower prevalence rate [5,22,23]. The inconsistency in findings is likely because of the different methods used in detection of SCT and SCD as previous studies reported lower rates based on hospital-based screening. The current study reported higher prevalence rates if SCT and SCD because of the population and hospital-based screenings.

On gender differences, the current study indicated that the prevalence of SCT was higher in females (6.6%) compared to males (5.8%). For SCD, prevalence was lower in

females (7.3%) in comparison to males (7.6%). The findings point out that females tend to be carries of SCD while clinical manifestations of SCD are more in males. The findings were similar to those by Qureshi et al. (2015) who found out that SCD is relatively frequent among males (56.4%) than females in patients with sickle cell hemoglobinopathies [24].

Findings of SCD & SCT prevalence according to age group revealed that the highest percentage of SCT positive cases was in 10 to 19 years' age group (10.8%), followed by cases from age group of 60 years and above (10.0%) and age group less than 10 years had the lowest prevalence at 2.4%. The findings on prevalence of SCD showed slightly different

findings with age group 10 to 19 years having the highest prevalence of positive cases for SCD (33.8%), followed by age group 20 to 29 years (11.9%), while the rest age groups

ranged between 6.8% and 1.0%. Interestingly, the current study findings showed the absence of SCD positive cases among age group 60 years and above (0.0%) that might be explained by the small sample size of 10 subjects only. The distribution of SCT and SCD positive cases across age groups did not follow a clear pattern in general. These findings indicate that the

prevalence of SCT and SCD may not strongly be associated with specific age groups but

rather influenced by other factors. However, findings strongly pointed the prevalence of SCT and SCD appeared more in the 10 to 19 years' age group that can be associated to the

effectiveness of the premarital program in detection of SCD in this age group as it is an age of early marriage in KSA.

To understand trends in prevalence of SCT and SCD between 2015 and 2020, the

findings from the current study revealed that positive SCT percentage ranged between 11.0% and 19.5% over the period. In 2016 and 2020, the positive percentage was highest at 19.5% and lowest in 2015 at 11.0%. Lower findings were reported by Alsaeed et al. (2018) in

Madinah between 2011 and 2015 at 1.37% and by Mir et al. (2020) whose prevalence rate in adult population of Al Majma'ah Saudi Arabia was 0.32% between 2016 and 2018 [23,25].

The difference in the findings can be justified by the different screening methods in the

detection of SCT. For SCD, the positive percentage varied between 9.2% in 2017 and 28.0% in 2019. Lower findings were reported by Alseed et al. (2018) in Madinah in KSA between 2011 and 2015 with a percentage of 0.08%, with the same explanation for the differences in the studies being similar to those in SCT screening [23].

Regarding the comparison of hematological parameters between healthy and SCT Subjects, the findings of the current study revealed that individuals with a positive result showed lower mean values compared to those with a negative result in terms of Hb (g/dL) (10.889 vs. 11.807), RBC (10^12/L) (4.119 vs. 4.558), MCV (fL) (80.98 vs. 82.20), Hb F

(%) (2.65 vs. 4.76), and Hb A (%) (60.70 vs. 91.78). However, the positive group of SCT had a higher mean value for MCH (pg) (26.87 vs. 26.77), MCHC (g/dL) (33.01 vs. 32.40), Hb A2 (%) (2.96 vs. 2.58), and Hb S (%) (34.97 vs. 0.00). Moreover, the mean result of Sickling test for SCT positive cases was (positive) and it was (negative) for SCT negative cases. These

findings were similar to those of Mir et al. (2018) excluding slight differences in the

parameters of MCH (pg) (24.59 vs. 29.27), MCHC (g/dL) (31.38 vs. 34.58) and Hb F (%)

(0.49 vs. 0.36) [25]. For SCD, the findings of the current study revealed that individuals with a positive result showed lower mean values compared to those with a negative result in terms of Hb (g/dL) (9.302 vs. 12.089), RBC (10^12/L) (3.130 vs. 4.726), Hb F (%) (10.45 vs.

4.76), and Hb A (%) (13.23 vs. 94.44). However, the positive group of SCD had a higher mean value for MCV (fL) (89.68 vs. 80.99), MCH (pg) (30.97 vs. 26.16), MCHC (g/dL)

(34.44 vs. 32.16), Hb A2 (%) (3.21 vs. 2.55), and Hb S (%) (78.59 vs. 0.00). Moreover, the

mean result of Sickling test for SCD positive cases was (positive) and it was (negative) for SCD negative cases. These findings were lower to those of Capanzana et al. (2018) in some particular hematological

parameters such as Hb (g/L) (100), MCV (fL) (72.6), MCH (pg)
(22.4), MCHC (g/dL) (30.6), and Hb A2 (%) (2.2), and the current study findings were higher than those of Capanzana et al. (2018) in the hematological parameters of Hb A (%) (97.8) and RBC (10^12/L) (4.5), these differences can be attributed to that the sample of SCD in
Capanzana et al. (2018) was from patients of Iron deficiency anemia only [26].

CONCLUSION

Sickle Cell Disease is a major concern in hemoglobinopathies and healthcare facilities dealing with it. This study revealed a recent trend in the occurrence of SCD and SCT over a
6-year period in Al-Madinah City, KSA. The findings of this study revealed that the
prevalence of SCT and SCD, in Al-Madinah City, KSA between 2015 and 2020 was 6.23% and 7.44% respectively. Therefore, hospital-based population screening of SCD is more
effective in detection of SCD than other methods of screening such as premarital or neonatal screening. The study findings indicated that the prevalence of SCT was higher in female cases, but the prevalence of SCD was observed more in male cases. There were varied
patterns in age groups analyzed but the findings strongly pointed the prevalence of SCT and SCD was more in the age group of 10 to 19 years which can be linked to the effectiveness of the premarital program in detection of SCD in this age group as it is the age of early marriage in KSA. The study also revealed variations in hematological parameters between health and SCT and SCD subjects. The data and findings of this study can set the stage for continued monitoring of hemoglobinopathy disorders in Al-Madinah City and other cities in KSA and aid facilitation of future evaluations of the efficiency of existing preventive programs, the study's data findings yield important information for decision makers in enabling prioritization of new programs and implementation of policy changes.

Limitations and Future Work

The sample size was small in comparison to the previous studies based on data
collected from premarital programs, making it difficult to get significant conclusions applicable to the Al-Madinah City population.
SCD was the most prevalent haemoglobinopathy in the study (7.44%), that is different from the findings of previous studies. Therefore, prospective, and systemic studies are needed in determining the prevalence and identification 0of epidemiology of
haemoglobinopathies in different KSA regions.
The data collected from King Fahd Hospital at Al Madinah in KSA has no exclusion criteria for population study which in certain instances could lead to misleading results.

Conflicts of Interest: There are no conflicts of interest in this study.

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