UTTAR PRADESH JOURNAL OF ZOOLOGY

43(24): 210-223, 2022
ISSN: 0256-971X (P)

PREVALENCE OF SICKLE-CELL DISEASE IN SAUDI ARABIA: A SYSTEMATIC REVIEW

NISREEN OMAR ASRAF [a++#*], SAAD ABDULRAHMAN ALJIBREEN [b], MUATH BADER ALOTAIBI [c], MOHAMMED HADI HADADI [d], H. ALTHOMALI FARIS AHMED [e], AFNAN ATEEG BATWIE [f], WALEED MOHAMMED ALGHAMDI [g], YASSER HUSSAIN AL-JAFFER [h], SALEH MOHAMMED ALHAI [i], KHALID ABDULLAH ALSHEHAB [j], TARIQ MOHAMMED ALSHAMI [k], MOHAMMED ALI ALSALMAN [l] AND NUHA ABDULAZIZ S ALHARBI [m]

[a] National Guard Hospital, Primary Health Care, Jeddah, Saudi Arabia.
[b] AlQuwayiyah General Hospital, Saudi Arabia.
[c] Shaqra University, Saudi Arabia.
[d] Baish General Hospital, Saudi Arabia.
[e] alsharqyah PHC Al Taif, Saudi Arabia.
[f] Al Doha PHC in Alkhobar, Saudi Arabia.
[g] Jubail General Hospital, Saudi Arabia.
[h] Alresford PHC in Qatif, Saudi Arabia.
[i] ALAWAMIA PHC in Qatif, Saudi Arabia.
[j] Al jafer General Hospital, Saudi Arabia.
[k] King Abdulaziz Hospital in Makkah, Saudi Arabia.
[l] Prince Saud Ben Jalawi Hospital, Saudi Arabia
[m] Kudi and Alhejrah PHC in Makkah, Saudi Arabia.

AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.56557/UPJOZ/2022/v43i243315

Editor(s):
(1) Dr. Juan Carlos Troiano, University of Buenos Aires, Argentina.
Reviewers:
(1) Emrah Yerlikaya, Siirt University, Turkey.
(2) Karen Cordovil, Brazil.

Received: 17 October 2022
Accepted: 24 December 2022
Published: 27 December 2022

Systematic Review Article

[++] *Consultant Family Medicine;*
[#] *Specialized Poly Clinic;*
**Corresponding author*

ABSTRACT

Background: A series of hemoglobinopathies known collectively as sickle cell disease (SCD) contain abnormalities in the gene encoding the beta component of haemoglobin. There are other subcategories that fall under the SCD umbrella, including sickle cell disease (SCD), haemoglobin SC disease (HbSC), and haemoglobin sickle-beta thalassemia (beta-thalassemia positive or beta-thalassemia negative). The prevalence of SCD varies greatly across Saudi Arabia, with the Eastern province having the greatest frequency and the southern regions having the second-highest prevalence. The reported sickle-cell prevalence ranges from 2% to 27%, and in some regions, up to 2.6% of people will have SCD.

Objectives: The study aims to summarize current evidences regarding Prevalence of Sickle-Cell Disease in Saudi Arabia.

Methods: For article selection, the PubMed database and EBSCO Information Services were used. All relevant articles relevant with our topic and other articles were used in our review. Other articles that were not related to this field were excluded. The data was extracted in a specific format that was reviewed by the group members.

Conclusion: Although the prevenance of sickle cell anemia is relatively high due to multiple reasons such as consanguinity, the prevalence of genetic diseases in Saudi Arabia may be significantly lowered during the following decades as a result of premarital screening there. Also, acute chest syndrome in SCD patients is relatively infrequent in Saudi Arabia's Eastern Province, it nonetheless has a major impact on morbidity and death. If patients with African haplotypes are compared, it has a low prevalence and recurrence.

Keywords: SCD; sickle cell anemia; hemolytic anemia; hemoglobinopathies; anemia in pediatrics; hemolysis.

1. INTRODUCTION

“A series of hemoglobinopathies known collectively as sickle cell disease (SCD) contain abnormalities in the gene encoding the beta component of haemoglobin. Dr. Africanus Horton published the first description of a condition that is similar to SCA in (1872). But it wasn't until 1910 that two medical professionals, Drs. James B. Herrick and Ernest Irons, noted "sickle-shaped" red blood cells in a dentistry student. Dr. James V. Neel and Col. E. A. Beet published independent findings in 1949 that detailed the inheritance patterns in SCD patients. In his article "Sickle Cell Anemia Hemoglobin" from the same year, Dr. Linus Pauling explained the molecular makeup of sickle haemoglobin (HbS). Ingram Vernon confirmed Linus Pauling's results in 1956 by describing the substitution of neutral valine with negatively charged glutamine using a fingerprinting approach” [1-3].

“One in 500 African Americans has sickle cell disease (SCD). The autosomal recessive mutation affects around 1 in 12 African Americans, and every year, 300,000 babies are born with sickle cell anaemia. There is still much to learn about how the illness manifests itself phenotypically. Infections, low foetal haemoglobin levels, cold climates, poor air quality, and other genetic subtypes all contribute to the disease's appearance. Clinical symptoms vary, have an impact on several systems, and typically result in a shorter life span” [4-7].

There are other subcategories that fall under the SCD umbrella, including sickle cell disease (SCD), haemoglobin SC disease (HbSC), and haemoglobin sickle-beta thalassemia (beta-thalassemia positive or beta-thalassemia negative). There are a few other minor variations among the SCDs, although they are not as prevalent as the aforementioned types. The sickle cell trait (HbAS), which has a heterozygous mutation and seldom exhibits any clinical signs or symptoms, should also be mentioned. The most prevalent kind of SCD is called SCA, and it is characterised by chronic hemolytic anaemia that necessitates blood transfusions, severe pain episodes, and organ damage. The first description of the use of hydroxyurea to raise HbF levels was made in 1984 by Platt et al. Since then, various new medications have been developed to treat sickle cell disease, including voxelotor, crinzalizumab, L-glutamine, and most recently, gene therapy [1].

Many patients have periods of chronic pain, exhaustion, hand-foot syndrome, recurrent infections, delayed development, and eyesight issues as a result of their illness, which frequently necessitates hospital stays. In addition, many SCD patients have shorter life expectancies and deal with a multitude of chronic, costly, and debilitating illnesses. As a result, there is a growing need for health services due to the rising prevalence of SCD, which is linked to a lack of skilled healthcare workers, efficient medications and immunizations, specialised medical facilities, and secure blood transfusions. In order to address the high burden of SCD in Saudi Arabia and to take steps to lower the morbidity and mortality that are related to this illness, it is crucial to take this into account [8].

The prevalence of SCD varies greatly across Saudi Arabia, with the Eastern province having the greatest

frequency and the southern regions having the second-highest prevalence. The reported sickle-cell prevalence ranges from 2% to 27%, and in some regions, up to 2.6% of people will have SCD. In Saudi Arabia, there is clinical and haematological variation in SCD, with two main phenotypes: a moderate phenotype and a severe phenotype. Additional research on the prevalence, molecular, and clinical epidemiology of SCD may aid in risk classification of patients and disease severity prediction to determine whether they should get early intensive care or ongoing symptomatic therapy [9]. The study aims to summarize current evidences regarding Prevalence of Sickle-Cell Disease in Saudi Arabia.

2. MATERIALS AND METHODS

2.1 Study Design

A systematic review of the current evidence on Prevalence of Sickle-Cell Disease in Saudi Arabia is considered a robust way of identifying and synthesizing the peer reviewed articles for evidence in this area to define a cohesive empirical research agenda that builds on prior knowledge. This review included qualitative evidence only to produce an interpretation. Further, a synthesis of qualitative data aims to generate findings that are meaningful, relevant and appropriate to individuals, to inform a research agenda and ultimately to more effectively practices on association between obesity and breast cancer. The review used methods of qualitative synthesis to combine, integrate and interpret, where possible, the evidence from the included papers.

The review aims to move beyond the aggregation of available data to provide further interpretive insights into Prevalence of Sickle-Cell Disease in Saudi Arabia, and define where future research can add to what is known.

2.2 Study Eligibility Criteria

The review included qualitative peer-appraised studies. Qualitative data from mixed methods-studies was screened for inclusion and included if the qualitative element was pertinent. We included those studies that have been conducted in twenty years. All peer-reviewed articles published in English, reporting association between obesity and breast cancer was included.

To be included for the review, the studies should have been published from October 2012 up to October 2022 to ensure the currency of the work while enabling a broad view of the emerging issues to be identified.

2.3 Study Inclusion and Exclusion Criteria

The articles was selected based on the relevance to the project, English and time restriction on ten years was considered. All other articles which do not have one of these topics as their primary end, or repeated studies, and reviews studies were excluded. The reviewers excluded any studies not available in English, conference abstracts, books or grey literature and editorial comments. Studies reporting only qualitative data was also excluded.

2.4 Search Strategy

A systematic search strategy was developed using a combination of Medical Subject Headings (MeSH) and controlled vocabulary to identify peer-reviewed articles on Prevalence of Sickle-Cell Disease in Saudi Arabia. The databases was from PubMed/MEDLINE, Scopus/Embase (Elsevier), EbscoHost, and Google Scholar. We limited our search from October 2012 to October 2022.

2.5 Selection of Study

The ENTREQ guidelines for reporting qualitative systematic reviews was used to demonstrate the selection processes and results. All retrieved studies was initially imported into Endnote library to assist removing duplicates. After removing the duplicates, the Endnote library was shared between the two reviewers to independently screen the articles by title and abstract, guided by the eligibility criteria. The studies which the two reviewers have agreed on was subjected to the full-text review. A third reviewer adjudicated any discrepancies between the two reviewers. The two reviewers independently reviewed the full text of all eligible studies. In the case where there are differences between the two reviewers, consensus was sought through discussion on the differences with the third reviewer. Finally, the full texts of all relevant studies found to meet the inclusion criteria was retained for the final framework synthesis.

2.6 Data Extraction

Data was independently extracted by two reviewers from eligible studies onto a customised data extraction form and populated with variables pertaining to the study population and phenomena of interest. Double checking and verification of extracted articles was done by the third review author. Study characteristics that were extracted included name of the first author and year of publication, data collection period and region in which the study was conducted. Specific study details including the study design,

study population, sample size, sampling procedures and data collection procedures was captured. Prevalence of Sickle-Cell Disease in Saudi Arabia was systematically identified.

2.7 Data Synthesis and Analysis

No software was utilized to analyze the data. The reviewers sorted the data by theme and presented the themes in the form of an analysis table (chart). The columns and rows of the table reflected the studies, and related themes enabled us to compare findings of the studies across different themes and subthemes.

2.8 Mapping and Interpretation

The reviewers used charts to define the identified concepts and map the range and nature of the phenomena. Our review explored associations between the themes to help clarify the findings. Our review mapped and interpreted findings in line with the review objectives and emerging themes.

3. RESULTS

Fig. 1 shows the selection and identification of studies. The search of the mentioned databases returned a total of 286 studies that were included for title screening. 198 of them were included for abstract screening, which lead to the exclusion of 52 articles. The remaining 146 publications full-texts were reviewed. The full-text revision led to the exclusion of 137 studies due to difference in study objectives, and 7 were enrolled for final data extraction (Table 1).

In Al-Qurashi MM, et al. Study which was done in Saudi Arabia found that Sickle cell disease had a frequency of 24 per 10,000 people and was found in 108 of 45,682 children and adolescents. The eastern area dominated the geographical distribution of sickle cell disease, with a prevalence of 145 per 10,000, followed by the southern region with a prevalence of 24 per 10,000, the western region with a prevalence of 12 per 10,000, and the central region with a prevalence of 6 per 10,000. The northern areas did not have any instances. The ratio of men to women was about 1:1 [10].

According to Memish, Z. A., & Saeedi, M. Y. (2011): Out of all the men and women who were evaluated, 70 962 (4.5%) and 29 006 (1.8%) had sickle cell disease or were sickle cell carriers, respectively. Between 2004 and 2009, the frequency of sickle cell disease remained steady, however the prevalence of -thalassemia rapidly declined from 32.9 to 9.0 per 1000 people who were subjected to testing (P.001). Between 2004 and 2009, the number of at-risk couples dropped by around 60%. Between 2004 and 2009, there was a more than 5-fold rise in the voluntary cancellation of marriage offers among at-risk couples (from 9.2% to 51.9%, P.001). In comparison to other regions of Saudi Arabia, the eastern region had 58% of all identified at-risk marriages and shown the highest reduction in detection and rise in prevention over time. [11] However, in AlHamdan, N., et al. 2007. study Sickle cell trait, sickle cell disease, thalassemia trait, and thalassemia disease were all detected in 4.20 percent of the 488,315 people that were tested. Both illnesses mostly affected the eastern, western, and southwestern regions of the nation. 2.14% of the 207,333 couples to whose certifications for matching were given were deemed to be at high risk. 89.6% of the 2,375 high-risk couples who were telephoned got hitched despite being aware of their high risk status [12].

The rest of results are detailed in Table 1.

4. DISCUSSION

“When a neutral valine replaces a negatively charged glutamine at the sixth position of the beta-globin chain, the sickle cell mutation results. The mutation is inherited in an autosomal codominant manner and is transmitted via Mendelian genetics. The most severe kind of SCD, also known as HBSS disease or SCA, is caused by a homozygous mutation. HBS-Beta-0 illness, which phenotypically mimics HBSS sickness, is caused by the coinheritance of beta-naught thalassemia and the sickle cell mutation. HbAS is inherited heterozygously. Patients with HbAS are not regarded as belonging to the SCD spectrum since they seldom have SCA-specific symptoms. Only screening measures used at births, blood donations, etc. may be able to find them” [1].

The two types of care for sickle cell anaemia are health maintenance and complication management. Screening and identifying risk factors and warning indicators of problems are the fundamental objectives of health maintenance. There is proof that invasive infection mortality and morbidity have been significantly decreased by pneumococcal vaccination, penicillin prophylaxis (from early infancy until at least age five), and teaching on how to control fever. Children with sickle cell disease may benefit from routine transcranial Doppler (TCD) scanning of the big cerebral blood arteries because it may not be widely available. Additionally, the therapy (chronic transfusion therapy) is impractical in many impoverished countries [4].

Table 1. Author, country, year of publication, methodology and outcome

Author, Publishing Year	Objective & Methodology	Outcomes	Population	Prevalence of disease	Conclusion
Al-Qurashi MM, et al. [10]	A multistage random probability sampling of the Saudi families from each of the 13 areas of the kingdom resulted in the selection of a sample size of 45,682 children and adolescents from newborn to 19 years of age. The study was carried out over a two-year period, from 2004 to 2005, and is cross-sectional and community-based. A house-to-house survey was	The eastern area dominated the geographical distribution of sickle cell disease, with a prevalence of 145 per 10,000, followed by the southern region with a prevalence of 24 per 10,000, the western region with a prevalence of 12 per 10,000, and the central region with a prevalence of 6 per 10,000. The northern areas did not have any instances. The ratio of men to women was about 1:1.	The total number of participants was 45,682 children and adolescents from newborn to 19 years old	24 per 10,000 people and in 108 of 45,682 children and adolescents	Planning should be done for national or regional newborn screening programmes for sickle cell disease using haematological assays. This study demonstrates the unequal geographic distribution of the people at risk. Because of this, national neonatal screening should probably be selected rather than universal.
Memish, Z. A., & Saeedi, M. Y. [11]	Saudi Arabia's nationwide premarital screening and genetic counselling program's six-year results for sickle cell disease and beta-thalassemia: Blood samples from all couples who received marriage proposals between 2004 and 2009 were examined for -thalassemia and sickle cell disease. All test subjects received the results, and all at-risk couples were given the opportunity to participate in genetic counselling.	Out of all the men and women who were evaluated, 70 962 (4.5%) and 29 006 (1.8%) had sickle cell disease or were sickle cell carriers, respectively. Between 2004 and 2009, the frequency of sickle cell disease remained steady, however the prevalence of -thalassemia rapidly declined from 32.9 to 9.0 per 1000 people who were subjected to testing (P.001). Between 2004	Premarital couples presenting marriage proposals at premarital and genetic counselling clinics between 2004 and 2009.	-	Six years of premarital screening in Saudi Arabia significantly decreased the number of marriages at risk, which could significantly lessen the burden of hereditary diseases in Saudi Arabia in the next decades.

Author, Publishing Year	Objective & Methodology	Outcomes	Population	Prevalence of disease	Conclusion
		and 2009, the number of at-risk couples dropped by around 60%. Between 2004 and 2009, there was a more than 5-fold rise in the voluntary cancellation of marriage offers among at-risk couples (from 9.2% to 51.9%, P.001). In comparison to other regions of Saudi Arabia, the eastern region had 58% of all identified at-risk marriages and shown the highest reduction in detection and rise in prevention over time.			
AlHamdan, N., et al. [12]	to calculate the prevalence of sickle cell disease and beta thalassemia in the adult population screened as part of the Saudi Premarital Screening Program, together with their regional distribution. The National Premarital Screening Program was a cross-sectional, population-based investigation. It applies to everyone who requested a marriage licence during the years 1425 and 1426 Hijra (February 2004 to January	Sickle cell trait, sickle cell disease, thalassemia trait, and thalassemia disease were all detected in 4.20 percent of the 488,315 people that were tested. Both illnesses mostly affected the eastern, western, and southwestern regions of the nation. 2.14% of the 207,333 couples to whose certifications for matching were given were deemed to be at high risk. 89.6% of the	All the people who submitted a marriage licence application between February 2004 and January 2005. The Ministry of Health operated a network of 123 reception centres, and 70 laboratories were dispersed throughout Saudi Arabia.		The findings demonstrated good access to the intended audience. However, the program's goal of reducing high-risk marriages was not as successful, highlighting the need for better health education programmes for the general population, increased counselling efforts for high-risk couples, and adjustments to the method of timing screening in relation to marriage.

Author, Publishing Year	Objective & Methodology	Outcomes	Population	Prevalence of disease	Conclusion
	2005). The Ministry of Health operated a network of 123 receiving centres, and 70 laboratories were dispersed throughout Saudi Arabia.	2,375 high-risk couples who were telephoned got hitched despite being aware of their high risk status.			
Al-Ali, A.K., et al. [13]	From 2016 to 2019, King Fahd Hospital, Al-Ahsa or King Fahd Hospital of the University, Imam Abdulrahman Bin Faisal University, Dammam, recruited patients from the Eastern Province of Saudi Arabia, ages 2 to 82. Standard criteria were used to determine clinical complications..	One in every 80 residents of Saudi Arabia's Eastern Province has sickle cell disease. The two main quantitative trait loci (QTL) that affect HbF gene expression are BCL11A and MYB. Only 4.2% of the variation in HbF was explained by the frequency of two sentinel minor alleles associated with this QTL, rs766432 in BCL11A and rs9399137 in MYB, respectively. The minor allele frequencies of rs766432 and rs9399137 were similar in 2040 sickle cell anaemia patients of African heritage, but they explained 14.7% of the variation in HbF. HBG2 accounts for 66% to 75% of globin in homozygotes for	From 2016 to 2019, participants from the Eastern Province of Saudi Arabia, ranging in age from 2 to 82, were sought out in King Fahd Hospitals in Al-Ahsa and Dammam, respectively, and King Fahd Hospital of the University at Imam Abdulrahman Bin Faisal University.		We don't have any mortality data for this cohort. Mortality and hemolysis are correlated. This shows that patients with AI haplotype sickle cell anaemia may live longer than those of African heritage. This theory is best supported by a longitudinal investigation of a birth cohort.

Author, Publishing Year	Objective & Methodology	Outcomes	Population	Prevalence of disease	Conclusion
		rs7482144 and sickle cell anaemia, vs 40% in healthy people.			
Alabdulaali M K. [14]	317 SCD patients, aged two or older, who were hospitalised to King Fahad Hospital Hofuf between January and May 2003 for a variety of etiologies participated in this retrospective analysis. 26 individuals presented with various ACS-related reasons; 11 patients appeared with various pathologies other than ACS but had a history of ACS; and 280 patients presented with various pathologies but never with ACS. The following variables were examined: clinical characteristics, CBC, Hb-electrophoresis, G6PD activity, cultures, chest X-ray, arterial oxygen saturation, blood transfusion rates, and outcome. To assess effect on ACS, univariate and multiple regression analyses were used.	37 patients (or 11.67% of the SCD patients hospitalised during the research period) with recent or prior bouts of ACS were examined. Five individuals (13.51%) experienced two or more episodes, compared to the majority of ACS patients who had just one. With one patient dying, the hospital mortality rate was 1 in 26 (3.8%). When ACS recurrence and mortality among SCD patients in Saudi Arabia's Eastern province were compared to those among patients with African haplotype, it was found that mortality was also lower, though not statistically significant, and ACS recurrence was significantly lower (P 0.025) in the Eastern province patients.	317 SCD patients who were two years of age or older who were admitted to King Fahad Hospital Hofuf between January and May 2003 for various etiologies participated in this study. 26 individuals presented with various ACS-related reasons; 11 patients appeared with various pathologies other than ACS but had a history of ACS; and 280 patients presented with various pathologies but never with ACS. The following variables were examined: clinical characteristics, CBC, Hb-electrophoresis, G6PD activity, cultures, chest X-ray, arterial oxygen saturation, blood transfusion rates, and outcome.	-	Although acute chest syndrome in SCD patients is relatively infrequent in Saudi Arabia's Eastern Province, it nonetheless has a major impact on morbidity and death. When compared to patients with African haplotypes, its prevalence and recurrence are minimal.
Ahmed, A. E. et al. [15]	At King Fahad Hospital in Hofuf, Saudi Arabia, 290	The sample contained 131 aberrant leukocyte	290 SCD patients who received regular care at King		About five out of ten Saudi SCD patients evaluated in this group had

Author, Publishing Year	Objective & Methodology	Outcomes	Population	Prevalence of disease	Conclusion
	SCD patients who were receiving regular care were the subjects of a cross-sectional and retrospective record review research. In addition to reviewing patient documents to gather information on blood test values for the past six months, an interview was done to evaluate clinical presentations.	counts (45.2%), with low WBC counts of 15 (5.2%) and high WBC counts of 116 (40%). Shortness of breath (P=0.022), fatigue (P=0.039), edoema of the hands and feet (P=0.020), and back discomfort (P=0.007) were all linked to high WBC levels. Patients with normal WBC counts had higher mean haemoglobin levels (P=0.024), whereas patients with high WBC levels had higher mean haemoglobin S levels (P=0.003). Male gender (adjusted odds ratio [aOR]=3.63) and patients with cough (aOR=2.18), low haemoglobin (aOR=0.76), and low heart rate (aOR=0.97) were predictors of elevated WBC counts when relevant confounders were taken into account.	Fahad Hospital in Hofuf, Saudi Arabia, participated in this study.		abnormal leukocyte counts. High WBC count was related to male gender, cough, poor haemoglobin, and low heart rate. Strategies that target high WBC counts may help SCD patients by preventing disease complications.
Memish, Z. A., et al. [16]	Between 2004 and 2009, routine blood tests were used to identify the sickle cell	Over the course of six years, 15,72,140 men and women were	Between 2004 and 2009, prospective spouses who used common blood testing.		Saudi adults are known to have a wide range of hemoglobinopathies, which should aid in better allocating

Author, Publishing Year	Objective & Methodology	Outcomes	Population	Prevalence of disease	Conclusion
	disease and beta-thalassemia carrier and case status in couples who were about to be married. Researchers computed and compared the prevalence of illnesses among several SA administrative and geographic regions, as well as the prevalence of at-risk marriages.	examined. This amounted to 0.06% of Saudi Arabia's total population. 45.1 out of every 1000 people investigated had a positive sickle cell test in a pair. The Eastern area had the greatest frequency (134.1 per 1000), followed by the Southern and Western regions (55.6 and 28.5 per 1000, respectively), while the Central and Northern regions had the lowest prevalence (28.6 per 1000). (13.7 and 13.5 per 1000, respectively). Per 1000 people screened, there were 18.5 couples with positive -thalassemia tests (18.5 for carriers and 0.5 for cases). The Eastern area had the greatest prevalence (59.0), while the Southern, Western, and Central regions had intermediate prevalences and the Northern region had the lowest prevalence (3.9).	15,72,140 men and women in all were examined		resources to the current preventive measures.

Table 2. Detailed description of studies on barriers to receipt of appropriate pain management

Study	Study design	Study population/location	No.	Summary of reported barriers
Al-Qurashi MM, et al. [10]	Cross-sectional study	children and adolescents from newborn to 19 years/ Saudi Arabia (SA)	45,682	NA
Memish, Z. A., & Saeedi, M. Y. [11]	Retrospective review	premarital couples/ SA	NA	NA
AlHamdan, N., et al. [12]	cross-sectional, population-based study	individuals who applied for a marriage license/SA	488,315	NA
Al-Ali, A.K., et al. [13]	NA	Individuals aged 2 to 82/SA	NA	NA
Alabdulaali M K. [14]	retrospective study	SCD patients who were two years or older, admitted to King Fahad Hospital Hofuf, SA	317	NA
Ahmed, A. E. et al. [15]	cross-sectional and retrospective chart review study	SCD patients who were routinely treated at King Fahad Hospital in Hofuf, Saudi Arabia	290	NA
Memish, Z. A., et al. [16]	NA	couples approaching marriage/SA	15,72,140	NA

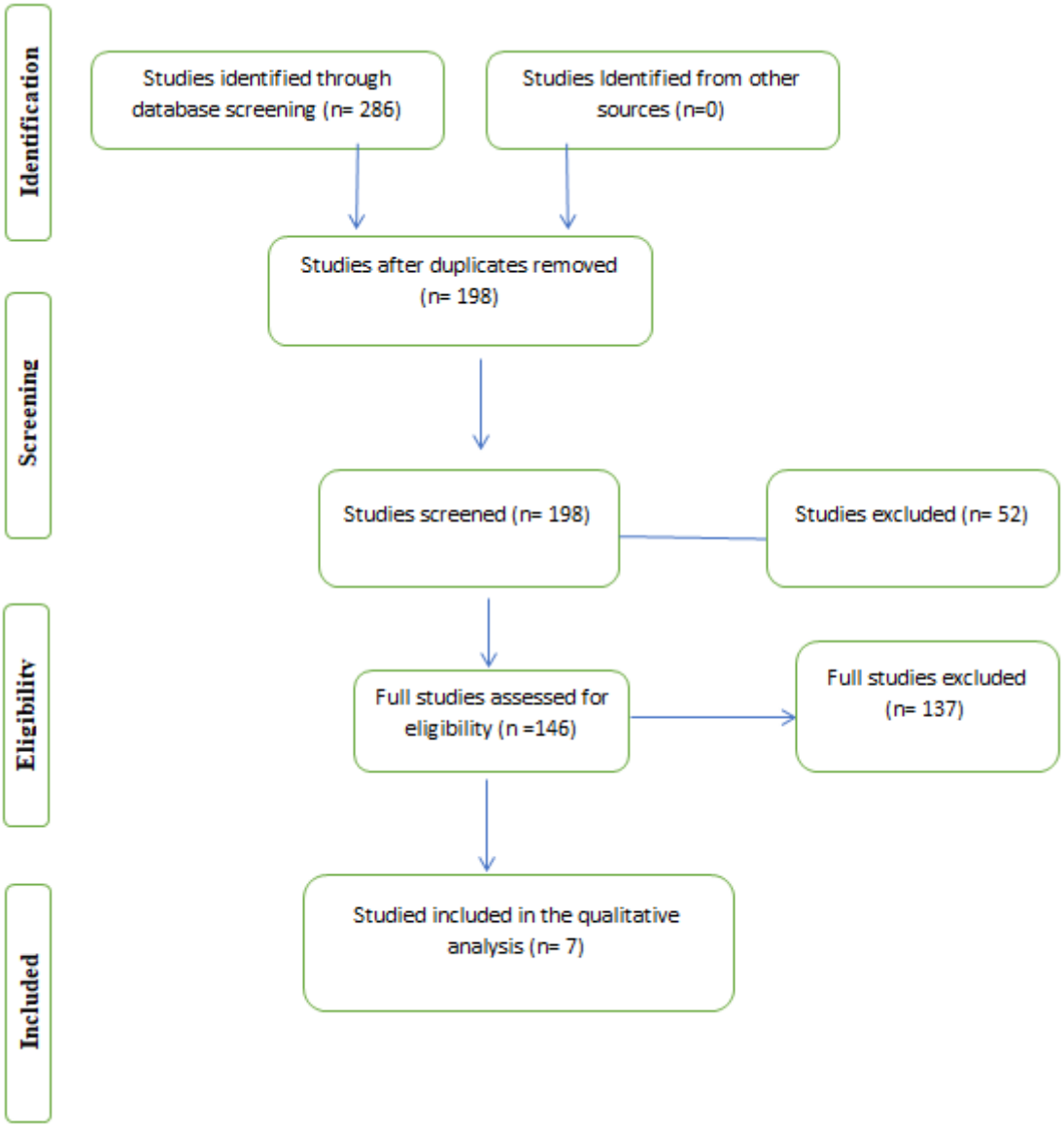

Fig. 1. The included studies had different study designs

"Even though Saudi Arabia's population has benefited greatly from the Premarital Screening Program and free genetic counselling, the country needs still create more programmes that are efficient at detecting new cases of SCD (e.g., through newborn screening). For instance, in other nations, parental counselling and follow-up care for impacted patients have decreased SCD-related morbidity and death. Saudi patients, however, face a number of obstacles to genetic counselling and screening, including restricted access to healthcare services, a shortage of qualified medical personnel, social and cultural stigmas, and religious views. Therefore, awareness campaigns must be started very early in Saudi Arabia in order to assist the public in overcoming these obstacles" [8,17].

"There are two main kinds of the clinical phenotype of SCD in Saudi Arabia. Eastern patients had greater amounts of foetal and total haemoglobin, lower levels of haemoglobin A2, mean cell volume, reticulocytes, and platelet counts, and more deletional alpha thalassemia. The illness has a moderate or benign clinical phenotype. However, the word "benign" is ambiguous because people with this kind of illness have a wide range of symptoms and acquired issues. For instance, avascular necrosis of the femoral head is more likely to occur in 27% of SCD patients from the Eastern province as opposed to 8% to 12% of African type individuals. A greater risk of splenic problems, such as sequestration crisis, chronic hypersplenism, and splenic infarction, is associated with late

persistent splenomegaly, which is documented in 50% to 80% of patients" [9,18-20].

According to recent studies, Saudi Arabia has a high incidence of -thalassemia (1.8%) and sickle-cell disease (4.5%). The bulk of these favourable findings (93.9% for sickle-cell disease and 97.3% for -thalassemia) were carriers. In a previous study covering the first two years of the PMSGC programme, sickle-cell disease was more common (4.2% carriers and 0.26% cases), but -thalassemia was far more common (3.2% carriers and 0.07% cases). This can be explained by the significant drop in -thalassemia prevalence that occurred in one study following the second year of the treatment (more than 70%) [11].

Blood transfusions are a crucial component of SCA treatment. Transfusions are intended to lower the HbS content and boost blood's ability to transport oxygen. To keep the HbS level below 30%, blood is transfused (simple or exchange) (STOP 1 and 2 trial). A more realistic aim for HbS in patients receiving routine exchange transfusions (history of stroke, intolerance to hydroxyurea, or contraindication to hydroxyurea) is 25% in order to prevent an increase in HbS over 30% 4 weeks after the patient stops getting exchange transfusions [1].

"In contrast to Hb SS homozygotes, persons with Hb S/-thalassemia or Hb SC often experience mild to moderate symptoms. People with Hb S/0 thalassemia have symptoms that are similar to those of Hb SS homozygotes. The median survival for SS illness was predicted to be 48 years for women and 42 years for men, and for SC disease to be 68 years for women and 60 years for men, according to an analysis of data from the Cooperative Study of Sickle Cell Disease (CSSCD) carried out in the 1980s. Despite improvements over time, Hb SC continues to have much greater child survival than Hb SS" [16].

"The impairments indicated in the following sections are a danger for children and adults with SCD, especially those who have sickle cell anaemia. A disability may result in activity restrictions and limited social engagement. The medical model of disability is most frequently used to treat impairments in clinical settings. This model acknowledges the cumulative harm that red blood cell sickling and inflammation cause to multiple organ systems, as well as the occurrence of unpredictable and debilitating pain episodes and chronic anaemia. The medical paradigm isolates the individual from the social environment and takes a physiological approach to sickness. Therefore, it has come under fire from social scientists using a social model of disability, which examines functional outcomes and interactions with the social and physical contexts, as being insufficient" [19].

"Blood transfusions are a crucial component of SCA treatment. Transfusions are intended to lower the HbS content and boost blood's ability to transport oxygen. To keep the HbS level below 30%, blood is transfused (simple or exchange) (STOP 1 and 2 trial). A more realistic aim for HbS in patients receiving routine exchange transfusions (history of stroke, intolerance to hydroxyurea, or contraindication to hydroxyurea) is 25% in order to prevent an increase in HbS over 30% 4 weeks after the patient stops getting exchange transfusions" [1].

5. STRENGTHS AND LIMITATIONS OF THE SYSTEMATIC REVIEW

The included studies had relatively small sample sizes, resulting in low power to our results. We were unable to conduct analyses to explore potential bias associated with the heterogeneity between studies because of the small number of included studies. The majority of the included studies used cross-sectional which reduces our confidence in these results because bias can be introduced.

6. CONCLUSION

Although the prevenance of sickle cell anemia is relatively high due to multiple reasons such as consanguinity, the prevalence of genetic diseases in Saudi Arabia may be significantly lowered during the following decades as a result of premarital screening there. Also, acute chest syndrome in SCD patients is relatively infrequent in Saudi Arabia's Eastern Province, it nonetheless has a major impact on morbidity and death. If patients with African haplotypes are compared, it has a low prevalence and recurrence.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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