# Sickle Cell Disease in Children in Saudi Arabia: A Systematic Review

**Nazim Faisal Hamid [1]*, Nader Mousa Rubayyi Albalawi [2], Fawaz Khalifah M Alanazi [2], Faisal Mohammed Alharbi [2], Moath Omar Aljabri [3]**

*[1] Pediatrics Consultant, Maternal and Child Health Care Center, Tabuk, KSA.*
*[2] Pediatrics Specialist, Maternal and Child Health Care Center, Tabuk, KSA.*
*[3] Pediatrics Resident, Maternal and Child Health Care Center, Tabuk, KSA.*

## ABSTRACT

**Background:** Sickle cell disorder is commonly found in Saudi Arabia. There is no reliable information on the influence of sickle cell and the mortality rate of people aged five years and younger. Several types of research have deliberated the occurrence of SCD. The researches in the Middle East Arab Nations have established the presence of precise risk influences assembly SCD extra prevailing in this portion of the world.
**Aim:** To review results of previous studies regarding prevalence and complications of sickle cell disease among children in Saudi Arabia
**Methodology:** This is a systematic review, including PubMed, Google Scholar, and EBSCO that by examining randomized controlled trials, observational, and experimental studies investigates sickle cell disease among children in Saudi Arabia.
**Results and Conclusion:** The research included 8 studies and concluded that results show elevation of the frequency of sickle cell disease in Saudi Arabia especially in the eastern and southern districts of the kingdom. Proper vaccinations and blood transfusions aimed at children at risk of complications are advised. Neonatal screening programs for sickle cell disease should be considered. Selective screening of the children at risk or with a history of consanguinity between parents rather than universal screening is more appropriate.

**Key Words:** *Sickle cell disease, SCD in Saudi Arabia, Sickle cell among children, Risk factors of SCD, Complication of SCD.*

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## INTRODUCTION

Sickle Cell Disease (SCD) is a communal expression for a sum of genetic illnesses in which hemoglobin is architecturally atypical, causing the sporadic development of sickle-shaped Red Blood Cells (RBCs) and a varied range of medical manifestations [1-3]. SCD resulted from transmutation in the hemoglobin beta series in which glutamic acid is replaced by valine at the site six chromosome11 [4]. The occurrence of the illness is extraordinary in the general public of Sub-Saharan Africa, South Asia, the Middle East, and the Mediterranean.
Wide-reaching, 257,000 sicklier out of 330,000 broods born with a chief hemoglobinopathy, lead it to be the communal worldwide hemoglobin illness [5]. The utmost communal genotype is homozygous hemoglobin SS (HbSS), then mutual heterozygous disorders are hemoglobin sickle beta zero thalassemias, hemoglobin sickle beta plus thalassemia (hemoglobin sickle beta plus thalassemia), besides hemoglobin sickle cell disease (HbSC) [6].
The medical appearance of SCD is mutable depending on the type of complication and the body system affected. Vaso-Occlusive Crisis (VOC) is the utmost chief appearance of SCD followed by Acute Chest Syndrome (ACS); the new existence of lung infiltrates on chest X-ray go together with high temperature and respirational symptoms, comprising a cough, tachypnea, and chest ache [7, 8]. Infections, Pulmonary Hypertension (PHTN),

**Corresponding author:** Nazim Faisal Hamid
**Address**: Maternal and Child Health Care Center, Tabuk, KSA.
**E-mail:** nazim_prof @ yahoo.com
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Cerebrovascular Accidents (CVA)/Stroke, Renal Complications, Eye Complications, and Splenic Sequestration are also common complications of SCD [9]. Management of sickle cell complications is tailored to the type of complication. The life expectancy in SCD is generally decreased (possibly 20 - 30 years) in comparison with undiseased persons, nonetheless, loans in treatment are extending survival. The consequences for utmost cases are protected and SC crises frequently need readmissions to the hospice [10].

Various strategies such as premarital screening, prenatal screening, and increasing the awareness of parents of children with sickle cell disease about the high risk of reoccurrence, have been introduced in different countries. These strategies have, in turn, been shaped by social, economic, medical, and legal influences [11].

Sickle cell disorder is commonly found in Saudi Arabia, India, Mediterranean countries, and sub-Saharan Africa [12]. There is no reliable information on the impact of sickle cell and the mortality rate of people aged five years and younger. Nonetheless, of survivors to adulthood, many suffer ongoing organ malfunction [13].

Several types of research have deliberated the incidence of SCD. It was reported that the precise risk factors of SCD are mostly prevailing in the Middle East Arab Countries, as it is rapidly increasing inhabitants in addition to the rise in consanguinity nuptial [12]

### Aim of the Study:

To review results of previous studies regarding prevalence and complications of SCD among children in Saudi Arabia

## METHODOLOGY:

PubMed and EBSCO Information Services were chosen as the search databases for the publications used within the study, as they are high-quality sources. PubMed is one of the largest digital libraries on the internet developed by the National Center for Biotechnology Information (NCBI) which is a part of the United States National Library of Medicine. Topics concerning SCD among children in Saudi Arabia other articles have been used in the making of the article. Restriction to the last 10 years, country restriction on Saudi Arabia, and English language due to unavailable resources for translation were used.

Established articles were examined by title, abstract review of abstracts resulted in 8 subjects recorded. Inclusion Criteria: The articles were carefully chosen founded on their significance to the mission and articles including one of the following topics: ‘sickle cell disease, SCD in Saudi Arabia, sickle cell among children, risk factors of SCD, a complication of SCD’ (Figure 1). Exclusion criteria: all other articles which did not have one of these topics as their primary end, or repeated and review studies have been excluded.

### Statistical Analysis:

No software has been utilized to analyze the data. The data was extracted based on a specific form that contains (Title of the publication, author’s name, objective, summary, results, and outcomes). These data were reviewed by the group members to determine the initial findings and the modalities of performing the surgical procedure. Double revision of each member’s outcomes was applied to ensure validity and minimize mistakes.

## RESULTS:

The search of the mentioned databases returned a total of 67 studies that were included for title screening. 44 of them were included for abstract screening, which leads to the exclusion of 12 articles. The remaining 32 publications full-texts were reviewed. The full-text revision leads to the exclusion of 24 studies, and 8 were enrolled for final data extraction (Table 1).

The included studies had different study designs.

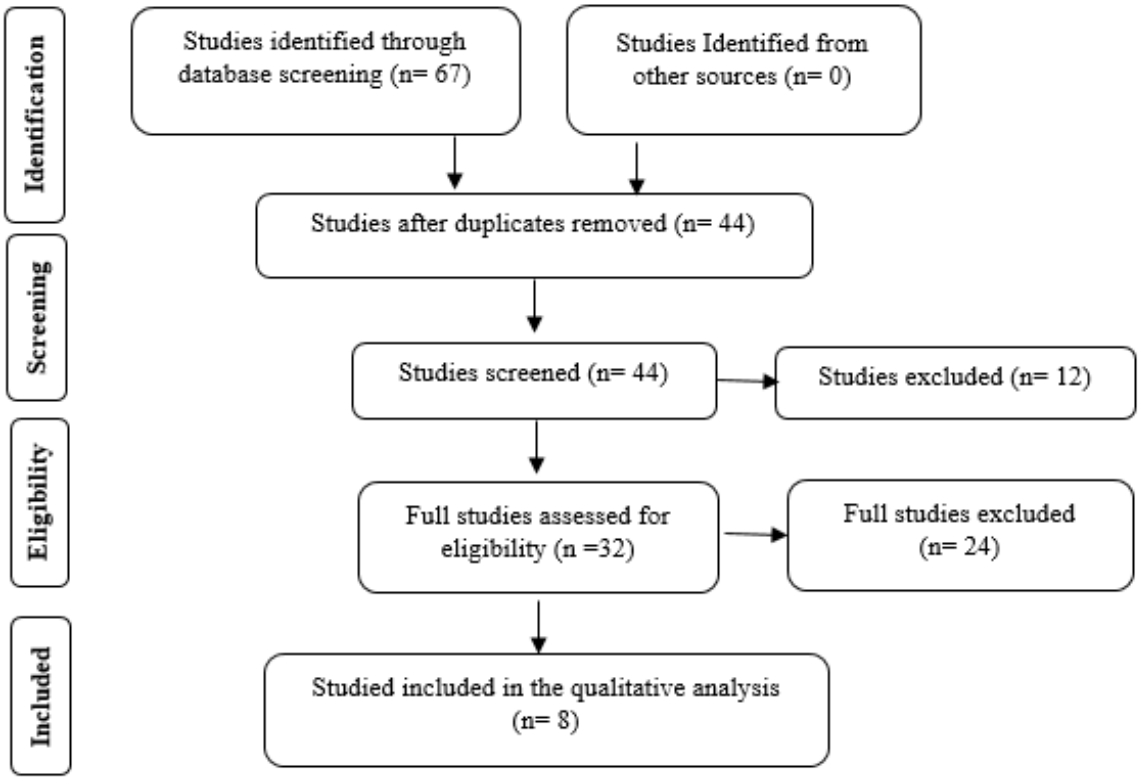


**Figure 1: Flow chart illustrates the data extraction process**

**Table 1: Author, Year of Publication, Study Type, and Study Outcome**

| Author | Study Region | Year of Publication | Study Type | Sample Size | Outcome |
|---|---|---|---|---|---|
| **Al-Qurashi, Mansour M, et al. [14]** | Saudi Arabia | 2008 | cross-sectional, community based | 45,682 children | Prevalence of SC was reported as 24 per 10,000. Eastern region of the Kingdom showed highest 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 difference in prevalence was reported between males and females. |
| **Elobied, S. et al. [15]** | King Abdulla Hospital, KSA | 2020 | cross-sectional study | 100 children | Mean age of the cases was 13.12±4.85 (SD), 95% reported consanguinity between parents. UTI was the highest reported infection and E. Coli was the most common organism isolated. |
| **el-Hazmi, M A et al. [16]** | South-western region of Saudi Arabia | 1990 | A cross-sectional study | 137 SCD children | α-thalassemia and variable levels of HbF was highly reported in SC patients and had the highest values for hematological parameters and lowest values of red cell indices. |
| **Alkot M, et al. [17]** | Makkah Al-Mukaramah, KSA | 2018 | A retrospective, analytic, nonintervention cohort study | 145 children | The most commonly reported complication was VOC (55.9%), followed by infection (9%). 41.4% of SCA children reported admission to hospital once whereas 25.5% were admitted more than 5 times. 3.1% of Saudi patients reported acute splenic sequestration. |
| **El Mouzan M, et al. [18]** | Eastern Province of Saudi Arabia | 1989 | Prospective study | 193 children | 7% presented in the first 12 months of age and 27% remained asymptomatic at 4 years. Aching attacks of bones and joints were the original symptoms, then dactylitis, abdominal pain and sever splenic confiscation (ASS), happening in 60%, 31.6%, 6.7%, and 1.7% of the cases, correspondingly. No one of the cases presented with severe bacterial infections. During this study, 175 sickle cell crises were documented, but only |

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| | | | | | 16 (9.1%) required hospital admissions. There were no deaths in this series. High hemoglobin F levels correlated with delayed clinical presentation and reduced number of crises. |
| **Pejaver RK, et al. [19]** | Saudi Arabia | 1995 | Prospective study | 41 children | Vaso occlusive crisis were reported to be the commonest cause of hospital admissions. Pneumococcal vaccine and prophylactic oral penicillin were reported to have no effect on the frequency of admissions and the admission rate per patient year. |
| **Hawasawi, Z M et al. [20]** | Al-Madinah Al-Munawarah, Saudi Arabia. | 1998 | a retrospective study | 6000 children | Prevalence of SCD was reported to be (0.88%) among studied children. 36 patients were homozygous SS and 17 were sickle thalassemic. Vaso-occlusive crisis (77.35%) was the most cause of admission followed by infection (67.92%), acute chest syndrome (22.64%), anemia (12.6%), and cerebrovascular accident (9.43%). 70% of the patients are still following up. |
| **Abd Elmoneim, Abeer A et al. [21]** | Al-Madinah Al-Munawarah, Saudi Arabia. | 2019 | A retrospective study | 739 SCD children | 49% of children existing by severe painful attacks. Sever chest syndrome was found in 20.9%. Infection causes admission in 17.5%, and severe anemia was found in 8.1% of the cases. |

## DISCUSSION:

Varied prevalence statistics have been published over the last 15 years. According to Al-Suwaid, Darwish, and Sabra(2015), the SCD gene was recognized in 1963, by Lehman, Maranjian, and Mourant, in the eastern area of Saudi Arabia. As Lehmannet al. (1963) later wrote: " The distribution of sickling in the Kingdom ofSaudi Arabia is of particular interest because of its relation to malarial distribution and the origin and movements of the population concerned" [22]. Previous findings regarding the high prevalence and uneven distribution of sickle cell disease in Saudi Arabia are supported by community-based studies conducted by Al-Qurashi et al. [14], and more recently by Al-Suwaid et al. (2015) [23]. Memish et al. (2011) suggested that regional differences reflect family size and frequency of consanguineous marriages. Knowledge levels also differ which means that the extent to which individuals with SCD are integrated into communities, and indeed health care systems, varies considerably. In the current research, it appeared that the experiences of individuals affected with SCD were largely hidden from the general community [24].

Regional variations in the prevalence of SCD were documented by Memishet al. (2011) [24] who examined the blood tests of couples who had undergone premarital screening over six years (2004-2009) and found a high prevalence of SCD in the eastern, southern, western, central, and northern provinces, respectively. Al-Qurashi, Mansour M et al. [14] showed regional differences in the prevalence of SC as 24 per 10,000. The Eastern region of the Kingdom showed the highest occurrence of 145 per 10,000, after that the southern region which has an occurrence of 24 per 10,000, the western area 12 per 10,000, and the central area has 6 per 10,000.

Ezenwa et al. (2016) found an association concerning the expectation of pain and self-reported satisfaction with the level of pain experienced by individuals with sickle cell disease. The authors concluded that measurement of the level of satisfaction of a patient with pain associated with sickle cell disease can assist with evaluation and the provision of adequate treatment [25]. El Mouzan M, et al. [18] reported that painful crises of bones and joints were the most common initial symptoms.

Opawoye et al. stated a 21.2% infection [26] in the Southern part of the Kingdom of Saudi Arabia (KSA), and Abu Srair et al. found an 8.6% infection rate from the Eastern part of Saudi Arabia [27]. The difference in the incidence of infection between the two studies might be caused by the presence of two different types of SCD in the country [28].

Urinary tract infection has been reported to be common in SCD patients, [29] as was observed in Elobied, S. et al. [14] and Hawasawi, Z M et al. [20].

Alkot M, et al. [17] found that the commonly stated consequence was VOC (55.9%), then infection (9%). Hawasawi, Z M et al. [20] reported that vaso-occlusive crisis (77.35%) was the most cause of admission followed by infection (67.92%), severe chest syndrome (22.64%), anemia (12.6%), and cerebrovascular accident (9.43%). Agreeing with Pejaver RK, et al. [19] who also reported that vaso occlusive crisis were reported to be the mutual reason for hospital admissions. In Kuwait, it was reported hospital admissions were mainly because of VOC (63.2%), splenic confiscation (9.2%), hemolysis attacks (8.8%), and severe chest syndrome (6.6%) whereas the individual case of every Transient Ischemic Attacks (TIAs) besides severe osteomyelitis caused by salmonella were reported, while no deaths were reported [30].

Previous research papers also established the results that, the most founded consequences of SCD and the common cause for hospital admission remained VOC [31-35].

## CONCLUSION:

The results show elevation of the prevalence of SCD in Saudi Arabia especially in the eastern and southern regions of the Kingdom. Suitable immunizations and blood donation for children at risk of complications are advised. Neonatal screening programs for SCD should be considered. Selective screening for children at risk or with a history of consanguinity between parents rather than universal screening is more appropriate. Additional research papers on the occurrence and risk factors of SCD could benefit in expecting illness severity and risk category of cases.

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