Prevalence and Incidence of Sickle Cell Disease in the Middle East: A Systematic Literature Review

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Background

- Sickle cell disease (SCD) is an inherited blood disorder caused by mutations in the hemoglobin subunit beta gene leading to production of abnormal hemoglobin and chronic complications such as vaso-occlusive crises, hemolytic anemia, and organ damage.[1]
- Regions with a high burden of SCD include areas historically endemic to malaria, such as parts of Africa, the Middle East, the Caribbean, and South Asia.[2]
- There remains a lack of comprehensive and up-to-date data on the incidence and prevalence of SCD across the Middle East.

Objective

- To conduct a systematic literature review (SLR) to synthesize the published peer-reviewed literature on the prevalence and incidence of SCD in the Middle East.

Methods

- An SLR was conducted by searching electronic bibliographic databases, Excerpta Medica Database (EMBASE) and Medical Literature Analysis and Retrieval System (MEDLARS/ MEDLINE). Searches were run in the electronic databases with a date range of January 1, 2009 to September 23, 2023; searches were updated in May 2024 to identify any additional studies published since the initial search date.
- Proceedings from key conferences held between 2021 and 2023 were also performed to identify studies, including the European Conference on Rare Diseases, the Global Congress on Sickle Cell Disease, the American Society of Hematology Annual Meeting, and the European Hematology Association Congress.
- Observational studies were eligible for inclusion if they reported prevalence or incidence estimates in a pediatric and/or adult SCD population in any Middle Eastern country. **Table 1** details the study eligibility criteria.
- Study selection and data extraction were performed by a single reviewer and validated by a second reviewer. Data were analysed qualitatively given the heterogeneity in patient populations, study designs, and outcomes reporting between studies.

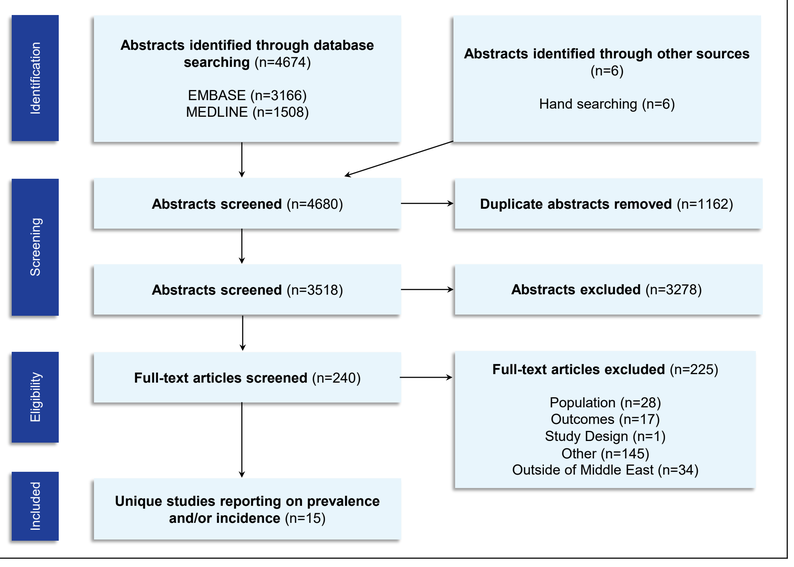
Table 1: Study eligibility criteria

Criteria	Description
Population	• Male or female children or adults who have confirmed sickle cell disease (homozygous for sickle cell disease [HbSS], heterozygous for sickle cell disease [HbSC], sickle β0 thalassaemia [HbSβ0], and sickle β plus thalassaemia [HbSβ+], and other genotypic variants)
Intervention	• Not applicable
Outcomes	• Prevalence • Incidence
Study design	• Observational studies (including, retrospective and prospective observational studies and cross-sectional studies) • Literature reviews
Publication year	• 2009 to present
Geography	• Afghanistan, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, Turkey, the United Arab Emirates, and Yemen

Results

- A total of 4680 abstracts were identified as potentially eligible from the bibliographic databases, conferences, and hand searching. After screening these abstracts, 240 advanced to full-text review, of which 225 were subsequently excluded for the following reasons: population not of interest (n=28 studies), prevalence or incidence outcomes not provided (n=17), study design not eligible (n=1), country not of interest (n=34), and other reasons (e.g., duplicate publications, commentaries, opinions, n=145).
- A total of 15 studies investigated prevalence and/or incidence of SCD (12 studies reported prevalence and 4 studies reported incidence) and were included (**Figure 1**).
- An overview of prevalence and incidence data are provided in **Table 2.** Countries captured across the 15 studies include: Afghanistan (n=1 study),[3] Algeria (n=1),[3] Bahrain (n=2), Egypt (n=1), Iraq (n=2),[3,4] Iran (n=2),[3,5] Jordan (n=2),[3,6] Kuwait (n=1, Lebanon (n=1), Libya (n=1),[3] Morocco (n=1),[3] Oman (n=4), Palestine (n=1),[3] Qatar (n=1), Saudi Arabia (n=8), Turkey (n=2), and UAE (n=1).[7,8]

Figure 1: PRISMA diagram of study selection



Prevalence

- Twelve studies provided data on the prevalence of SCD in the Middle East. The Global Burden of Disease (GBD) provided the most comprehensive data, with prevalence ranging from 168/100,000 in 2000 to 98/100,000 in 2021.
- As of 2021, prevalence of SCD was lowest in Kuwait, Lebanon, Turkey and UAE (<50/100,000) and highest in Bahrain, Oman, and Saudi Arabia (>250/100,000).
- More than one study provided estimates for Bahrain, Jordan, Oman, and Saudi Arabia:
  - In Bahrain, a cohort among eleventh grade students, 1999-2008, showed that among 60,424 students, 1.1% had SCD; whereas, a modelling study showed a prevalence of 949/100,000 and 618/100,000 in 2000 and 2021 in the general population.
  - In Jordan, prevalence, 2009-2018, among patients referred to a single-center (0.73%) was similar to a modelling study in the general population (72/100,000 and 65.4/100,000 in 2000 and 2021).
  - In Oman, 0.47% of patients at a single-center, 2004-2006, had SCD; whereas, a modelling study showed a prevalence of 289/100,000 and 273/100,000 in 2000 and 2021 in the general population.
  - In Saudi Arabia, a pre-marital genetic screening program showed prevalence of 270/100,000 in 2004 and 240/100,000 in 2009.

Incidence

- Four studies provided data on the incidence of SCD in the Middle East. The Global Burden of Disease (GBD) provided the most comprehensive data, with incidence ranging from 242/100,000 to 164/100,000 in 2021.
- As of 2021, incidence of SCD was lowest in Algeria, Turkey, Morocco, and UAE (<50/100,000) and highest in Bahrain, Libya, Oman, and Saudi Arabia (>250/100,000).
- More than one study provided estimates for Oman, Saudi Arabia, and Turkey:
  - In Oman, blood samples collected from newborns at Sultan Qaboos University Hospital between 2005 and 2007 revealed an incidence of 19 cases out of 7,837 for SCD; whereas, a modeling study estimated an incidence of 481 per 100,000 in 2000 and 503 per 100,000 in 2021 in the general population.
  - In Saudi Arabia, among pregnant Saudi women with homozygous SCD or normal hemoglobin phenotype treated at King Khalid University Hospital, the incidence of SCD was 392 out of 34,811; whereas, a modeling study estimated an incidence of 1,510 per 100,000 in 2000 and 379 per 100,000 in 2021 in the general population.
  - In Turkey, in a National Hemoglobinopathy Registry 17 out of 1988 were diagnosed with SCD; whereas, a modeling study estimated an incidence of 21.1 per 100,000 in 2000 and 13.2 per 100,000 in 2021 in the general population.

Table 2: Incidence and prevalence estimates for the Middle East region

Author (Year)	Countries	Population	Population Details	Year	Incidence	Prevalence
GBD 2021 Sickle Cell Disease Collaborators[3]	Afghanistan	SCD population (All ages 2000)	Modelling approach informed by hospital codes and insurance claims data among children and adults	2000-2021	131/100,000	84.5/100,000
		SCD population (All ages 2021)			131/100,000	82.2/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]	Algeria	SCD population (All ages 2000)		2000-2021	22.7/100,000	11.2/100,000
		SCD population (All ages 2021)			22.7/100,000	9.9/100,000
Al Arrayed et al. (2011)[9]	Bahrain	Adolescent with SCD (Overall)	Secondary school students	1999-2008	--	676/60,424
		Adolescent with SCD (1999)				68/5685
		Adolescent with SCD (2000)				75/5694
		Adolescent with SCD (2001)				68/6244
		Adolescent with SCD (2002)				64/5894
		Adolescent with SCD (2003)				74/5418
		Adolescent with SCD (2004)				78/6237
		Adolescent with SCD (2006)				73/6358
		Adolescent with SCD (2005)				59/6352
		Adolescent with SCD (2007)				67/6376
		Adolescent with SCD (2008)				50/ 6166
GBD 2021 Sickle Cell Disease Collaborators[3]	Bahrain	SCD population (All ages 2000)	Modelling approach informed by hospital codes and insurance claims data among children and adults	2000-2021	1260/100,000	949/100,000
		SCD population (All ages 2021)			1040/100,000	618/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]	Egypt	SCD population (All ages 2000)		2000-2021	151/100,000	110/100,000
		SCD population (All ages 2021)			151/100,000	104/100,000
Nezhad et al. (2018)[5]	Iran	SCA population	Volunteer couples living in Khuzestan Province, Southwest Iran	February 2014-December 2017	--	1240/17,581
GBD 2021 Sickle Cell Disease Collaborators[3]	Iran	SCD population (All ages 2000)	Modelling approach informed by hospital codes and insurance claims data among children and adults	2000-2021	227/100,000	170/100,000
		SCD population (All ages 2021)			154/100,000	94.7/100,000
Al-Hakeim et al. (2020)[4]	Iraq	SCA patients	Patients admitted to Al-Zahraa hospital for recording and treatment of hemoglobinopathies	October 2003-December 2018	--	101/1033
GBD 2021 Sickle Cell Disease Collaborators[3]	Iraq	SCD population (All ages 2000)	Modelling approach informed by hospital codes and insurance claims data among children and adults	2000-2021	215/100,000	111/100,000
		SCD population (All ages 2021)			214/100,000	97.6/100,000
Oudat et al. (2021)[6]	Jordan	SCD patients	Patients referred to Princess Iman Research and Laboratory Sciences Center	2009-2018	--	216/29,712
GBD 2021 Sickle Cell Disease Collaborators[3]	Jordan	SCD population (All ages 2000)	Modelling approach informed by hospital codes and insurance claims data	2000-2021	103/100,000	72/100,000
		SCD population (All ages 2021)			103/100,000	65.4/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]	Kuwait	SCD population (All ages 2000)		2000-2021	71.5/100,000	39.2/100,000
		SCD population (All ages 2021)			71.6/100,000	33.7/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]	Lebanon	SCD population (All ages 2000)		2000-2021	77.6/100,000	49.5/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]		SCD population (All ages 2021)			79.2/100,000	45.7/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]	Libya	SCD population (All ages 2000)		2000-2021	867/100,000	299/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]		SCD population (All ages 2021)			873/100,000	227/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]	Morocco	SCD population (All ages 2000)		2000-2021	29/100,000	13.1/100,000
		SCD population (All ages 2021)			29.1/100,000	11.2/100,000
Adly and Rajappa et al. (2008)[10]	Oman	SCD patients	Patients referred or admitted to Khoula Hospital	January 2001-December 2004	--	128/27,403
Alkindi et al. (2010)[11]	Oman	SCD patients	Blood samples of newborns at the Sultan Qaboos University Hospital	April 2005- March 2007	19/7837	--
GBD 2021 Sickle Cell Disease Collaborators[3]	Oman	SCD population (All ages 2000)	Modelling approach informed by hospital codes and insurance claims data	2000-2021	481/100,000	289/100,000
		SCD population (All ages 2021)			503/100,000	273/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]	Palestine	SCD population (All ages 2000)		2000-2021	99.9/100,000	73/100,000
		SCD population (All ages 2021)			99.5/100,000	67.4/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]	Qatar	SCD population (All ages 2000)		2000-2021	117/100,000	72.6/100,000
		SCD population (All ages 2021)		2000-2021	118/100,000	66.7/100,000
Al Kahtani et al. (2012)[12]	Saudi Arabia	SCD population	Pregnant Saudi women with homozygous SCD or with normal hemoglobin phenotype who received treatment in King Khalid University Hospital	August 2001-December 2010	392/34,811	--
Alhamdan et al. (2007)[13]	Saudi Arabia	SCD population	All premarital couples in the general population	February 2004-January 2006	--	1251/488,315
Hanafy et al. (2020)[14]	Saudi Arabia	SCD patients admitted to pediatric intensive care unit	Pediatric patients <14 years of age with confirmed diagnosis of SCD at King Salman Armed Forces Hospital	2013-2019	--	58
Memish and Saeedi et al. (2011)[15]	Saudi Arabia	Adult SCD population (Overall)	Premarital couples attending premarital and genetic counseling clinics with marriage proposals	2004-2009	--	4313/1,572,140
		Adult SCD population (2004)				645/241,825
		Adult SCD population (2005)				606/246,490
		Adult SCD population (2006)				706/236,629
		Adult SCD population (2007)				812/255,894
		Adult SCD population (2008)				823/295,018
		Adult SCD population (2009)				721/296,284
GBD 2021 Sickle Cell Disease Collaborators[3]	Saudi Arabia	SCD population (All ages 2000)	Modelling approach informed by hospital codes and insurance claims data	2000-2021	1510/100,000	1260/100,000
		SCD population (All ages 2021)			379/100,000	289/100,000
Ezzat et al. (2023)[16]	Saudi Arabia	SCA patients - Neonates	Blood samples collected from newborns at Al-Ahsa Health Cluster	--	--	25/5715
Ezzat (2023)[17]	Saudi Arabia	Adolescent with SCD	Secondary school students	--	--	4/1030
Zuair et al. (2023)[18]	Saudi Arabia	SCD patients on general internal medicine unit at hospital	Patients >14 years of age with SCD at King Saud University Medical City	2016-2021	--	160
Aydınok et al. (2017)[8]	Turkey	SCD patients	National Registry for Hemoglobinopathies	--	77/1988	--
GBD 2021 Sickle Cell Disease Collaborators[3]	Turkey	SCD population (All ages 2000)	Modelling approach informed by hospital codes and insurance claims data	2000-2021	37.8/100,000	21.1/100,000
		SCD population (All ages 2021)			31.3/100,000	13.2/100,000
GBD 2021 Sickle Cell Disease Collaborators[3]	UAE	SCD population (All ages 2000)	Modelling approach informed by hospital codes and insurance claims data	2000-2021	29.6/100,000	21.1/100,000
		SCD population (All ages 2021)			28.8/100,000	16.5/100,000

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Abbreviations

EMBASE, Excerpta Medica Database; GBD, Global Burden of Disease; MEDLARS/MEDLINE, Medical Literature Analysis and Retrieval System; SCA, sickle cell anemia; SCD, sickle cell disease; SLR, systematic literature review.

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Conclusions

- Prevalence and incidence of SCD in the Middle East is highest in Bahrain, Saudi Arabia, and Oman.
- Differences in data sources and research methodology in the source studies have created challenges in understanding and comparing epidemiology estimates in the region.
- Continued implementation of newborn screening programs and registries will likely allow for more accurate estimates and thus optimized care for individuals with SCD.

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