Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Short Communication

COVID-19 and sickle cell disease in Bahrain

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ABSTRACT

Introduction: Coronavirus disease 2019 (COVID-19) is caused by a newly identified strain of the coronavirus family that has been shown to affect the hemoglobin beta chain, the same chain that has sickle cell disease (SCD) mutation. This study was undertaken to see if COVID-19 infection increased disease severity in patients with SCD.
Methods: Mass screening of the Bahraini population was undertaken between February and April 2020.
Results: A total of 38,092 Bahraini people were tested for COVID-19 during this period; 378 (1%) were SCD patients. Six patients with SCD had COVID-19 (1.6%): three remained asymptomatic, two had mild symptoms and one required oxygen therapy. The SCD patients had a similar average length of stay when compared with non-SCD COVID-19 patients (10.7 days).
Conclusion: The infection rate, clinical course and viral clearance seen for the SCD patients with COVID-19 were no different to those without SCD.

Introduction

Coronavirus disease 2019 (COVID-19) is caused by a newly identified strain of the coronavirus family: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Anon, 2020) Virus isolation and nucleic acid sequencing have shown that the novel coronavirus is a positive-stranded RNA8 (Wenzhong and Hualan, 2020a). It has been suggested that the virus acts through ACE2, CD147 and CD26 receptors on the erythrocytes, resulting in a hemoglobinopathy interaction with the hemoglobin molecule; viral ORF8 surface glycoproteins combine with porphyrin to form a complex with 1-beta chain of hemoglobin, with or without hemolysis forming a dysfunctional hemoglobin, resulting in decreased heme oxygen-carrying capacity (Wenzhong and Hualan, 2020a; Liu and Li, 2020; Wenzhong and Hualan, 2020b).

Sickle cell disease (SCD) is an inherited hemoglobinopathy due to a mutation in the hemoglobin-beta gene found on chromosome 11. SCD affects 1% of the Bahraini population (Al Arrayed and Haites, 1995) and causes the red blood cells to sickle, causing a sickle cell crisis that may result in hypoxic injury to organs. The prevalence of SCD in Bahrain has decreased from the 1980s when the prevalence was 2%, due to education and a premarital testing program that tests for both sickle cell and thalassemia (Al Arrayed and Haites, 1995). Couples with risk of passing on hemoglobinopathies are referred for genetic counselling. In addition, a screening program for SCD has been introduced, where all newborn babies are screened for the disease (Shaikha Al Arrayed et al., 2009). Sickle cell disease diagnosis is established by hemoglobin electrophoresis and confirmed by a positive sickling test result. Patients with SCD are all in a regular follow-up program and managed with disease modifying agents such as hydroxyurea. Patients are referred for hematopoietic stem cell transplantation when possible.

Infections may induce sickle cell crisis requiring hospital admission (Booth et al., 2010). Several anecdotal reports have suggested worse COVID-19 complications in SCD (McCloskey et al., 2020; Hussain et al., 2020; Beerkens et al., 2020; De Luna et al., 2020). A review of the literature on COVID-19 and 19 SCD cases highlighted that SARS-CoV-2 infection should be considered to be an important triggering factor of sickle cell crisis and that there are many unanswered questions, including the potential increased risk of SARS-CoV-2 infection in SCD and if there is a role for preventative red blood cell exchange (Sahu et al., 2020). This

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study was undertaken to determine if patients with SCD are a high-risk group, as has been suggested (Roy et al., 2020).

Methods

Mass population screening for COVID-19, including mobile clinics, was established in Bahrain. In this cross-sectional study, all COVID-19 testing data on the Bahraini population was reviewed from the start of the screening in February until 25 April 2020. The SCD status of subjects was acquired from hospital medical records and the E-government authority of open data portals. Further details on the length of stay and time to viral clearance were collected from the medical records of all patients with COVID-19. The diagnostic test used for SARS-CoV-2 was real-time RT-PCR: all were tested for E gene and positive samples were confirmed after being tested for N gene and RdRp gene (from Tib Molbiol) (Corman et al., 2020). Viral clearance was defined as two RT-PCR-negative tests 24 h apart. Ethical permission was granted by the National Research Committee of COVID-19.

Statistical analysis

Statistical analysis was performed using the STATA statistical computer package (StataCorp 2013, Stata Statistical Software). Differences between the patients with and without SCD were compared by a two-way *t*-test.

Results

Table 1 shows the demographics between those with and without SCD. The Bahraini population is 689,714, and a total of 6933 (1%) Bahraini people are affected by SCD. During this period 38,092 Bahraini people were tested for COVID-19, of whom 378 (1%) were SCD patients. Of the 38,092 individuals tested for COVID-19, 696 (1.83%) were infected; 387 (1% of those tested) also had SCD, of whom six (1.6%) had COVID-19 ($p = 0.55$). Of the six SCD with COVID-19 (Table 2), three remained asymptomatic and one developed mild symptoms of an upper respiratory tract infection. Two patients developed moderate symptoms and one of them required oxygen therapy. These two patients did not require ventilator support or ICU care. The maximum length of stay was 12 days. All six patients were discharged; their average length of stay was 9.8 days. The SCD patients had a similar average length of stay when compared with non-SCD COVID-19 patients (10.7 days), which is the time to viral clearance (two RT-PCR negative tests 24 h apart) ($p = 0.11$, not significant).

Discussion

Whilst there were six patients with SCD who developed COVID-19 disease, it can be seen that severity of COVID-19 disease was no worse compared with those without SCD. The time to viral clearance was no different between those with and without SCD, with a similar hospital stay; further, in the course of the infection, one patient required oxygen therapy and none required ventilator support. In addition, no SCD patient suffered a sickle cell crisis as had been hypothesized, given that the SARS-CoV-2 virus may affect the hemoglobin beta chain (Wenzhong and Hualan, 2020a) and that infection may precipitate a crisis (Booth et al., 2010). Others have hypothesized that in beta-thalassemia, where there is a fault in hemoglobin beta-chain synthesis, this may result in immunity to SARS-CoV-2 infection (Lansiaux et al., 2020) and may therefore be protective, but that was not seen in the SCD patients who were studied.

At the time of writing, the prevalence of COVID-19 disease in Bahrain was approximately 0.1%, with 2464 documented cases. A total of 114,110 tests had been conducted, reaching about 71 tests per 1000 people. Of the 2464 cases, eight deaths had been recorded, 1189 cases had recovered and 1447 cases had been admitted. All COVID-19 cases had been admitted to either an isolated COVID-19 ICU, hospital or isolation facility, depending on the patients' medical requirements.

The percentage of the tested SCD people (1%) reflected the overall population with SCD within the Bahraini community. 1.8% of all COVID-19 tested individuals in this study were positive, including those with and without SCD, suggesting that there is no increased infection rate in those with SCD. However, the main limitation of this observational study was the low number of SCD who had COVID-19 and the possibility of a type 2 statistical error due to low power.

In conclusion, the infection rate, clinical course and viral clearance seen for SCD patients with COVID-19 were no different to those without SCD. It is therefore encouraging that people with SCD are not at increased risk during the course of COVID-19 infection, nor at risk of a sickle cell crisis.

Table 1
Characteristics of non-sickle cell and sickle cell disease patients who were tested for SARS-CoV-2 infection.

Factor	Level	Non-sickle cell disease	Sickle cell disease
N		37,705	387
Age in years, median (IQR)		33 (24, 46)	30 (23, 40)
Gender	Female	14,305 (37.9%)	165 (42.6%)
	Male	23,400 (62.1%)	222 (57.4%)

Ethics approval and consent to participate

The study was approved by the National Covid-19 Ethics Committee.

Consent for publication

All authors gave their consent for publication.

Availability of data and materials

All the data for this study will be made available upon reasonable request to the corresponding author.

Funding

None declared.

Conflict of interest

None declared.

Author contributions

AA and SA analyzed the data and wrote the manuscript. OY, MS and SA contributed to study design, collected, analyzed, and interpreted data and edited the manuscript. MA supervised data collection, analyzed data and edited the manuscript. SLA and SO interpreted data and the wrote the manuscript. All authors reviewed and approved the final version of the manuscript.

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Table 2
Characteristics of the six patients with sickle cell disease and SARS-CoV-2 infection.

Age (years)	Gender	SCD genotype	Chief complaints	SARS-Cov2 PCR	Chest X-ray	Hb (g/dL)	WBC (x10^9/L)	CRP (mg/L)	Maximum oxygenation support	Management	Discharge day
23	Male	HbSS	Asymptomatic: tested positive on return from travel	Positive	Normal	17.1	3.28	N/A	None	Observation alone	10
40	Male	HbSS	Fever, myalgia, cough and diarrhea	Positive	Infiltrates	7.4	13.73	137	Nasal cannula 2 L O_2	Blood transfusion, antibiotics	10
52	Male	HbSS	Asymptomatic: tested positive on return from travel	Positive	Normal	10.2	6.77	7.3	None	Observation alone	12
25	Male	HbSS	Asymptomatic: tested positive on contact tracing	Positive	Normal	12.8	3.71	4.5	None	Observation alone	8
21	Female	HbSS	Fever, loss of smell and taste	Positive	Normal	13.8	4.61	4.22	None	Supportive and IVF	8
24	Female	HbSS	Fever and myalgia	Positive	Normal	8.5	11.63	1.48	None	Antibiotics, supportive care	9

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