Case Series

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# Coronavirus disease 2019 (COVID-19) in special groups: A single-center experience in sickle cell disease patients in Saudi Arabia

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**Abstract:**

**BACKGROUND:** Sickle cell disease (SCD) is a group of hereditary diseases, inherited as autosomal recessive disorder, which causes mutation in the β-globin gene. As a result, there is a change in the sixth amino acid from glutamic acid to valine. The affected red blood cell is then prone to polymerization and sickling crisis under conditions of low oxygen tension. One of the major causes of mortality in SCD is acute chest syndrome (ACS). On the other hand, coronavirus disease 2019 (COVID-19) is a pandemic disease that carries significant mortality and morbidity worldwide with unknown outcomes in the affected SCD population. This study was created for that reason.

**MATERIALS AND METHODS:** We report a case series of ten SCD patients who were affected by COVID-19 and required admission between May 1, 2020, and October 30, 2020, at a tertiary care hospital in Dhahran, eastern region of Saudi Arabia. Historical data were obtained retrospectively from electronic records. MS Excel was used for data entry, and SPSS version 23 was used for data analysis.

**RESULTS:** The mean age of the patients involved in the study was 32 years, and the mean duration of symptoms was 5.7 days. None required critical care admission, and there was no mortality. All patients were discharged from hospital in good condition with no requirement of home oxygen.

**CONCLUSION:** Although we expected a fatal outcome of SCD patients affected by COVID-19 infection, our limited case series showed favorable disease behavior and outcome, with a suspicion of underlying unclear protective mechanism from serious complications. However, further studies are required to better understand COVID-19 behavior in SCD patients.

**Keywords:**

Blood transfusion, coronavirus disease 2019, hydroxyurea, mechanical ventilation, mortality, sickle cell disease

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## Introduction

Sickle cell disease (SCD) is a widely distributed hereditary disease, with an estimated global incidence up to 400,000 neonates per year.[1] Although the majority of cases detected in sub-Saharan Africa are one-third of adults carrying sickle cell-defected genes, the Middle East countries have many cases.[1,2] The prevalence of SCD in Saudi Arabia varies among provinces, with the highest in the Eastern province (1.2%).[3] However, owing to unavailability of Saudi registry for SCD, data taken from previous hospital-based studies showed mortality rate as a result of acute chest syndrome (ACS).[3] ACS is manifested by fever, chest pain, dyspnea, and cough with decreased oxygen saturation to less than 94% and lung infiltration



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in chest X-ray. The presentation of ACS is similar to the respiratory presentation of coronavirus disease 2019 (COVID-19) infection, which was announced as a pandemic disease early in March 2020. Since then, there have been expectations of high mortality rates as a result of the combination of the two fatal pulmonary conditions, COVID-19 infection and SCD/ACS. In a study by Panepinto *et al*., in the United States which reported 122 SCD patients affected by COVID-19, 69% of the patients required admission to hospital, 11% required admission to the critical care unit, 3% required mechanical ventilation support, and there was a mortality rate of 7%.[4] The authors concluded that people who have SCD and get affected by COVID-19 are at a higher risk for severe disease and higher fatality rate.[4] However, in a study by Jean *et al.*, done in France, in which 83 SCD patients infected by COVID-19 were enrolled, they concluded that there was neither increased morbidity nor mortality.[5] In view of different ethnicities and SCD genotypes and phenotypes in Saudi Arabia in comparison to other countries, the severity and outcome of COVID-19 in SCD patients among Saudi citizens are worth reporting. Thus, the main question behind this study is to evaluate the impact of COVID-19 infection on SCD patients' morbidity and mortality. In this case series, we present ten cases of SCD patients affected by COVID-19 who required hospital admission as a unicenter study, but with a view to a future national multicenter study for a better understanding of the behavior of COVID-19 on affected SCD patients.

## Materials and Methods

Approximately 383 candidates of COVID-19–positive cases were admitted to the hospital between May 1, 2020, and October 30, 2020. A retrospective observational study in a tertiary care hospital was conducted on ten patients with sickle cell. Any SCD patient, i.e., HB SS, HBS-beta beta [HB SB], HB SC, HB SE, or HB SD, aged ≥18 years, affected by COVID-19 and admitted to the hospital was eligible for the study. Sickle cell trait or non-SCD, as well as pediatric age group and SCD patients not requiring admission, were excluded.

Ethical approval was obtained from the institutional review board (IRB) vide letter No. AFHER-IRB-2021-009 dated 23/05/2021 and informed written consent was taken from all participants involved in this case series. Moreover, all data taken in this study were used only for the purpose of this study. Patients' names were not collected; instead, each file was encoded with a number for further analytical purposes.

Historical data were obtained retrospectively from electronic records. Data on the presenting symptoms, laboratory results, the need for blood transfusion (simple or exchange), oxygen or/and intubation requirement, as well as the outcome of the disease were evaluated.

Laboratory data were obtained retrospectively from previous results. On admission and before discharge, some parameters including hemoglobin level, white cell count, lymphocyte count, neutrophil count, platelet count, lactate dehydrogenase, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were assessed. Total bilirubin, C-reactive protein, D-dimer, ferritin, and creatinine, as well as baseline Hb S and Hb F levels were also taken.

Confirmation of all SCD patients with SARS-CoV-2 (COVID-19) was done by nasopharyngeal swab. Those who were clinically stable and did not require oxygen by high-flow nasal cannula maintaining peripheral oximetry saturation >94% were admitted to COVID-19 unit. Critical care admission was required if oxygen requirement increased or the patient was unable to maintain oxygen above 94% with high-flow oxygen or if the patient showed any elements of hemodynamic instability.

As most of the patients presented with pain crises, with or without respiratory symptoms resembling pneumonia/ACS, all cases were managed with hydration and pain control measurement, in addition to home medications such as folic acid and hydroxyurea with individualized dose. Requirements for thromboprophylaxis, antibiotics, steroids, as well as other anti-COVID-19 measures, were administered on the basis of indication and patient situation guided by the Ministry of Health (MOH) recommendations.[6] If the oxygen saturation of the patient dropped below 94%, suggestive of ACS, they received a top-up with simple blood transfusion (if hemoglobin level is <8 g/dl) or exchange transfusion (if hemoglobin level ≥8 g/day).

Patients were discharged from critical care, COVID-19 unit, or hospital according to the recommendations of the MOH.

Our primary end point was to assess the clinical course of SCD in the presence of COVID-19 infection. Thus, the main question in this study was to evaluate the impact of COVID-19 infection on SCD patients' morbidity and mortality.

After collecting the data, MS Excel was used for data entry, and SPSS version 23 (IBM Corp., Armonk, NY) was used for data analysis. Frequency and percentage were used to describe categorical variables, while mean and standard deviations (SDs) were used to describe continuous variables. Chi-square test and *t*-test were used to describe the relation among variables. We used

the paired *t*-test to compare admissions and discharge. Wilcoxon's singled-rank test was used to test the significance. All data were normally distributed. All statements were considered statistically significant when $P \leq 0.05$.

## Results

In this study, we collected the data of 10 SCD patients with a mean age of 32 years infected by COVID-19. Of these 10 patients, 6 were females and five were from the southern region of the Kingdom. According to the genotypes of SCD, eight patients had HB SS and two had HB SB thalassemia. The most common reported symptoms of COVID-19 were bone pain, fever, and cough. Moreover, 60% of patients had other comorbidities, including treated pulmonary tuberculosis, bronchial asthma, diabetes mellitus type one, alloimmunization, glucose 6 phosphate dehydrogenase deficiency, and Grave's diseases. The mean duration of symptoms was 5.7 days, with a SD of 4.24 days. All patients had anemia, elevated ferritin, and elevated bilirubin on admission, but 60% had leukocytosis, 40% had elevated AST, and 20% had elevated ALT [Table 1].

In Table 2, we show the clinical characteristics of each patient, indicating that most of the patients had had at least one hospital admission per year, while half the number had complications of SCD. Moreover, cholecystectomy was the most common procedure (60%).

Laboratory values at baseline and during hospitalization are summarized in Table 3. Here, we find that hemoglobin was significantly increased after treatment with and without transfusion from 8.44 on admission to 9.32 upon discharge ($P = 0.012$). White blood cell was significantly decreased from 12.84 on admission to 9.72 upon discharge ($P = 0.032$). Moreover, neutrophils, lymphocytes, and creatinine had decreased after treatment; however, the difference was not significant. On the other hand, there was a significant reduction in D-dimer level with a mean of 5.35 on admission to 2.68 upon discharge ($P = 0.021$). All other laboratory results had decreased upon discharge compared to baseline; however, the differences were not significant.

All patients (100%) had high HB F level with a mean of 13.65 (SD 6.36) [Table 3].

Radiological investigation for all cases was done, including chest X-ray upon presentation and whenever needed. We present the worst chest X-ray during admission for each patient, two of which (20%)

**Table 1: Biological characteristics of sickle cell disease patients with coronavirus disease-2019 infection (*n*=10)**

| Characteristics | *N* (%) |
|---|---|
| Age | |
| Mean±SD | 31.8±14.5 |
| Gender | |
| Male | 4 (40.0) |
| Female | 6 (60.0) |
| Geographical area | |
| Central | 2 (20.0) |
| Northern | 1 (10.0) |
| Southern | 5 (50.0) |
| Western | 2 (20.0) |
| Eastern | 0 |
| SC type | |
| HB SS | 8 (80.0) |
| HB SB Thai | 2 (20.0) |
| Symptoms | |
| Fever | 4 (40.0) |
| Bone pain | 8 (80.0) |
| Cough | 4 (40.0) |
| Nausea | 1 (10.0) |
| Vomiting | 0 |
| Shortness of breath | 0 |
| Chest pain | 1 (10.0) |
| Comorbidities | |
| Alloimmunization | 6 (60.0) |
| Treated Tb | 2 (20.0) |
| BA | 1 (10.0) |
| Diabetes mellitus type 1 | 1 (10.0) |
| G6PD deficiency | 1 (10.0) |
| Grave's disease | 1 (10.0) |
| Procedures (past surgical history) | |
| Cholecystectomy | 6 (6.0) |
| Splenectomy | 3 (30.0) |
| Bronchoscopy with positive BAL for PCP | 1 (10.0) |
| Caesarean section (C-section) | 2 (20.0) |
| Umbilical hernia repair | 1 (10.0) |
| Tubal ligation | 1 (10.0) |
| Appendectomy | 1 (10.0) |
| Adenoidectomy | 1 (10.0) |
| Tonsillectomy | 1 (10.0) |
| Duration of symptoms | |
| Mean±SD | 5.7±4.24 |
| Laboratory findings | |
| Anemia | 10 (100) |
| Elevated bilirubin | 10 (100) |
| Elevated ferritin | 10 (100) |
| Leukocytosis | 6 (60.0) |
| Elevated AST | 4 (40.0) |
| Elevated ALT | 2 (20.0) |

SD=Standard deviation, BA=Bronchial asthma, AST=Aspartate aminotransferase, ALT=Alanine aminotransferase, G6PD=Glucose 6 phosphate dehydrogenase, TB=Tuberculosis, HB=Hemoglobine, SC=Sickle cell, SB=Sickl/beta thalssemia, SS =Homozygous disease, BAL=Broncho-alveolar lavage, PCP =Pneumocystis carinii pneumonia

**Table 2: Clinical characteristics, comorbidities, and complications of coronavirus disease-2019 among persons with sickle cell disease**

| | Age | Gender | Geographic area | Sickle cell type | Symptoms at presentation | Comorbidities | Duration of symptoms | Complications | Procedures | Past 1 year admission |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 24 | Male | Southern | HB SS | Fever, cough | Treated pulmonary TB | 12 | NA | Cholecystectomy, splenectomy, positive bronchial alveolar lavage for PCP | 1 |
| 2 | 37 | Female | Southern | HB SS | Bone pain | Alloimmunization, bronchial asthma | 14 | History of hepatopathy 3 times requiring exchange transfusion, history of abortion | Cholecystectomy | 14 |
| 3 | 30 | Male | Central | HB SS | Bone pain | NA | 4 | NA | Cholecystectomy | 2 |
| 4 | 49 | Female | Central | HB SS | Fever, cough, bone pain | NA | 4 | NA | Cholecystectomy, Cesarian section, umbilical hernia repair, tubal ligation | 1 |
| 5 | 40 | Female | Northern | HB SS | Bone pain | NA | 1 | Acute Chest Syndrome | Appendectomy, adenoidectomy | 2 |
| 6 | 25 | Male | Southern | HB SB Thal | Fever, bone pain | NA | 6 | NA | Cholecystectomy, splenectomy | 6 |
| 7 | 18 | Female | Southern | HB SB Thal | Cough, bone pain, nausea | T1DM | 2 | NA | NA | 24 |
| 8 | 60 | Male | Southern | HB SS | Fever, cough | G6PD def | 4 | AVN of hip joints, Iron overload | Cholecystectomy | 1 |
| 9 | 18 | Female | Western | HB SS | Bone pain | Grave's disease | 3 | Osteomyelitis | Splenectomy, tonsillectomy | 3 |
| 10 | 19 | Female | Western | HB SS | Bone pain, Chest pain | Alloimmunization | 7 | Postcentral nervous system crisis | NA | 0 |

G6PD def=Glucose 6 phosphate dehydrogenase deficiency, HB SB Thal=HBS-beta thalassemia, T1DM=Diabetes mellitus type one, Pulmonary TB=Pulmonary tuberculosis, NA=Not applicable, HB=Hemoglobine, SS=Homozygous disease, SB=Sickl/beta thalssemia, AVN=A vascular necrosis, PCP=Pneumocystis carinii pneumonia

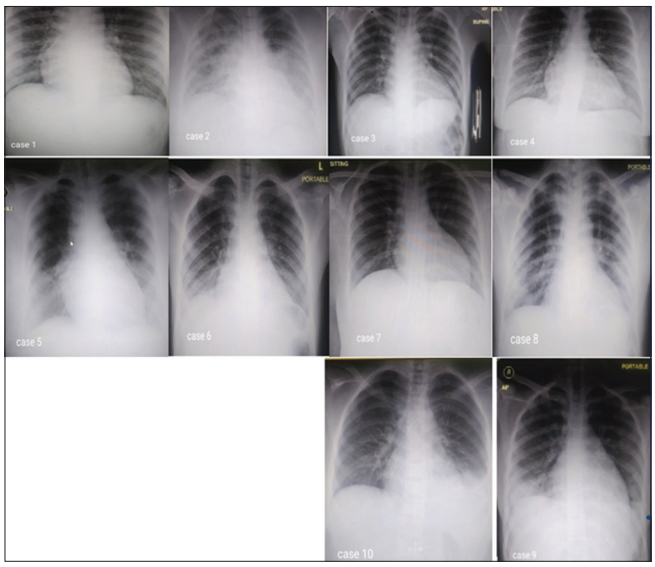

**Figure 1:** Chest X-rays with worst appearance during admission with COVID-19 for each sickle cell disease case involved in the study

showed normal study (case #3 and 7,) three (30%) showed chest infiltrates or consolidation (case #2, 9, and 10), and the remaining five cases (50%) represent typical COVID-19 peripheral chest hazy appearance (case # 1, 4, 5, 6, and 8) [Figure 1].

Maintenance of hydroxyurea was continued in the 3 cases (30%), and the remaining 70% were not on hydroxyurea because of either allergy or previous refusal of the drug. Dexamethasone, a modality for treating and reducing complications of COVID-19, was required in 30% of the cases. However, neither tocilizumab nor hydroxychloroquine was used. For one patient, favipiravir 1800 mg twice a day for 1 day was prescribed and then 800 mg bid for 7 days. The 3 patients who were on hydroxyurea did not require dexamethasone, favipiravir, or tocilizumab. Furthermore, there was no correlation between the use of hydroxyurea and the need for transfusion (simple or exchange) [Table 4].

All patients were discharged after treatment with zero mortality; 40% of patients needed oxygen supplement; 90% needed simple transfusion; and 30% needed exchange transfusion; but none required intensive care unit admission or intubation [Table 4]. The median length of stay in hospital was 5.3 days; only two cases exceeded 10 days of admission.

**Table 3: Laboratory data for coronavirus disease-2019 cases among persons with sickle cell disease**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Mean | *P* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hb (A) (g/dl) | 8.23 | 6.67 | 10.40 | 8.00 | 8.63 | 7.99 | 8.92 | 8.37 | 7.80 | 9.35 | 8.44 | 0.012* |
| Hb (D) (g/dl) | 10.30 | 8.08 | 9.27 | 9.00 | 8.58 | 10.20 | 10.00 | 8.49 | 8.69 | 10.60 | 9.32 | |
| WBC (A) (×10³/ul) | 13.00 | 15.40 | 14.00 | 9.11 | 14.60 | 14.70 | 8.31 | 7.67 | 21.00 | 10.60 | 12.84 | 0.032* |
| WBC (D) (×10³/ul) | 7.94 | 8.10 | 9.55 | 8.68 | 10.90 | 15.90 | 7.42 | 8.03 | 10.80 | 9.90 | 9.72 | |
| Neutrophils (A) (×10³/ul) | 9.95 | 8.38 | 8.61 | 4.69 | 8.83 | 9.13 | 3.87 | 2.76 | 16.60 | 7.27 | 8.01 | 0.123 |
| Neutrophils (D) (×10³/ul) | 3.71 | 2.83 | 5.11 | 3.21 | 5.56 | 12.30 | 5.30 | 4.69 | 6.80 | 8.10 | 5.76 | |
| Lymphocytes (A) (×10³/ul) | 1.48 | 4.33 | 3.12 | 3.44 | 3.36 | 2.99 | 3.29 | 3.51 | 1.87 | 2.19 | 2.96 | 0.315 |
| Lymphocytes (D) (×10³/ul) | 2.94 | 3.70 | 2.32 | 4.68 | 3.29 | 1.63 | 1.73 | 2.44 | 1.98 | 1.40 | 2.61 | |
| Creatinine (A) (umol/L) | 47.00 | 41.00 | 73.00 | 40.00 | 26.00 | 44.00 | 36.00 | 71.00 | 60.00 | 41.00 | 47.90 | 0.675 |
| Creatinine (D) (umol/L) | 44.00 | 51.00 | 52.00 | 36.00 | 51.00 | 46.00 | 32.00 | 62.00 | 58.00 | 30.00 | 46.20 | |
| D-dimer (A) (mg/L) | 11.72 | 1.45 | 4.49 | 2.94 | 2.88 | 10.42 | 1.91 | 4.18 | 11.01 | 2.51 | 5.35 | 0.021* |
| D-dimer (D) (mg/L) | 7.09 | 0.00 | 4.49 | 0.95 | 1.88 | 1.38 | 1.15 | - | 3.96 | 3.19 | 2.68 | |
| CRP (A) (mg/L) | 82.00 | 2.00 | 111.00 | 5.00 | 21.00 | 16.60 | - | 152.00 | 132.00 | 101.00 | 69.18 | 0.621 |
| CRP (D) (mg/L) | 9.00 | 1.00 | 13.00 | 5.00 | 14.30 | 166.00 | 7.40 | 165.00 | 51.30 | 41.00 | 47.30 | |
| Ferritin (A) (ng/ml) | 1411.00 | 5653.00 | 473.00 | 459.00 | 836.00 | 3930.50 | 439.00 | 7819.00 | 271.00 | 2454.00 | 2374.55 | 0.213 |
| Ferritin (D) (ng/ml) | 1411.00 | 3809.00 | 556.00 | 564.00 | 782.00 | 878.70 | 1029.00 | 5298.00 | 267.00 | 2123.00 | 1671.77 | |
| T.BIL (A) (umol/L) | 106.00 | 14.00 | 7.60 | 20.00 | 14.30 | 19.20 | 23.00 | 59.10 | 65.00 | 45.90 | 37.41 | 0.9 |
| T.BIL (D) (umol/L) | 41.00 | 7.00 | 40.00 | 20.00 | 29.20 | 11.20 | 17.80 | 54.00 | - | 57.00 | 30.80 | |
| AST (A) (U/L) | 134.00 | 156.00 | 47.00 | 34.00 | 30.20 | 55.60 | 35.80 | - | - | 32.80 | 65.68 | 0.21 |
| AST (D) (U/L) | 107.00 | 67.00 | 101.00 | 35.00 | 33.50 | 22.30 | 48.20 | 63.60 | 18.80 | 37.60 | 53.40 | |
| ALT (A) (U/L) | 93.00 | 33.00 | 30.00 | 32.00 | 35.80 | - | - | 65.60 | 34.90 | 42.00 | 45.79 | 0.123 |
| ALT (D) (U/L) | 138.00 | 268.00 | 37.00 | 29.00 | 34.50 | - | - | - | - | 40.00 | 91.08 | |
| LDH (A) (U/L) | 868.00 | 845.00 | 547.00 | 419.00 | 609.00 | 455.00 | 390.00 | 528.00 | 478.00 | 349.00 | 548.80 | 0.058 |
| LDH (D) (U/L) | 561.00 | 609.00 | 698.00 | 430.00 | 472.00 | 401.00 | 390.00 | 429.00 | 350.00 | 279.00 | 461.90 | |
| HB F (A) (%) | 4.6 | 12.4 | 7.3 | 18 | 16 | 5.2 | 18 | 21 | 22 | 12 | 13.65 | 0.9 |
| HB F (D) (%) | 2.3 | 6 | 4 | 16.9 | 10 | 2.9 | 8.4 | 13.7 | 14 | 3.9 | 8.21 | |
| HB S (A) (%) | 86 | 70 | 78 | 67 | 74 | 83 | 59 | 70 | 73 | 75 | 73.5 | 0.71 |
| HB S (D) (%) | 30 | 41 | 56 | 58 | 60 | 43.6 | 47.7 | 44.5 | 78 | 40 | 49.88 | |

*(A) upon Admission and (D) upon Discharge. Hb=Hemoglobin level, WBC=White cell count, lymphocyte count, neutrophil count, platelet count, LDH=Lactate dehydrogenase, AST=Aspartate aminotransferase, ALT=Alanine aminotransferase, T.BIL=Total bilirubin, CRP=C-reactive protein, HB S=Hemoglobine S, HB F=Hemoglobine F

Furthermore, we found that the need for oxygen supplementation during treatment was age related (35.75 years compared with 29.5 years of patients who did not need oxygen supplementation), gender related, and HB S genotype. In contrast, we found that more younger patients and males required exchange transfusion [Table 4].

## Discussion

Sickle cell patients are known to have structural defects in the defense against infection.[7-9] Patients' susceptibility to infections appears to be associated with dysfunction of the immune system and decreased organ reserves.[7,10] The cause of sinopulmonary and recurrent urinary tract infections in patients is impaired phagocyte function due to asplenia.[9] However, it is not clear whether there is a significant predisposition to viral infections. On the other hand, the cytotoxic function of NK cells is enhanced, and naive cytotoxic T lymphocytes secreting interferon-γ are activated.[11] Tissue and organ damage worsens the natural barrier against infectious agents. Vaso-occlusive crises, endothelial activation, and lifelong inflammatory conditions cause varying degrees of tissue and organ damage in patients.[12] Infections are major causes of morbidity and mortality in SCD individuals because of tissue hypoperfusion, functional hyposplenism, disproportionately high inflammatory overload, or hypoventilation.[13,14] The reason for this difference is not clear.

It seems that patients with SCD adhered more than everyone to the protective measures set by the World Health Organization and applied by society because of the consequences of the COVID-19 epidemic. Referral rates, a monitoring system that is part of the Basque Sickle Cell Care (BAS-CARE) program, and social media accounts used by patients support this observation.[15] However, the incidence of COVID-19 infections reported in the BAS-CARE system was found to be higher than in the general population. It is hypothesized that in addition to susceptibility to infection, other family factors may contribute to the high incidence of COVID-19 infection in patients. Almost all SCD patients living in the Eastern Mediterranean have an Eti-Turkish lifestyle with large families. The factor may be infection of the family members of the patients.[16,17]

**Table 4: Patient's needs for $O_2$, intensive care units, intubation or transfusion, and drug required during stay in the hospital**

| | $O_2$ requirement | | ICU admission | | Intubation | | Transfusion simple | | Transfusion exchange | | Hydroxyurea | | Steroid | | Convalescent plasma | | Tocili zumab | | Anti-viral | | Chloroquine | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | | No | Yes | No | Yes | No | Yes | No | Yes | No |
| 1 | | * | | * | | * | * | | * | | * | | | * | | * | | * | | * | | * |
| 2 | | * | | * | | * | * | | | * | * | | | * | | * | | * | | * | | * |
| 3 | | * | | * | | * | | * | | * | | * | | * | | * | | * | | * | | * |
| 4 | | * | | * | | * | * | | | * | | * | | * | | * | | * | | * | | * |
| 5 | * | | | * | | * | * | | | * | | * | Dexamethasone 8 mg bid for 3 days | | | * | | * | | * | | * |
| 6 | * | | | * | | * | * | | * | | * | | Dexamethasone 8 mg od for 1 day | | | * | | * | | * | | * |
| 7 | | * | | * | | * | * | | | * | | * | Dexamethasone 5 mg od for 3 days | | | * | | * | | * | | * |
| 8 | * | | | * | | * | * | | | * | | * | | * | | * | | * | | * | | * |
| 9 | * | | | * | | * | * | | | * | | * | | * | | * | | * | | * | | * |
| 10 | | * | | * | | * | * | | * | | | * | | * | | * | | * | Favipiravir | | | * |
| Total | 4 | 6 | 0 | 10 | 0 | 10 | 9 | 1 | 3 | 7 | 3 | 7 | | 7 | | 10 | | 10 | 1 | 9 | 0 | 10 |

ICU=Intensive care unit

Mortality rate from COVID-19 in Saudi Arabia is lower than other countries. However, understanding the behavior and pathogenesis of the disease in concomitance with other chronic illnesses such as SCD, which affects a significant number of Saudi citizens, is required.

Therefore, we retrospectively reviewed clinical data of 10 SCD patients who were positive for SARS-CoV-2 (COVID-19). The mean age was 32 years, which is in agreement with the study by Ramachandran *et al*., in which the mean age ranged between 19 and 40.[18] However, this was slightly different from the study by Arlet *et al*., which covered a wide age range (12 and 74 years).[5]

The most common presenting symptoms were bone pain, cough, and fever in 80%, 40%, and 40% of cases, respectively. Strikingly, presentations with chest pain and other respiratory symptoms were insignificant. In comparison to the French study, 54% of cases developed body pain or vaso-occlusive crisis, which is in agreement with the presentation of our cases. However, approximately 28% of cases in the French study presented with ACS, which is unlike our cohort.[5] Although body pain was one of the most common presenting symptoms, this was not supported by some other case series, in which fever or being asymptomatic was superior to body pain when the diagnosis of COVID-19 infection was made.[18,19] When it comes to the outcome of SCD genotypes with COVID-19 infection, HB SS/SB thalassemia seems to be more common but less fatal than HB SC, which has a worse outcome as reported in other studies.[18,5]

The severity of COVID-19 infection and progression of the disease, as well as the need of oxygen supplementation, critical care admission or intubation, and mortality were evaluated. Four cases (40%) required oxygen supply therapy to maintain $SaO_2$ saturation ≥94%, but none required intubation or critical care admission. This is contrary to some studies in which some cases required intubation and critical care admission, and some died.[5,18,20]

Pre-existing comorbidities were reported as a risk factor for poor outcomes in SCD patients affected by COVID-19; however, this was not so in our study sample.[18,20,21] The reason may be that our case cohort involved a younger age group with fewer comorbidities.

All our cohort had a high HB F level at baseline with a mean of 13.65%. The reason could be that our SCD patients had a milder course and hence a better outcome. Moreover, almost all our cases required blood transfusion, whether simple or exchange transfusion, regardless of the SCD genotypes and phenotypes, which agrees with other cohorts.[5,18,22,23]

Hydroxyurea has changed the prognosis of SCD patients. A study showed that hydroxyurea could reduce frequency, length of hospitalization, as well as severity of the crisis. In our cohort, three cases were getting their maintenance dose of hydroxyurea, whereas seven were not on hydroxyurea either because of allergy or refusal. However, there was no difference in outcome or the need for intubation between those who received hydroxyurea and those who did not. On the other hand, the length of hospital stay was longer in 65% of the patients receiving hydroxyurea, but it was not significant for the limited number of cases. These data agree with the study by Arlet *et al*., in which findings did not support any indication of a protective mechanism of hydroxyurea in SCD with COVID-19 as it did not provide protection from critical care unit admission or stop the need for transfusion.[5]

Pain management (paracetamol and morphine as needed), as well as intravenous fluid and antibiotics (ceftriaxone intravenously and oral azithromycin) if indicated together with such vitamin support as Vitamin D and C, was the main strategy in treating our patients. None required hydroxychloroquine, tocilizumab, or convalescent plasma. One case required favipiravir, and three cases required dexamethasone. There was no standard guideline in managing SCD with COVID-19 during the first peak of the pandemic. Most of the reviewed reports from other studies treated patients with pain management, hydration, and antibiotics with or without blood transfusion even in ACS such as in cases.[18,19,21,24] Treatment with tocilizumab in SCD complicated by ACS in COVID-19–positive cases was reported by De Luna *et al*., and by Odièvre *et al*., but there has been no large study or case series on the efficacy of this biological agent.[25,26] Furthermore, dexamethasone has been suggested as a modality of COVID-19 treatment in many guidelines and protocols. It was reported that the use of dexamethasone could reduce 28-day mortality in COVID-19 patients who required oxygen therapy or mechanical ventilation support.[27] Interestingly, dexamethasone helped in the treatment of patients with SCD complicated by ACS in a pediatric age group study, but there are no data on its efficacy in adult age groups.[28] With regard to the use of favipiravir in SCD, no reported cases or studies have yet been detected.

In general, our cohort showed favorable prognosis of SCD patients who got infected by COVID-19, but no clear reason was revealed for this outcome. Furthermore, even with diverse ethnicity, different genotypes, and geographic distribution of the study population, our data are in consonance with most other reports, which give good outcomes.

As most of the SCD patients are considered immunocompromised due to hyposplenic state or auto-splenectomy, with some defect in cell-mediated immune response, we can assume this to be the reason for the favorable outcome, since hyperimmune reaction or cytokine storm was the major cause of severe COVID-19 diseases. However, some reports have pointed to immune activation in SCD, especially with frequent transfusions. Whether this is useful or not, in the case of COVID-19 infection, this is an area for more elucidation and study.[29,30]

This study had some limitations which could affect its reliability. First, the sample was small and related to unicenter, a military center with rules, and eligibility criteria for admission. Second, because of the nature of the study, data were retrieved as retrospective information; therefore, causality could not be determined. Third, our end result could have been affected by the youthful samples with limited concomitant comorbidities, so outcomes could be varied. Further larger multicenter studies need to be conducted to better explore and investigate COVID-19 and possible complications in SCD.

## Conclusion

Despite the expected fatal outcomes for SCD patients infected by COVID-19, the behavior and outcome of the disease in our cohort were favorable, with unclear underlying protective mechanisms from serious complications. However, further extensive studies and national multicenter data are required for a better understanding of the behavior of COVID-19 infection in SCD patients.

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### Conflicts of interest
There are no conflicts of interest.

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