COVID-19 in patients with sickle cell disease: A single center experience from Ohio, United States

Dear Editor,

Coronavirus disease 2019 (COVID-19) pandemic is expanding at an enormous pace and has already affected over 15 million population. Individuals with comorbidities are the worst affected with risk factors like old age, diabetes, chronic airway disease, immunosuppressed, and cancer. Sickle cell disease (SCD) is a common genetic disease and needs special care owing to impaired immunity and compromised cardiopulmonary system. Hereby, we share our institutional experience with SCD patients during the COVID-19 pandemic.

In our chart review (approved from the institutional review board), we captured five laboratory-confirmed COVID-19 patients with SCD. Four patients required inpatient treatment, while the other one was managed as an outpatient. The average age of the patients was 32.6 years (range 21–47 years) with three females and two males. Only two out of five were on chronic therapy with hydroxyurea. Importantly, two out of the five patients presented to us only with generalized body aches. Three patients had classical imaging findings suggestive of COVID-19 disease. None of the patients required intensive care or mechanical ventilation with only one patient had a new oxygen requirement (Table 1). Only one patient (Patient no. 1) required transfusion support for symptomatic anemia. The same patient did receive remdesivir therapy for COVID-19 pneumonia. All patients except one (Patient no. 5) received prophylactic anticoagulation as per institutional policy with 1 mg/kg enoxaparin once daily. Patient no. 5 was never hospitalized and hence did not require any anticoagulation. None of the patients develop any thrombotic complications like deep venous thrombosis or pulmonary embolism. During the hospital stay, none of the patients developed lymphopenia, thrombocytopenia, coagulopathy. There was 100% recovery with an average hospital stay of 8.75 days (Table 2).

The severe acute respiratory syndrome coronavirus 2 virus can act as a potential trigger to acute chest syndrome (ACS) in SCD patients. Factors, such as hypersplenism, vasoocclusion, iron overload, and recurrent veno-occlusive crisis (VOCs) leads to impaired immunity that can lead to more fatal outcome than non-SCD patients in COVID-19 pneumonia. Also, to note that the clinical presentations of COVID-19 related ACS, COVID-19 pneumonia, and bacterial pneumonia can overlap (Figure 1). This could be challenging especially in a scenario when one or more entities co-exist in a same patient. In general, diffuse ground glass appearance in imaging is more commonly seen in COVID-19 pneumonia than ACS or bacterial pneumonia. Other classical findings like hemolysis, rapid falling hemoglobin, bone aches could be more suggestive of ACS than COVID-19 per se. However, in practical scenario it might be extremely difficult to definitively rule out one possibility over the other.

SECURE-SCD global registry, an initiative by The Medical College of Wisconsin is an excellent platform to collaborate the cases of SCD acquiring COVID-19 and their outcome (https://covidscdregistry.org). The latest data (updated till July 17, 2020) shows 260 cases of SCD registered from across the world (mostly from the US) with an average age of 26.83 years, and African American females being the worst affected population. Just like our patient series, the majority of the patients from the registry were on hydroxyurea and without any chronic transfusion therapy. An interesting observation which we also noted in our case series that, 31.15% of patients (81 out of 260) presented with symptoms of pain only. The majority of the patients (54.62%) had mild symptoms with a mortality rate of 6.15%. The second-largest study reported includes a French experience with 83 SCD patients with COVID-19 (multicentric study, 24 hospitals). The French group showed that the prevalence of intensive care admission was more with advanced age (53% in the older group, the median age of 54 years vs. 13% in the younger group, the median age of 28 years). The majority of the patients have associated VOCs (54%, 44 out of 81 patients), followed by ACS (28%, 23 out of 82 patients). 20% of the patients required ICU care which is almost like the results reported by SECURE-SCD global registry (25% were severe or critically ill). In addition to the above-mentioned studies, the other two largest single-center studies reported till now, both from the UK included 10 patients each.

In conclusion, treating COVID-19 in SCD patients’ needs a multidisciplinary approach with the management of pneumonia, VOCs, ACS, and supportive care at the same time for the best outcome.

CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS
All the authors played a significant role (manuscript writing, data collection, literature search, reviewing the paper, editing, and proofread) in the paper.
| SN | Age/sex | Genotype | Comorbidities | On treatment if any | Symptoms | RT-PCR | Imaging findings | Maximum oxygen requirement | ICU stay/ mechanical ventilation | RBC exchange therapy | Simple transfusion | Treatment given for COVID | hospital stay (in days) | Outcome |
|----|---------|----------|---------------|---------------------|----------|--------|------------------|----------------------------|--------------------------------|----------------------|-----------------|---------------------------|--------------------------|---------|
| 1  | 38/M    | SS       | Iron overload | Hydroxyurea, DDefera-sirox | Cough, malaise, abdominal pain, nausea, vomiting, anorexia X 3 days | Positive | Bilateral pulmonary congestion, multifocal opacities | 3 L (via Nasal Cannula) | Not required | Not required | Yes, 4 units PRBCs | Remdesivir | 6 | Discharged |
| 2  | 28/F    | SC       | Obesity (BMI 54) | None | Pain, Shortness of breath, dyspnea on exertion X 5 days | Positive | Right lower lobe opacity | Not required | Not required | Not required | Not required | Not required | 15 | Discharged |
| 3  | 47/F    | S B-thal | Asthma | None | Body pain X 2 days | Positive | Patchy bibasilar infiltrates | 2 L at night (chronic, home O₂) | Not required | Not required | Not required | Not required | Not required | 11 | Discharged |
| 4  | 29/M    | SS       | Hypertension | Hydroxyurea | Body pain X 3 days | Positive | Normal | 1 L at night (chronic, home O₂) | Not required | Not required | Not required | Not required | 3 | Discharged |
| 5  | 21/F    | SC       | Anoxic brain injury, seizures | None | None | Positive | Not done | Not required | Not required | Not required | Not required | Not required | 0 | Improved |

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; ICU, intensive care unit; RT-PCR, reverse transcription-polymerase chain reaction.

*a*Patient no. 2 got readmitted within 24 h of discharge after initial 5 days of hospitalization due to dyspnea on exertion. Second hospitalization was for 10 days (total duration of hospitalization was 15 days).

*b*Patient no. 5 never required admission and was managed as an outpatient.
**TABLE 2**  Laboratory parameters of patients

| SN | Nadir Hb | Nadir reticulocyte count | Nadir ALC | Nadir WBC count | Nadir Platelet count | Nadir D-dimer | Nadir CRP | Nadir Ferritin | Nadir LDH | Nadir PT | Nadir APTT | Nadir AST | Nadir ALT | Zenith Total/Direct Bilirubin | Zenith S. creatinine |
|----|----------|--------------------------|-----------|----------------|---------------------|---------------|-----------|---------------|---------|---------|-----------|---------|---------|-----------------------------|-------------------|
| 1  | 6.8      | 0.092                    | 2.45      | 6.4            | 263                 | 4283          | 4.8       | 3840          | 617     | 14.5    | 29        | 58      | 42      | 2.7/0.6                     | 0.86              |
| 2  | 8.8      | 0.077                    | 1.87      | 9.5            | 534                 | 1197          | 4.63      | 131           | 471     | 13.2    | 22        | 38      | 42      | 1.8/0.4                     | 0.72              |
| 3  | 9.2      | 0.262                    | 1.92      | 8.5            | 368                 | 21567         | 6.96      | 187           | 409     | 13.8    | 68        | 30      | 12      | 0.9/0.2                     | 0.52              |
| 4  | 9.2      | 0.516                    | 2.96      | 8.3            | 310                 | 3918          | 0.39      | 425           | 561     | 11.4    | 27        | 65      | 38      | 2.7/0.5                     | 0.87              |
| 5  | Not done | Not done                 | Not done  | Not done       | Not done            | Not done      | Not done  | Not done      | Not done| Not done| Not done  | Not done| Not done| Not done                    | Not done          |

Note: Reference range: Hb, 13.5–17.5 g/dL; reticulocyte count, 0.022–0.118 × 10¹²/L; ALC, 1.2–4.8 × 10⁹/L; WBC count, 4.4–11.3 × 10⁹/L; platelet count, 150–450 × 10⁹/L; D-dimer, <500 ng/ml; CRP, <1.0 mg/dL; ferritin, 20–300 mcg/L; LDH, 84–246 U/L; PT, 9.7–12.7 s; APTT, 25–36 s; AST, 9–39 IU/L; ALT, 10–52 IU/L; T/C Bil. Total, 0.0–1.2 mg/dL and direct, 0.0–0.3 mg/dL; S. creatinine, 0.5–1.3 mg/dL.

Abbreviations: ALC, absolute lymphocyte count; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein; Hb, hemoglobin; LDH, lactate dehydrogenase; PT, prothrombin time; WBC, white blood cells.
Three common differentials for respiratory complaints in a patient with SCD during COVID-19 pandemic. COVID-19, coronavirus disease 2019; SCD, sickle cell disease.

REFERENCES

1. Sahu KK, Kumar R. Current perspective on pandemic of COVID-19 in the United States. J Family Med Prim Care. 2020; 9(4):1784.
2. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. Clin Infect Dis. 2020.
3. Sahu KK, Siddiqui AD, Cerny J. Managing sickle cell patients with COVID-19 infection: the need to pool our collective experience. Br J Haematol. 2020.
4. Panepinto JA, Brandow A, Mucalo L, et al. Early release—coronavirus disease among persons with sickle cell disease, United States, March 20–May 21, 2020. Emerging Infect Dis J. 2020(10). https://wwwnc.cdc.gov/eid/article/26/10/20-2792_article
5. Arlet J-B, de Luna G, Khimoud D, et al. Prognosis of patients with sickle cell disease and COVID-19: a French experience. Lancet Haematol. 2020.
6. Chakravorty S, Padmore-Payne G, Ike F, et al. COVID-19 in patients with sickle cell disease—a case series from a UK Tertiary Hospital. Haematologica. 2020.
7. McCloskey KA, Meenan J, Hall R, Tsitsikas DA. COVID-19 infection and sickle cell disease: a UK centre experience. Br J Haematol. 2020; 190(2):e57-e58.

Correspondence
Ankit Mangla, MD, Hematology and Oncology, Developmental Therapeutics Program, Case Comprehensive Cancer Center, Case Western Reserve University School of Medicine, Cleveland 44106, OH.
Email: Ankit.Mangla@UHhospitals.org

ORCID
Kamal Kant Sahu https://orcid.org/0000-0002-0382-6882
Ankit Mangla https://orcid.org/0000-0002-6789-4315