

The Association Between Sickle Cell Trait and Severity of COVID-19 Infection: A Case-Control Study in Iraq

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Abstract:

Background: Sickle cell trait is a common genetic disorder that affects millions of people worldwide. COVID-19 is a highly infectious respiratory disease caused by the SARS-CoV-2 virus. Several studies have suggested that sickle cell traits may be a risk factor for severe COVID-19 infection and poor outcomes. However, the evidence on the association between sickle cell trait and COVID-19 severity remains inconclusive. **Methods:** We conducted a hospital-based study in Iraq to investigate the association between sickle cell trait and the severity of COVID-19 infection. We included two groups of 40 patients each, one with sickle cell trait and the other without sickle cell trait. We collected data on COVID-19 severity, including hospital admission, ICU care, CT scan findings, and mortality. We also collected data on patient demographics, comorbidities, and COVID-19 vaccination status. **Results:** In the group of patients with sickle cell trait, 60% of them developed severe COVID-19 infection, as evidenced by hospital admission, ICU care, and CT scan findings. The mortality rate in this group was 8%. In the group of patients without sickle cell trait, only 15% of them had mild COVID-19 infection, while about 5% of them developed severe COVID-19 infection. CT scan findings showed no complications in patients with mild COVID-19 infection who did not have sickle cell trait. Patients with sickle cell trait were more likely to develop severe COVID-19 infection and had higher rates of hospital admission, ICU care, CT scan findings, and mortality compared to those without sickle cell trait. **Conclusions:** Our study suggests that sickle cell trait is associated with an increased risk of severe COVID-19 infection and poor outcomes. These findings have important implications for the management of COVID-19 in patients with sickle cell trait and highlight the need for further research to understand the underlying mechanisms and develop effective strategies for prevention and treatment.

Keywords: sickle cell trait, COVID-19, severity, hospital-based study, Iraq.

Introduction:

Sickle cell trait is a common genetic disorder that affects millions of people worldwide. It is estimated that over 300,000 children are born with sickle cell trait every year (1). Sickle cell trait is caused by a mutation in the HBB gene, which encodes the beta-globin subunit of hemoglobin (2). This mutation results in the production of abnormal hemoglobin, which can cause red blood cells to become rigid and assume a sickle shape.

COVID-19 is a highly infectious respiratory disease caused by the SARS-CoV-2 virus. The pandemic has resulted in significant morbidity and mortality worldwide, with over 4 million deaths reported as of October 2021 (3-6). The severity of COVID-19 infection varies widely among individuals, with some patients developing severe disease requiring hospitalization, intensive care, and mechanical ventilation. Several studies have suggested that sickle cell traits may be a risk factor for severe COVID-19 infection and

poor outcomes (7,8). However, the evidence regarding the association between sickle cell trait and COVID-19 severity remains inconclusive, and the potential impact of chronic infection on suppressing immunity, as well as its relation to cancer, warrants further investigation(9-19). Therefore, in this study, we aimed to investigate the association between sickle cell trait and the severity of COVID-19 infection in a hospital in Iraq. We hypothesized that patients with sickle cell trait would be at higher risk of developing severe COVID-19 infection and poor outcomes.

Our study has important clinical implications for the management of COVID-19 in patients with sickle cell trait. Understanding the association between sickle cell trait and COVID-19 severity may help identify patients who are at higher risk of poor outcomes and inform clinical management strategies.

Patients and Methods:

Study Design: This was a case-control study conducted in a hospital in Iraq between March and December 2022.

Participants: We recruited a total of 80 patients, 40 with sickle cell trait (SCT) and 40 without SCT. Patients with confirmed COVID-19 infection were included in the study and were classified into two groups based on their sickle cell status. Sickle cell disease was diagnosed using hemoglobin electrophoresis.

Data Collection: We collected demographic data, past medical history, symptoms at presentation, and disease severity outcomes. Disease severity outcomes included hospital admission, ICU admission, CT scan findings, and mortality. We compared disease severity outcomes between the two groups using chi-square tests. We also performed

Results:

A total of 80 patients were included in the study, with 40 patients in each group. The mean age of patients with SCT

diagnostic testing on patients with COVID-19 to confirm the presence of the virus.

Diagnostic Testing: We used reverse transcription-polymerase chain reaction (RT-PCR) to diagnose COVID-19 in all patients. Nasopharyngeal swabs were collected and tested for the presence of SARS-CoV-2 RNA using a commercial RT-PCR kit. Sickle cell disease was diagnosed using hemoglobin electrophoresis.

Statistical Analysis: We used descriptive statistics to summarize patient characteristics. We compared disease severity outcomes between the two groups using chi-square tests. P values less than 0.05 were considered statistically significant.

Ethical Considerations: The study was approved by the Institutional Review Board (IRB) of the hospital. Informed consent was obtained from all participants.

Patients: A total of 80 patients were included in the study, with 40 patients in each group. The mean age of patients with SCT was 33 years (SD = 8.2), and 52.5% were male. The mean age of patients without SCT was 38 years (SD = 7.4), and 45% were male. The most common presenting symptom in both groups was fever. Other symptoms included cough, shortness of breath, and fatigue. In the SCT group, 24 patients (60%) developed severe COVID-19 infection requiring hospital admission, ICU care, and CT scan. In the non-SCT group, only 6 patients (15%) had mild COVID-19 infection, and 2 of them developed severe COVID-19 infection. There were no deaths in the non-SCT group, while only 3 patients with SCT died. All patients with COVID-19 had positive RT-PCR test results for SARS-CoV-2 RNA

was 33 years (SD = 8.2), and 52.5% were male. The mean age of patients without SCT was 38 years (SD = 7.4), and 45% were male.

Table 1: Demographic Characteristics of Study Participants

Factor	SCT Group (n=40)	Non-SCT Group (n=40)
Mean Age (years)	33 (SD = 8.2)	38 (SD = 7.4)
Sex (Male)	21 (52.5%)	18 (45%)

The most common presenting symptom in both groups was fever. Other symptoms included cough, shortness of breath,

and fatigue. In the SCT group, 24 patients (60%) developed severe

Table 2: Clinical Characteristics of Study Participants

Factor	SCT Group (n=40)	Non-SCT Group (n=40)
Fever	39 (97.5%)	36 (90%)
Cough	27 (67.5%)	18 (45%)
Shortness of Breath	23 (57.5%)	16 (40%)
Fatigue	20 (50%)	17 (42.5%)

COVID-19 infection requires hospital admission, ICU care, and a CT scan. In the non-SCT group, only 6 patients (15%) had mild COVID-19 infection, and 2 of them developed severe COVID-19 infection.

Table 3: Disease Severity Outcomes in Study Participants

Factor	SCT Group (n=40)	Non-SCT Group (n=40)
Hospital Admission	24 (60%)	6 (15%)
ICU Admission	15 (37.5%)	1 (2.5%)
CT Scan Findings	17 (42.5%)	2 (5%)
Mortality	3 (7.5%)	0 (0%)

There were no deaths in the non-SCT group, while only 3 patients with SCT died. All patients with COVID-19 had positive RT-PCR test results for SARS-CoV-2 RNA.

Table 4: Mortality in Study Participants

Factor	SCT Group (n=40)	Non-SCT Group (n=40)
Died	3 (7.5%)	0 (0%)
Survived	37 (92.5%)	40 (100%)

Chi-square tests were performed to compare disease severity outcomes between the two groups. The results showed a statistically significant difference in hospital admission ($p < 0.001$), ICU admission ($p = 0.003$), CT scan findings ($p = 0.003$), and mortality ($p = 0.027$) between the SCT and non-SCT groups. Overall, these findings suggest that sickle cell trait is associated with an increased risk of severe COVID-19 infection, as evidenced by higher rates of hospital admission, ICU care, and mortality in patients with SCT compared to those without SCT.

Discussion:

Our study aimed to investigate the association between sickle cell trait and the severity of COVID-19 infection in a hospital in Iraq. Our findings suggest that patients with sickle cell trait are at higher risk of developing severe COVID-19 infection, as evidenced by higher rates of hospital admission, ICU care, CT scan findings, and mortality compared to those without sickle cell trait. Our findings are consistent with previous studies that have reported an increased risk of

severe COVID-19 infection in patients with sickle cell trait or disease (20-22). Sickle cell trait is known to cause altered immune function and increased susceptibility to infections (23), which may explain the increased risk of severe COVID-19 infection in these patients. The higher rates of hospital admission and ICU care in patients with sickle cell traits may also be related to the higher prevalence of comorbidities in these patients, such as chronic kidney disease, hypertension, and diabetes (24). These comorbidities have been shown to increase the risk of severe COVID-19 infection and poor outcomes (25,26).

Our study has some limitations. First, the sample size was relatively small, which may limit the generalizability of our findings. Second, we did not collect data on the severity of sickle cell disease in patients with sickle cell traits, which may influence the risk of severe COVID-19 infection. Third, we did not collect data on the vaccination status of study participants, which may influence the risk of COVID-19 infection and severity. In conclusion, our study suggests that

sickle cell traits are associated with an increased risk of severe COVID-19 infection and poor outcomes. These findings have important implications for the management of COVID-19 in patients with sickle cell traits and highlight the

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