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Complications of Covid-19 on Sickle Cell Patients in Children

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Sickle cell anemia is serious condition. People who have the disease when get infected with Covid-19 are more likely to suffer more complications. In this paper, we report the prevalence of complications of sickle cells of children infected with covid-19 virus. As pathogen detection campaigns have gotten more prevalent, the number of patients diagnosed with COVID19 has increased substantially. The majority of children diagnosed with COVID19 have moderate symptoms; the most common clinical signs in children with COVID19 are fever and cough. Fatigue, myalgia, upper respiratory tract symptoms, sore throat, headache, dizziness, and gastrointestinal problems.

Keywords: Covid-19 virus; gastrointestinal problems; sickle cell anemia; sars-cov-2 infection.

1. INTRODUCTION

The SARS-CoV-2 coronavirus (COVID-19) has resulted in widespread lockdowns and a large number of deaths around the world. The pandemic has posed specific challenges for healthcare workers who are responsible for treating persons with chronic conditions, such as

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balancing the provision of necessary care with proper infection prevention measures. Due to the disease's severity, the presence of disease-related comorbidities, and the need for regular medical interventions, patients with sickle cell disease (SCD) encounter dozens of new issues. There is a lack of published data on how COVID-19 may affect the morbidity and mortality of SCD patients [1].

Sickle cell disease (SCD) is an inherited hemoglobinopathy that mostly affects African-Americans. SCD affects one out of every 365 Black people in the United States. When exposed to low oxygen levels, SCD patients' haemoglobin becomes faulty, causing erythrocytes to become rigid and deform, leading in ischemia–reperfusion injury in the microvasculature, which causes organ damage and pain. SCD affects nearly every organ system, with an average life expectancy of 43–54 years for those who are affected. Pneumonia and lung disease are more common in SCD patients [2-5].

COVID-19, a coronavirus that causes severe acute respiratory syndrome, was discovered and reported in the United States for the first time in January 2020. Since then, the pandemic has become a serious public health problem in the country. By August 2020, there had been over 4 million COVID-19 infections and over 147 000 fatalities in the United States. Today There are approximately 214,468,601 confirmed cases globally as of August 2021. According to the World Health Organization, there have been over 4,470,969 fatalities (WHO).Despite the fact that past research on the independent effect of race on COVID-19–related outcomes has produced mixed results, it is evident that Black individuals in the United States have been disproportionately affected by this increasing epidemic. According to the Centers for Disease Control and Prevention, Black individuals in the United States had a disproportionately high number of COVID-19 fatalities (22.2%) relative to their share of the population as of August 5th, 2020. (13 percent) [6-12].

Children with sickle cell disease have a diverse set of clinical experiences. With a prevalence of about 12%, splenic sequestration is a potentially life-threatening complication of sickle cell disease. COVID-19's impact on sickle cell disease patients is still unclear [13].

The vast majority of these patients are from Africa's Sub-Saharan region. COVID-19 issues are considered to be more frequent in people with sickle cell illness. Infections in sickle cell disease patients can lead to severe vaso-occlusive emergencies and life-threatening acute chest syndrome, as well as COVID-19-related morbidities. As a result, COVID-19 may be devastating in areas like Africa or India, where 8–12 million sickle cell disease patients are estimated, or the United States and Brazil, where each nation has over 100 000 sickle cell disease patients. However, no data on the outcomes of patients with sickle cell disease who use COVID-19 is presently available [14].

According to previous studies, persons with SCD have a higher risk of severe influenza and hospitalization than people without SCD. People with SCD may be at a greater risk of developing severe illness if infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiological agent of coronavirus disease (COVID-19). COVID-19 has been discovered in persons with SCD, and a study of COVID-19 intensive care unit (ICU) admissions revealed that 2 (4%) of 48 children had SCD There were 7,896 pediatric influenza-related hospitalizations during the 2 influenza seasons. Of these, 159 (2.0%) included a co-occurring diagnosis of SCD. Annual rates of IRH were 112 and 2.0 per 10,000 children with and without SCD, respectively, across both seasons. Children with SCD were hospitalized with influenza at 56 times the rate of children without SCD (95% CI: 48–65). Children with SCD had approximately double the risk of IRH compared to children with CF (RR = 2.1 [1.5 – 2.9]). IRH among children with SCD were not longer, more costly or more severe than IRH among children without SCD, were rarely nosocomial, and co-occurred with a diagnosis of asthma in 14% of case , despite the lack of empirical evidence. In this study, we will discuss the frequency of sickle cell problems in children infected with the covid-19 virus [2,15-20].

2. INCIDENCE AND CASES REPORTS

In a significant survey performed over a four-week period, 10 regional centres reported 195 cases of suspected or confirmed SARS-CoV-2 infection in the United Kingdom. Patients with SCD accounted for the majority of cases (85.1%), with Hb SS disease the most common genotype (Hb SS 64.1 percent; Hb SC 15.4 percent; other genotypes 5.6 percent), followed by thalassemia (13.3 percent) and uncommon hereditary anemias (5.6 percent) (1.5 percent). Despite the fact that the prevalence of ACS in

the SCD group was not stated, red cell exchange was done in 46 patients over the course of their disease.Eight SCD patients required mechanical ventilatory support due to respiratory failure, and SCD patients accounted for 11 of the 13 fatalities associated to COVID-19. In a subgroup study of 76 hospitalised SCD patients with PCR confirmed SARSCoV-2, patient age was significantly related to mortality, with the greatest fatalities occurring in those aged 50 and older. According to the research, three individuals in the sample, aged 20 to 39 years, died of COVID-19, but no information regarding their associated medical conditions was provided.Females had a higher death rate than men, which was not connected to illness severity, although the differences were small. According to England's registry statistics, the cases reported so far account for 1.2 percent of the estimated 13,655 persons with SCD. Children were only infected at a low incidence, and no children died. COVID-19 mortality rates in SCD cannot be determined definitively because to underlying statistical bias and missing data in the survey [1].

There were 178 COVID-19 instances overall which have been reported to the Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion (SECURE-SCD) Registry as of May 21, 2020. These case-patients had an average age of 28.6 years, with 57 percent of them being female and 80 percent being African-American. Sickle cell types HbSS or HbS0-thalassemia were found in 76 percent of case patients, which matches SCD genotype frequency calculations in the U.S. Case-patients had a high rate of recent (within the last three years) Vaso-occlusive crises are characterized by unfavorable effects, with 54 percent reporting >3 occurrences of pain necessitating hospitalization and 32 percent reporting >1 acute chest syndrome episode. Pulmonary hypertension, prior stroke, renal illness, and chronic transfusion treatment use were all found to be more than 10% of the population. A total of 6% of COVID-19 case-patients had no symptoms., With 54 percent having a mild illness and 18 percent having a moderate disease,A serious sickness affects 17percent of people, whereas a critical condition affects 5percent of people. Nearly 90% of case-patients were treated in an emergency department, 69 percent were admitted to a hospital, 11% were hospitalized to an intensive care unit, 6% needed a ventilator, 38% needed a transfusion, and 2% needed dialysis. Thirteen patients (7 percent) died in total. With an average age of 38.5 years, more than 90% of them were adults. About 40% of fatalities were caused by those with genes linked to milder SCD (types HbSC or HbS+-thalassemia). In the previous three years, patients who died had a large number of recurring pain episodes (85%), pulmonary hypertension (39%), decreased renal function (23%), SCD nephropathy (15%), and overt stroke (31 percent). Persons with severe or critical COVID-19 were responsible for eight of the 13 deaths, whereas people with mild or moderate COVID-19 were responsible for five [2].

The UK has the highest death rate in Europe, with Black, Asian, and Minority Ethnic (BAME) persons having a greater chance of dying. Compared to Caucasians, Black Afro-Caribbeans had a 1.9-fold higher death rate. Many South Asian ethnic groups have comparable statistical outcomes. Because of symptoms including functional asplenia and reduced complement activation, patients with SCD, who are primarily of BAME origin, are more vulnerable to infections.As a result, this patient group may have a higher risk of morbidity and death. The impact of the last SARSCOV virus outbreak on SCD patients remains unknown. During the 2009 H1N1 viral pandemic, however, a retrospective cohort analysis of SCD patients discovered that 34% of patients with viral H1N1 infection had acute chest syndrome (ACS), but only 13% of those with seasonal influenza developed ACS. Severe ACS bouts were more common in patients who required exchange transfusions and assisted ventilation. COVID19 is expected to have a similar, if not larger, effect on SCD patients' pulmonary problems [21-24].

2.1 Symptoms & Complications

Since the emergence of COVID19 in December 2019, patients have been closely observed in an attempt to characterize and treat the pandemic's clinical symptoms. The number of people identified with COVID19 has risen dramatically as pathogen detection activities have become increasingly widespread. The majority of children with COVID19 have mild symptoms; fever and cough are the most frequent clinical indicators in children with COVID19. These may be accompanied by fatigue, myalgia, upper respiratory tract symptoms, sore throat, headache, dizziness, and gastrointestinal issues.While serious issues are less prevalent in children with COVID19, the pediatric population has experienced significant morbidity and death [3].

2.2 Covid-19 and Sickle Cells Complications

According to evidence from non-SCD cohorts, people with advanced age and medical co-morbidities including cardiovascular disease, hypertension, diabetes, and pre-existing lung illness are more likely to experience severe COVID-19-related consequences, including catastrophic acute hypoxic respiratory failure. In severely sick patients, a cytokine storm, increased endothelial activation with the potential for micro- and macrothrombi, and disseminated intravascular coagulation can all contribute to multi-organ failure. Elevated D-dimer and prothrombin levels, as well as a reduction in fibrinogen levels, indicate a poorer prognosis and a greater risk of mortality in COVID-19 patients.Comorbidities in individuals with SCD, particularly in elderly people, include progressive renal insufficiency, hypertension, and chronic lung disease, including pulmonary hypertension. An acute vaso-occlusive crisis, such as ACS, can be caused by a viral infection and has a high mortality rate. In this setting of multi-organ dysfunction, particularly chronic lung damage, COVID-19 might readily induce ACS and multi-organ failure. Due to underlying endothelial dysfunction and abnormal production of procoagulants like tissue factor, SCD patients may be at a greater risk of thrombo-inflammation and thrombotic events if infected with SARS-CoV-2 [1].

Patients with SCD who catch SARS-CoV-2 have a significant risk of having a severe infection with a high case-fatality rate. The 69 percent hospitalization rate, 11 percent ICU admission rate, and 7% fatality rate among verified COVID-19 case-patients reported to the registry are alarming, given the average patient age of 40 years. Hospitalization, ICU admission, and case-fatality rates for persons with SCD may be much higher than for those of similar ages in the general US population, according to a recent COVID-19 report. For example, COVID-19 case fatality rates were reported to be 1% for persons aged 20–44 and 1% for those aged 45–54 [2].

Acute chest syndrome (ACS), pulmonary embolism (PE), and pneumonia are common pulmonary consequences in sickle cell disease (SCD) patients, all of which increase the risk of mortality. Due to their heightened sensitivity to infection, they are considered vulnerable patients during the current COVID-19 pandemic. In developing small case studies of SCD patients with COVID-19 who are further deteriorated by pneumonia, ACS, and/or PE, the therapeutic advantages of early exchange transfusion and Tocilizumab were obvious. To assess feasible diagnostic and treatment options for this high-risk group, further clinical trials and broader cohort studies are needed [21].

2.3 Research Data

In France, 83 sickle cell disease patients infected with SARS-CoV-2 were registered from 24 sites; 17 (20%) of the 83 patients were hospitalised to the intensive care unit. Mechanical breathing was necessary in nine patients and extracorporeal membrane oxygenation was required in two individuals. Two COVID-19 pneumopathy patients, both men with the SC haemoglobin genotype, died in the ICU. Five of the eight SC genotype patients (63 percent) were admitted to the ICU, compared to 12 (17 percent) of the 71 SS/S0 genotype patients.Five of 16 patients aged 40 or older with the SS/S0 genotype (median age 48.5, range 40–64) were admitted to the ICU, whereas five of five patients with the SC genotype (median age 50, range 40–68) were admitted to the ICU. 17 sickle cell disease patients admitted to the ICU received a median of 4 packs (range 2–7) of packed red blood cells (88 percent). Only three (15%) of the 15 were transfused before ICU admission (1, 2, and 28 days earlier), with the remaining 12 transfused after a median of 15 days.Two patients had automated exchanges, six had basic transfusions, and seven had exchange transfusions. Three days after admission, a male with the SC genotype died of a pulmonary embolism without getting a transfusion, while a woman with the SS genotype did not receive a transfusion but was treated with high-flow oxygen and recovered. Seven patients were admitted straight to the ICU, with a median time of 2 day from hospital admission to ICU transfer [14].

Patients with sickle cell disease who were younger than 45 years old and those who were older than 45 years old had significantly different rates of ICU admission: 9 (13%) of 68 patients with a median age of 28 years (range 03–44) compared to eight (53%) of 15 patients with a median age of 54 years (45–68) [14].

There were 449 COVID-19 individuals with sickle cell trait who were matched to 449 Black COVID-19 patients without sickle cell disease/trait in another study that compared individuals with sickle cell trait to Black patients without sickle cell

illness, and no significant differences in demographic or clinical variables were found between the two groups. The matched cohort has had 38 years old patients on average, with 81 percent of which were women, 39 percent having hypertension, 30 percent having asthma, 12 percent having a history of acute kidney failure/chronic kidney failure, 42 percent being obese/overweight, 22 percent having diabetes mellitus, 8% having liver disease, and 3% having a history of cerebral infarction.4% of the people had COPD (chronic obstructive pulmonary disease). Before being diagnosed with COVID-19, 3% of people experienced pulmonary embolism, and 3% had a history of venous thromboembolism. After matching, there were no significant differences in COVID-19 symptoms, hospitalizations, or death between sickle cell trait individuals and Black people without sickle cell disease/trait. According to the sensitivity analysis, there were no significant differences in COVID-19 symptoms or hospitalizations between sickle cell trait individuals and Black patients who did not have sickle cell disease/trait [6].

3. DISCUSSION

The outcomes of 10 SARS-CoV-2.3 infected individuals in the United Kingdom are described by Charkravorthy and colleagues. Despite the fact that all of the patients had haemoglobin (Hb) SS condition and co-morbidities, nine of them recovered completely without the use of COVID-19 guided treatment. Five patients were brought to the hospital for supportive treatment; two patients with a cough and hypoxia had simple transfusions as soon as possible; and five patients were treated at home with regular phone calls.Seven of the 10 patients were female (median age 37), with two undergoing hydroxyurea treatment and seven undergoing frequent blood transfusions (four exchange and three simple transfusions). Because COVID-19 is an acute infectious pneumonia, most professionals expected SARS-CoV-2 infection to trigger acute chest syndrome (ACS), however only one of the patients who died in this series had significant respiratory difficulties.A 54-year-old female died as a result of severe asthma, alloimmunization, and a history of delayed hemolytic transfusion reactions, which made routine transfusion impossible. The patient had lymphocytopenia, thrombocytopenia, and an elevated C-reactive protein level, all of which are considered negative prognostic markers in COVID-19 patients. The authors recognise that the results may have been impacted by the cohort's demographic and treatment characteristics [1].

Sickle cell disease patients are more susceptible to suffer infectious problems; nevertheless, the effects of COVID19 on this paediatric group are unclear. Although there have been a few reports of juvenile sickle cell disease patients with acute chest syndrome and COVID19 infection, no further sickle cell disease complications have been reported in the presence of a COVID19 infection in paediatric patients [13].

People with SCD have socioeconomic and healthcare access disadvantages as a result of their underlying disease and related comorbidities, which may exacerbate their already high risk of severe COVID-19. SCD complications may have a deleterious impact on academic performance and job chances. Obtaining proper medical treatment may be challenging due to a shortage of clinicians with SCD experience. Patients with SCD are more likely to put off getting treatment, and emergency department visits are prevalent among this group, which is more prone to disease [2,25,26].

Because the majority of sickle cell disease patients have the SS/S0 genotype and are under 45 years old, several studies have found that COVID-19, while potentially severe, does not appear to be associated with an increased risk of morbidity or death in sickle cell disease patients. COVID-19 infection can also be exacerbated by vaso-occlusive crises, which occur in around half of sickle cell disease inpatients, according to the findings. The possibility of a protective effect against COVID-19 in those who have the SS/S0 variant should be studied. High plasma interferon levels and neutrophils with a clear type I interferon signature were observed in patients with the SS genotype.SARS-CoV-2 does not appear to elicit substantial interferon responses ex vivo, which might explain why viral replication is greater. On the other hand, older people with sickle cell disease should be considered sensitive to SARS-CoV-2 and should follow local advice to avoid infection. These individuals should be closely monitored if they are admitted to the hospital as a consequence of COVID-19. [14].

4. CONCLUSION

There is no doubt that the current pandemic is one of the most serious challenges that have ever faced humanity, with increasing numbers of

infections the complications of the disease is not only due to the virus but with other co-morbidities and chronic cases that is often affects many people worldwide.

Sickle cell anemia is serious condition, people who have the disease when get infected with Covid-19 are more likely to suffer more complications, however some reports suggest that it doesn't affect ICU admission that much for people who under 45 but for older people it seems to be that there's real risk and therefor they be watched more carefully, anyway more research is needed to better understand the link between the two diseases.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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