COVID-19 Infection in Sick Cell Patients in a Developing Country: A Case Series

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Keywords

Sickle cell disease · ABO blood group · SARS-CoV-2 · COVID-19

Abstract

Sickle cell disease is characterized by vaso-occlusive phenomena and haemolytic anaemia. There is a significant concern that the overlap of COVID-19 lung disease with acute chest syndrome that occurs in sickle cell patients may result in serious complications. Case reports of sickle cell patients with COVID-19 have been published. Here, we present a case series of COVID-19 infection in sickle cell patients in a developing country (Brazil). Only 10 patients tested positive so far for SARS-CoV-2 of 600 patients followed at our institution, of which 8 needed hospitalization (one in the intensive care unit), with no deaths. Even in a middle-income country, COVID-19 was reported to be relatively mild in sickle cell patients. In relation to risk factors, blood type O seems to confer some protection against developing severe COVID-19, a finding that could guide clinicians to adopt more clinical surveillance for patients with non-O blood type in sickle cell patients.

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Introduction

Sickle cell disease (SCD) is a hereditary group of disorders characterized by the presence of haemoglobin S, either in homozygosity or in composed heterozygosity with another β -globin mutation ($S\beta$ thalassaemia, SC, and SD haemoglobinopathies). Together, SCD is characterized by vaso-occlusive phenomena and haemolytic anaemia [1, 2].

One of the main causes of mortality in SCD patients is acute chest syndrome (ACS). ACS can result from sickling in the small blood vessels, infarction or pulmonary embolism, or viral or bacterial pneumonia. The treatment of ACS is challenging and requires surveillance by the medical team, hospitalization, often in the intensive care unit (ICU), ventilatory support, transfusion, and antibiotic therapy [3, 4].

COVID-19 is a mild viral infection in 80% of cases. Nevertheless, 20% of patients develop interstitial pneumonia, acute respiratory syndrome, sepsis, and septic shock [5]. There is a significant concern that the overlap of COVID-19 lung disease with the ACS might result in severe outcomes in this population. In addition, both

Table 1. Clinical characteristics of the patients included in the study

Patients	Age	Sex	Genotype	Previous treatments	Previous complications	Complication during hospitalization	Blood group	BMI	Length of stay, days
1	30	F	SS	Clinical trial	ACS	VOC	A	22.4	5
2	28	F	SC	Chronic transfusion	ACS	ACS	AB	20.9	5
3	30	F	SBETA0	HU	ACS	ACS	A	24.8	10
4	33	F	SC	None	Myocarditis	ACS	A	22.4	4
5	45	M	SS	Chronic transfusion	Stroke + leg ulcers	VOC	A	25.6	22
6	30	F	SS	HU	Stroke	ACS	O	20.2	14
7	31	M	SBETA+	HU	ACS + hyperhaemolysis syndrome	ACS	A	17.5	20
8	36	F	SS	HU	ACS + VOC	ACS	O	23.32	11
9	31	F	SS	HU	VOC	–	A	22.93	–
10	8	F	SS	HU	ACS	–	B	16	–

M, male; F, female; SS, sickle cell anaemia; SBETA0, S β thalassaemia; SC, haemoglobinopathy SC; HU, hydroxyurea; ACS, acute chest syndrome; VOC, vaso-occlusive crisis; BMI, body mass index.

COVID-19 and SCD favour the occurrence of thromboembolic events, so the association of these 2 diseases could greatly increase the risk of occurrence of complication [6]. In Europe and in the USA, case reports of SCD patients with COVID-19 have already been published, and the relatively good clinical outcome was somehow surprising, considering the susceptibility of SCD patients to infections and vaso-occlusion complications [6–8].

In a case series of 4 sickle cell patients treated in the USA, the authors showed a mild clinical course in most of them, despite having a previous history of ACS in 3 patients and pulmonary embolism in the other one, with no deaths [6]. In another case series, from a UK tertiary hospital, 10 patients (7 females) with SS genotype and ages between 25 and 54, the authors reported only 1 death. Five patients had mild COVID-19 infection and were not hospitalized and 4 recovered after a short period of hospitalization [7]. The French national consortium published the clinical outcome of 83 SCD patients with COVID-19. The median age was 33.5 years for the adult population and 12 for paediatric patients (0.3–17); 58% had a history of ACS and 20% were admitted to ICU. Only 2 patients died, both with the SC genotype. Patients aged above 45 years were at higher risk of admission to ICU. Hence, the authors suggested that COVID-19 was mild in most of the patients, especially those younger than 45 years [8]. Brazil is being greatly affected by the pandemic. Over 17 million people across the country were infected so far, and >480,000 people died of COVID-19. According to our Ministry of Health, there are between 30 and 70,000 sickle cell

patients in Brazil [9], and the clinical outcome of those patients with COVID-19 is largely unknown; however, we believe that this report can contribute to show the outcomes in patients with SCD and COVID-19 in this country.

Case Series

This is an observational retrospective study of all the SCD patients diagnosed with COVID-19 followed at our institution. The study was approved by the institutional ethics committee, which waived the need for the informed consent from the patients. We report here 10 (1.7% of 600 patients followed at our institution) SCD patients with COVID-19 (confirmed by RT-PCR; all cases caused by the original variant). Their clinical characteristics and outcomes are described in Table 1. Nine patients were adults, and one was an 8-year-old child with the SS genotype. Eight adult patients were admitted to the hospital, of which 1 patient ($n = 8$) was admitted to ICU and underwent mechanical ventilation support. The overall mean length of hospitalization was 11.4 days (range 4–22 days). The causes of hospitalization were vaso-occlusive phenomena in 2 patients and ACS in 6 patients. We performed descriptive statistics for general data and Fisher's exact test to analyse categorical variables.

The ABO blood group types of the patients were 6 type A, 1 type AB, 1 type B, and 2 type O. The control subjects were the SCD population followed at our institution who had their blood typing performed ($n = 204$). Blood groups A, AB, and B were overrepresented (80%) in the COVID-19 group related to the control group (56%), whereas blood group O was less represented: 20% in the COVID-19 group versus 44% in the sickle cell population. Although this result did not reach statistical significance, the prevalence of the O blood group among the COVID-19 patients was less than half of the control group.

Discussion

Interestingly, as observed in this case series and in other published studies [6–8], the low number of SCD patients needing to be hospitalized for COVID-19 was somewhat surprising and raises the hypothesis that SCD patients are perhaps not as vulnerable to COVID-19 as has been supposed at the beginning of the pandemic. Some of the recognized risk factors for COVID-19 infection, such as obesity, diabetes, and hypertension, are very rare in SCD patients. SCD patients tend to be younger than the general population, with a lower percentage of older individuals, who are known to be more vulnerable to COVID-19. The median age of our 9 adult patients was 31 years, with no patients above 45 years of age, a risk factor for COVID-19 complication in sickle cell disease [8]. Besides, none of our patients had obesity, type II diabetes, or hypertension. An additional protective factor could be the chronic inflammatory status present in SCD, which may play a role in reducing the vulnerability to the virus and even the intensity of the inflammatory storm that frequently occurs in COVID-19, as suggested by others [8]. Nevertheless, although mortality in SCD patients with COVID-19 is less than had been expected, it is still high compared to the healthy population when corrected for age and comorbidities [10].

It has been previously proposed that group O confers a relative protection against SARS-CoV-1 infection [11]. In that study, blood group O healthcare professionals were less susceptible to become infected than nongroup O individuals. Zhao and colleagues [12] were the first to show that the proportion of blood group A patients infected with SARS-CoV-2 was higher than that observed in healthy subjects (39.3% vs. 32.3%). Additional studies confirmed the association between blood group A and COVID-19 infection [13–16]. One possible explanation is the higher plasma levels of von Willebrand factor and the higher risk of thrombosis in comparison with group O subjects [17–19]. Additionally, it is possible that anti-A antibodies (present in blood type O individuals) may interfere with SARS-CoV-2 and target cell integration, as previously demonstrated for SARS-CoV-1 [20]. These hypotheses need to be addressed in further studies. Here, we suggest that there could be an association between ABO blood group and COVID-19 in patients with SCD.

We acknowledge some limitations of our study. First, the number of patients is relatively small; however, we included all SCD patients diagnosed for COVID-19 at our institution, so far. Second, we do not provide mecha-

nistic evidence for this association and the reason(s) why non-O blood group SCD patients seem to be more vulnerable to develop severe COVID-19.

In conclusion, we have shown that SCD patients with COVID-19 have a relatively favourable outcome, even in a middle-income country. Another finding is that blood type O seems to confer some protection against developing COVID-19, a finding that could, possibly, guide clinicians to adopt a closer clinical surveillance for patients with non-O blood type in sickle cell patients.

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Statement of Ethics

This research was conducted ethically in accordance with the Declaration of Helsinki. The study was approved by our local institutional ethics committee, which dismissed the need for the written informed consent from the patients. Ethical approval date: September 15, 2020 (Process No. 4.277.529).

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Ana Cristina Silva-Pinto, Letícia Santos-Oliveira, Flávia Leite Souza Santos, and Gil Cunha De Santis. The first draft of the manuscript was written by Ana Cristina Silva-Pinto, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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