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Case Report

The Study of COVID-19 in an Iranian Family with Sickle Cell Disease

Seyedeh Moloud Rasouli Ghahfarokhi[1], Asghar Dasmeh[2], Amir Yousef Farahmandi[3], Azam Khedri[4], Fatemeh Asadi[5]*, Fahimeh Piryaei[6], Leila Moradi[7]

[1]School of Nursing and Midwifery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[2]Unit of Health, Mahshahr petrochemical industries hospital, Bandar Mahshahr, Khuzestan, Iran
[3]Department of English, School of Paramedical Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
[4]Department of Clinical Biochemistry, Faculty of Medicine, Ahvaz Jundishapur University of Medical Science, Ahvaz, Iran
[5]Department of Molecular Genetics, Science and Research Branch, Islamic Azad University, Fars, Iran
[6]Department of Molecular Medicine and Genetics, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
[7]Department of Epidemiology, School of Public Health, Hamadan University of Medical, Hamadan, Iran

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**Corresponding author:*
Fatemeh Asadi,
Department of Molecular Genetics, Marvdasht Branch, Islamic Azad University, Marvdasht, Iran
Tel: +98-71-43311172
Fax: +98-71-43112201
Email: fatemehasadi@miau.ac.ir

ABSTRACT

Coronavirus Disease 2019 (COVID-19) is a significant medical and public health problem in the world. It is believed that it can worsen in extreme conditions. Also, it is suggested that blood disorders such as sickle cell disease (SCD) may increase the risk of COVID-19 symptoms. The present study reports a family facing COVID-19, in which one of two members with SCD presented with fever, repeated cough and dizziness followed by acute chest syndrome leading to death. The remained members that had sickle cell trait manifested mild symptoms based on our findings. Although COVID-19 in individuals with SCD showed an increased risk for COVID19 compared with individuals with sickle cell trait, it seems that SCD cannot lead to worse condition in our patients.

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Introduction

The emergence of Coronavirus Disease 2019 (COVID-19) in China on December 2019 caused a pandemic around the world.[1] More than five million cases have been reported worldwide with 355,942 deaths by May 2020.[2] In Iran, the first confirmed positive case for COVID-19 was reported in Masih Daneshvari Hospital in Tehran on February 2020.[3] This novel virus can cause severe inflammation, respiratory tract infections and subsequent injury to the lungs.[4] The severity of COVID-19 cases varies from mild to severe pneumonia and thromboembolism events with high morbidity and mortality.

There are various potential risk factors which predispose affected patients to the severe forms of the disease. Among different underlying disorders, patients with sickle cell disease (SCD) are thought to be at higher risk of complications such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

SCD is one of the most common inherited hematological disorders. Sickle hemoglobin results from a point mutation replacing a T at codon 6 of beta globin chain (HBB: *c.20A>T*; p. Glu6Val).[5] This inherited disorder affects African Americans in the United States as well as those in sub-Saharan Africa, the western hemisphere including South America, the Caribbean, and Central America, and some Mediterranean countries.[6] In Iran, SCD is one of the most common hemoglobinopathies reported in Khuzestan province.[7-9]

The main clinical manifestations of patients with SCD are hemolysis and episodes of vaso-occlusive crisis. In this condition, the lifespan of RBCs is decreased from 120 days to 10-12 days leading to jaundice and gall stones. Similarly, obstruction of normal blood flow by sickled red blood cells can result in ischemic injuries in various

organ systems.[10]

SCD patients are at risk of severe complications once infected by a viral pathogen. Viral pathogens are a frequent cause of acute chest syndrome (ACS) in patients with SCD; however, it is still unclear whether patients with SCD fare worse when they contract COVID-19.

There are reports of the coexistence of COVID-19 and SCD in the world. A prospective study of African Americans demonstrated a two-fold increase in the risk of pulmonary embolism[11] in carriers of sickle cell trait, while in English case reports as in the largest registry to date as well as the French registry published recently the authors underline that SARS-COV2 does not seem to carry an increased risk of mortality or morbidity in patients with SCD.[12, 13]

Here, we report an Iranian family affected by COVID-19, two members of which had SCD, but the other siblings were carriers of Hb S variant (HBB: *c.20A>T*; p. Glu7Val). The patients' consent was obtained before reporting the case.

Case 1

A 54-year-old man with SCD presented with fever, dry cough, tachypnea, and dizziness during the pandemic of COVID-19 which led to hospital admission. The laboratory test revealed positive result for corona virus. Azithromycin and hydroxychloroquine were administered to treat severe pneumonia. He was admitted to ICU due to ACS; however, succumbed to death after progression of pulmonary involvement and worsening of respiratory symptoms.

Case 2

A 37-year-old woman, a case of sickle cell trait referred to the emergency department with fever and severe cough. Viral diagnostic testing (RT-PCR) for corona came positive. Azithromycin was administered to treat her symptoms. She recovered after 15 days of home quarantine.

Case 3

A 46-year-old woman with SCD with history of chronic anemia and minor pain episodes referred to the emergency department with high fever and severe cough. After being hospitalized, throat and nose swabs were reported to be positive for COVID-19 based on her laboratory test. Azithromycin, hydroxychloroquine, and multivitamin were administered. She was discharged after 16 days of hospitalization with good general condition.

Case 4

An asymptomatic 35-year-old man who was a sickle cell carrier, performed PCR testing for corona virus after being febrile. He was recommended to be quarantined 14 days in home without referring to the hospital, since he was well without any other symptoms. He got to be afebrile in three days.

The results of complete blood cell count of the patients were listed in Table 1, and the pedigree of family was shown in figure 1.

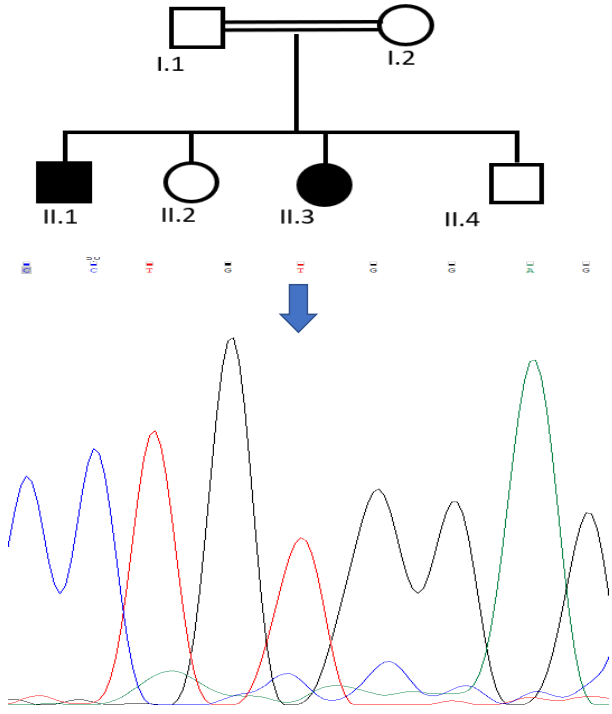

Figure 1: a) The pedigree of family by one sickle cell disease, b) Electropherogram of beta globin gene presenting HBB: c.20A>T mutation in homozygous state in the patients with sickle cell disease.

Discussion

COVID-19 resulting from SARS-CoV-2 has become an important medical public health concern in the world.[1, 4] We reported an Iranian family infected with COVID-19. Two siblings who had SCD were affected with severe symptoms; one of them expired due to COVID-19; however, family members with sickle cell trait showed very mild symptoms.

In subjects who inherit Hb S variant, red blood cells are transformed from a round shape into a sickle shape because of sickling process resulting in getting stuck in the arteries and, in turn, blocking the blood flow. Polymerization and aggregation of sickled erythrocytes in the microvasculature lead to the inhibition of oxygen delivery to the blood vessels since sickled RBCs are less flexible and damage the cellular membranes.[14]

ACS is a known complication of SCD in patients who are admitted to the hospital with vaso-occlusive crisis (VOC). As mentioned above, one of the patients with SCD developed ACS in the setting of COVID-19. Beerkens and colleagues reported a patient with SCD who primarily manifested severe pneumonia and then developed ACS in the setting of COVID-19.[15]

Nur and co-workers reported two patients with SCD who primarily presented with VOC and then developed ACS. In SCD, COVID-19 can potentially cause severe pulmonary complications, either by directly causing severe pneumonia or by initiating a VOC and/or ACS. They concluded that it is necessary to search for SARS-CoV-2 in the evaluation of SCD patients presenting VOC.[16]

Other studies showed that SCD cannot have a severe effect on COVID-19; for instance, a french study by Jean-

Table 1: Results of complete blood cell of four siblings

Laboratory study	Result				Reference
	Case 1	Case 2	Case 3	Case 4	
WBC	12.5 H	10.2	11.5 H	10.5	4-10 X1000/mm^3
RBC	4.06	6.1	4.2	5.2	M:4.5-6.0 F:4.2-5.2/ Mill/ mm^3
HB	8.2 L	15.6	10.9 L	16.2	M:14.0-18.0 F:12.0-16.0 g/dl
Hct	33.7	42.35	34.2	47.2	M:39-52 F:36-46 %
M.C. V	60.8	86.9	74.5	82.5	80-96 fL
M.C.H	26.8	31.6	25.2	30.2	27.0-34.0 pgm
M.C.H.C	27.6	33.1	28.8	32.8	32.0-36.0 %
Platelet	355	411	367	343	140.0-450 X1000/mm^3
RDW	15.9	13.4	15.1	13.9	11-16 %

Benoît Arlet *et al*. indicated that COVID-19 does not increase the risk of morbidity or mortality in patients with SCD and it was also suggested that the hypothesis of a protective effect against COVID-19 in patients with SCD can be surveyed.

A single center experiment by Preethi Ramachandran et al. 2020 reported that SCD patients who are assumed to be at high risk of COVID-19 may be protected from severe complications of COVID19.[17] Hussain *et al*. 2019 studied case series of SCD patients and demonstrated a milder COVID-19 course in four SCD patients.

In our study, the subjects who were carriers of HBS did not present severe symptoms. Given the heterozygous state, red blood cells have one copy of normal hemoglobin (Hb) and one copy of mutant Hb (HbS known as genotype of HbAS. It is expected that the presence of HbA can reduce the probability of polymer formation and attuned phenotype of SCD; thus, hematological parameters are normal in the majority of individuals with sickle cell trait; however, increasing evidence indicates that hypoxia may trigger complications such as splenic infarction, thromboembolism, rhabdomyolysis, and necrosis in patients with sickle cell trait.[18] Sickle cell trait has been associated with an increased risk of coronary artery diseases in African American men who have chronic kidney diseases.

Based on medical literature, sickle cell trait can potentially increase the risk of hypercoagulability; however, there are no reported cases of sickle cell trait infected with COVID-19 manifesting severe symptoms in clinical scientific literature as of May 16, 2020.

Conclusion

Given our findings, the severity of COVID 19 symptoms among SCT subjects is lower than SCD; however, it seems SCD cannot increase the risk of COVID-19.

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Conflict of Interest: None declared.

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