



Sickle cell individuals are less vulnerable for Corona Virus Disease 2019 - An Enigma

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ABSTRACT

The "Coronavirus Disease 2019 (COVID-19)" caused by "Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)" has emerged in December 2019 and was announced as a pandemic by "World Health Organization". As of today, no specific therapeutics drugs are available for COVID-19. Thus patients have to rely on symptomatic adjuvant therapies. Iron is critical in various physiological processes like DNA/RNA synthesis and generation of ATP. In pathological condition, iron is vital for the host as well as the pathogen. Literature search revealed iron chelation therapy is one of the promising and emerging treatment modality for COVID-19. In pathological condition, iron is essential for the host as well as the pathogen like viruses which require intracellular iron for replication and propagation. Sickle cell anaemia is hemolytic anaemia, where "Sickle haemoglobin (HbS)" is a structural variant of normal adult haemoglobin. Haemoglobin composed of haem and globulin molecules. An iron atom of haem helps in binding of oxygen molecules. In sickle cell individuals, haemoglobin concentration is reduced. Thus viruses do not succeed in replication and proliferation due to deprived iron concentration; they may be less vulnerable for COVID-19 due to reduced iron load. Another fact is that sickle cell individuals are immune to Malaria due to HbS. Some reports say that the incidence of COVID-19 is less in Malaria population counties. Thus it may be postulated that sickle cell individuals may also develop immunity to SARS-CoV-2, as evidenced by less incidence of COVID-19 in Malaria patients.



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avirus 2 (SARS-CoV-2)" has appeared in December 2019 and continues to spread worldwide. The disease creates a significant threat to public health worldwide affecting more than 200 countries (De Simone *et al.*, 2020)

Coronaviruses belong to the "Coronaviridae" family including single, large plus-stranded RNA as the genome (Fehr and Perlman, 2015; Gorbalenya *et al.*, 2006), "SARS-CoV-2" can attach to the "human angiotensin-converting enzyme 2 (ACE-2)", which is present on the cell surfaces and has been identified as target receptor for "COVID-19" virus for entry into the host cells (Sarode *et al.*, 2020).

INTRODUCTION

The "Coronavirus Disease 2019 (COVID-19)" caused by "Severe Acute Respiratory Syndrome Coron-

Fever, shortness of breath, cough, myalgia (muscle pain), and tiredness are the common clinical symptom of the patients suffering from "COVID-19".

Whereas it may also show, symptoms like hemoptysis, headache, dizziness, stomach pain diarrhoea, nausea, and vomiting (Fini, 2020)

As on today, no specific therapeutics drugs are available for COVID-19. Thus patients have to rely on symptomatic adjuvant therapies. The literature search revealed iron chelation therapy is one of the promising and emerging treatment modality for COVID-19 (Liu *et al.*, 2020)

Iron is critical in various physiological processes like DNA/RNA synthesis and generation of ATP (Drake-smith and Prentice, 2008). In pathological condition, iron is important for the host as well as the pathogen. In hepatitis B and C infection, there is iron overload, which is correlated with poor prognosis (Kaufmann and McMichael, 2005; Galli *et al.*, 2005).

Intracellular iron is fundamental in the process of replication and propagation of various viruses like HIV, hepatitis B and C, including "SARS-CoV-2." The pathogenesis of viral infection by SARS-CoV-2 is much less understood as compared with "HIV-1", hepatitis B and C. Thus in line with other viral infections it is reasonable that deprivation of iron supply to the virus serves as a helpful adjuvant therapy in treating SARS-CoV-2 infections (Liu *et al.*, 2020).

Sickle cell anaemia is hemolytic anaemia, where "Sickle haemoglobin (HbS)" is a structural variant of normal adult haemoglobin. Adult haemoglobin (HbAA) is made up of 2 alpha and two beta-globin chains. HbS is the result of a single point mutation (Glu→Val) on the sixth codon of the "beta-globin gene" (Bunn, 1997). In heterozygous individuals, about 40 % of haemoglobin is HbS which develops sickle cell trait, whereas in the homozygous individuals nearly all haemoglobin is HbS resultant to sickle cell anaemia (Lervolino *et al.*, 2011).

Haemoglobin composed of heme and globulin molecules. An iron atom of heme helps in binding of oxygen molecules. In sickle cell individuals, haemoglobin concentration is reduced, and thus viruses do not succeed in replication and proliferation due to deprived iron concentration (Koduri, 2003).

Another factor in sickle cell individuals is that they are resistant to Malaria. "Malaria" is a vector born disease which is caused by "Plasmodium falciparum", and it has been a significant reason for morbidity and mortality throughout human history. The life cycle of Plasmodium falciparum takes place in the erythrocyte. In sickle cell individuals presence of innate factor for Plasmodium falciparum help to reduce the growth and multiplication of parasites.

Even these individual develops acquired immunity against Malaria (Williams *et al.*, 2005). The association of sickle cell disease and Malaria is scientifically established (Gong *et al.*, 2013).

CONCLUSION

With this premise, it may be hypothesized that the sickle cell individuals may be less vulnerable for the SARS-CoV-2 infection due to reduced iron load. Another factor in sickle cell individuals is that they develop immunity to Malaria due to HbS. Thus it may be postulated that sickle cell individuals may also develop immunity to SARS-CoV-2, as evidenced by less incidence of COVID-19 in Malaria patients. To prove this hypothesis, detailed studies on the pathogenesis of COVID-19 in sickle cell individuals should be carried out, and the data can be utilized for the therapeutic modalities against SARS-CoV-2.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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