**The haemoglobinopathy patients in COVID 19 pandemic: A perspective.**

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**Abstract**

Haemoglobinopathic patients are high-risk group since due to their susceptibility to various types of infections and which contribute to the morbidity and mortality. Haemoglobinopathic patients, especially sickle cell disease and thalassemia patients are at high risk due to their non-functional spleen, immunodeficiency, and respiratory disorders in the context of COVID 19 pandemic. Lack of specialised advice and improper attention towards COVID 19 cases among haemoglobinopathic communities make the situation more severe. The urgency of developing a proper treatment protocol is very essential due to the rapid transmission of pandemic zoonotic infections to save the lives of millions of haemoglobinopathic patients around the globe.

Keywords: Haemoglobinopathies; viral diseases; COVID 19; pandemic; SARS; fatality; clinical ethics

**Introduction**

Haemoglobin disorders result from either the production of a mutated globular polypeptide in case of abnormal haemoglobin haplotype or the underproduction of any of the globular polypeptide in the case of thalassemia (1). Vaso-occlusion and haemolysis are the main pathophysiological conditions of sickle cell disease (SCD) and severe anaemia (2) and pulmonary problems are the trademarks of thalassemia. Among the haemoglobinopathies, SCD has got global attention since due to its ability to confer resistance to malaria (3). But the condition renders high susceptibility to many other infections many a time severely related to pulmonary as well as circulatory failure. The genetic change that happened in the 6th codon of the beta-globin chain happened as a boon sometimes turning to a curse in case of some severe pathogenesis. The cases of thalassemia cases are not ignorable in the same context.

Haemoglobinopathic patients are high-risk groups since due to their susceptibility to various types of infections and which contribute to the morbidity and mortality of this group especially in case of sickle cell anaemia (2). These groups are prone to various types viral of infections and end up with severe clinical complications. Being a chronic disease SCD has got a high risk of being affected by Dengue fever (4). Vaso-occlusion triggered by severe inflammation is a common risk factor in the case of SCD, SCA, and DENV (Dengue virus) infection (Rees *et al*. 2010 5). If the affected patient is a sickle cell case, the severity of viral infection becomes more complex. Endothelial damage, plasma leakage, high inflammation, profound shock, and hemorrhage may put the patients to the high-risk group (6). Chances of thrombotic complications also exist with bleeding which happens in some severe cases (7). Immunopathological aspects like activated monocytes and subsequent activation of endothelial cells produce a wide variety of cytokines and end in SCD mediated vaso-occlusion (8). The fatality rate is high among cell sickle patients, who are infected with DENV (8, 9). Dengue hemorrhagic fever (DHF) is also reported from thalassemia prevalent regions of South Asian countries. Thalassemia patients with DENV infection suffer from severe anaemia formed as a result of suppression of haematopoiesis, extra-vascular haemolysis and haemophagocytosis (10, 11). Severe anaemia and iron deficiency observed in the case of sickle cell disease and thalassemia may increase vector permissiveness of DENV (12, 13) and the people are in the high risk category. Zika virus infection is also reported in sickle cell disease. The disease severity of SCD in combination with arboviral infections like Zika virus infection is critical and should be closely monitored (14). The infection by Zika is reported from tropical Africa, South West Asia, and America, where haemoglobinopathies are prevalent (15). Ebola virus disease (EVD) may less severe in the case of SCD since the severity of EVD is complex when it co-exists with malarial infection (16). Sickle cell disease prevents the *P. falciparum* infection and it is an advantage for sickle cell patients affected with Ebola up to an extent and mortality rate is lower than groups co-infected with malaria and Ebola.

**Relatedness of COVID 19 and haemoglobinopathies**

Due to the onset of the zoonotic infection SARS-COV-2 coronavirus, haemoglobinpathic patients are becoming a risk group, since they are susceptible to acute chest syndrome and severe alveolar damage (17). Acute chest syndrome includes pathological conditions such as recurrent pulmonary infraction and related cough, pleuritic chest pain, hemoptysis, and finally leads to respiratory failure (18, 19). Cardiomegaly and congestive cardiac failure and increase the death risk factor.

The terminal infection in sickle cell disease was heralded by upper respiratory tract syndrome (72.6%). Pulmonary hypertension, obliterative pulmonary vasculopathy, pulmonary thrombi or emboli, and interstitial pulmonary fibrosis are the problems of sickle cell patients. Pulmonary thromboembolism (20, 21, 22) concentric pulmonary vascular intimal hyperplasia leading to endothelial damage and in situ thrombosis (23, 21) are the key pathological factors formed as a result of pulmonary hypertension in SCD (24, 25 ). Pulmonary hypertension plays an important role in pulmonary failure in sickle cell disease (22) and haemolysis is associated with pulmonary hypertension (25). Pulmonary problems are also usual events in thalassemia major cases (26, 27).

The onset of coronavirus exhibits symptoms like fever, cough, headache, diarrhea, dyspnoea, fatigue, etc (28, 29, 30, 31), In later stages complications like severe pneumonia, acute respiratory distress syndrome, RNAaemia, acute cardiac injury and gland-glass opacities in the lungs and subpleural regions of the lungs leading death can be observed (17, 31). The acute respiratory syndrome is the main lethal factor to the COVID-19 pandemic by the infection of SARS-Cov-2 (Severe acute respiratory syndrome coronavirus 2. COVID-19 pneumonia leads to acute pulmonary embolism (32, 33). Thrombocytopenia, prolonged prothrombin time, elevated D-dimer, and disseminated intracellular coagulation is observed among patients (34). The lack of antiviral treatment and lagging in the invention of vaccines against COVID 19 pushing the patients towards treatment based on the symptoms and intensive care units in case of acute chest syndrome (35). Haemoglobinopathic patients suffering from intensive respiratory problems and severe anaemia need utmost care and proper treatment strategies.

**COVID 19: Indian scenario**

According to Ministry of health and family welfare, Government of India (<https://www.mohfw.gov.in/>), as on August 23rd, India reported 22, 80, 556 COVID-19 positive cases and the major part is shared with the states of Maharashtra (4, 80, 114), Tamil Nadu (3, 13, 280), Andhra Pradesh (2, 52, 638), Karnata ( 1, 84, 568) and Delhi (1, 44, 138). This was followed by Uttar Pradesh (1, 31, 295), West Bengal (1, 04, 959), and Bihar (94, 858). Within one month, more than 9 lakhs of cases were newly reported. An on July 25th, 2020, the positive cases were 13, 36, 861 COVID-19, and the major part is shared with the states of Maharashtra, Tamil Nadu, and Delhi. All these states are center for haemoglobinopathies and the uncontrollable spreading rate of coronavirus make people in trouble who are suffering from various haemoglobin disorders. Since it is a novel infection, the dynamicity of infection is unclear apart from certain mathematical modeling and simulation approaches (36, 37). In the present scenario, the predictions and control measures are not going as expected. Haemoglobinopathic patients, especially SCD and thalassemia patients are at high risk due to their non-functional spleen and immunodeficiency (38). Spleen and lymphoid atrophy were also reported from COVID-19 cases (39). Difficulty in getting specialised advice and improper attention towards these rare haemoglobinopathies making the situation more severe (40). The situation is getting worse since due to its spreading among African, South American, and South Asian tribes and ethnic groups, who are more suffering from haemoglobinopathies. In Kerala, the first tribal COVID 19 death has been reported from the Attappadi tribal colony of Palakkad district. Unknown cases or even death may happen in various tribal communities. Many more tribal people are under close surveillance since 17 more cases so far reported from the area. Haemoglobinopathies are also prevalent in these Attappadi tribal colonies. Other tribal regions of India are at high risk due to the rapid community spreading of COVID 19 pandemic. If the government and health care systems fail to control the spread of COVID 19 among tribal people, it will end up with a great disaster. The tribal, as well as the other ethnic population all over the globe, are already under the pressure of malnutrition, immune deficiency, and different types of genetic disorders especially haemoglobin disorders. In this special context of COVID 19, they need more attention. Even though the national recovery rate nears 75% in India and fatality rate is above 1.5% (as per Augst 2020) when comparing with the previous month (July 2020) the urgency of developing a proper treatment protocol is very essential due to the rapid transmission of pandemic zoonotic infections to save the lives of millions of haemoglobinopathic patients around the globe. The persons, who are suffering from haemoglobin disorders need immediate attention and the cases should be considered with a special reference under the medical ethics of our country.

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