Editorial

Covid-19: Factors for Global Variations in Disease Severity and Mortality

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The coronavirus disease 2019 (COVID-19) has claimed around 1 million lives across the globe and infected over 30 million word population since its origination from Wuhan china in December 2019. The clinical symptoms, presentation, and mortality rate of COVID-19 are highly variable among different world populations. The Chinese population of Wuhan city has a 3% mortality rate, from the beginning of this epidemic to till date, but the mortality rate increased twofold in Italy, Spain, and the USA after China[1,2]. The European countries and the USA emerged as the new epicentre of COVID-19 after china. The severity of the disease in Italian patients and rapid deterioration of patient health, resulting in increased mortality rate indicate the involvement of other factors, which alleviate the viral pathogenicity. The severity of the disease and response of the patients to available management strategies have shown significant diversity and success rates among people of different ethnic backgrounds.

Pakistan is the country in south Asia, where 1st COViD -19 patient was reported in February 2020. The progression of the infection, clinical severity, and the mortality rates are low in the Pakistani region as compared to its ethnically matched neighbour country India and the developed countries of European and American regions. World health organisation has listed Pakistan among the countries where the report of new cases of COVID-19 and the death toll is going towards lower side with every passing day. In addition, the successful efforts of the government of Pakistan, for controlling the spread of the infection and managing hospitalized patients have been commended by world health leaders. Apart from the successful administrative strategies for combating the disease; several other factors, contributing towards low mortality and severity of the COVID-19 are in debate.

Several theories and scientific reasons have been postulated to underline the scientific link with low clinical severity and morality of COVID-19 in the region. One of the hypotheses is the use of the BCG vaccine as the cause of resistance to COVID-19 infection. The off-target protective role of BCG against other infections and boosting effects on the immune system have been observed previously[3-5]. However, its effect on the COVID-19 infection, comorbidities and mortalities are not clear and debatable[6,7]. The BCG vaccination may reduce the COVID-19 viral load, leading to less severe clinical manifestation and early clearance of the virus[7]. The BCG vaccine is included in the Enhanced Programme of Immunization of Pakistan and is being administered at the time of birth for the last 70 years[8]. There is a need to explore the scientific evidence for any relationship between COVID-19 pathogenicity and BCG associated immunity in Pakistani patients.

The genetic polymorphisms in the host immune genes may also play a crucial role in the variable clinical presentation and diversity in the pathogenic effects of the COVID-19. The coronavirus uses ACE2 receptors to enter the host cell and the host genetic variations in the ACE2 gene may impact the successful viral entry into the host cell. The variable expression of the ACE2 gene has been observed in the lungs of Asian and European patients[9]. A Comparative genetic study has described the controversial role of ACE2 gene mutations and expression related to COVID-19 disease pattern[10]. Previous genetic studies have revealed genetic heterogeneity in the Pakistani population and various novel genes and alleles have been found with the help of Pakistani patients[11]. There is a high probability that the Pakistani population may have unique alleles of ACE2 gene resulting in differential expressionand may be one of the reasons of low mortality and clinical severity among Pakistani COVID-19 patients.

The role of antibodies against SARS-CoV2 has proved invaluable; a significant number of COVID-19 recovered patients failed to develop antibodies; furthermore, patients who developed antibodies lost it by 90 days[12,13]. A recent study has described the role of another hidden immunity, based on CD4+ and CD8+ T cell responses. It is noteworthy that SARS-CoV-2-cross-reactive T cell responses were found in healthy subjects and may be a reason for pre immunity in the studied population[14]. The majority of the Pakistani individuals remained uninfected and may have the T cell based pre immunity against COVID-19.

In summary, the progression of COVID-19 infection in the Pakistani population, the recovery rate, clinical severity, and mortality are variable other than the rest of the world. There is a need to explore the reasons of extraordinary immunity and resistance shown by the people of this region. It may be based on the use of other vaccines, host genetic variations, or the specific innate immunity. The information will be helpful to

better understand the pathogenesis of the COVID-19 and may also pave the path for the synthesis of an effective vaccine.

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