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COVID-19 pandemic: Mechanistic approaches and gender vulnerabilities

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ABSTRACT

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a highly pathogenic virus that causes coronavirus-19 disease (COVID-19), a severe respiratory damaging syndrome with serious health complications worldwide. SARS-CoV-2 was unfamiliar before the epidemic started in Wuhan, China, in December 2019. COVID-19 is currently a pandemic influencing several countries worldwide. One of the mysteries of the new coronavirus is that it is deadlier for men than women with the male mortality rate is twice as high as that of females.

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1. Summary

Since its emergence in Wuhan, a city in Hubei province of China, COVID-19 has provoked widespread infectivity around the globe. According to Global Health 5050, a society that encourages gender-specific similarities in health care (Sharma, Volgman, & Michos, 2020; Sohrabi et al., 2020) male populations infected with the 2019 novel coronavirus-19 (COVID-19) are prone to more acute infections following deaths as compared to females (Xie, Tong, Guan, Du, & Qiu, 2020). The report suggested a role of sex biology in humans' risk of infectivity and death as a consequence of COVID 19.

CoV-19 attaches to the body's immune cells, triggering the antibody reaction in both COVID 19-infected and non-symptomatic individuals. Typically, males produce fewer robust immune responses than females and are highly prone to a selection of contagious means (Conti & Younes, 2020; Klein & Flanagan, 2016). Several reports propose variances between males and females in their immune reaction to communicable and inflammatory illnesses like TB, malaria, hepatitis, HIV-1, mumps, measles, and flu (Rettew, Huet-Hudson, & Marriott, 2008).

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Females are functional tessellations for X-lined genes that are related to immunity hence qualify them to incite stronger innate and adaptive immune responses resulting in low infectivity (Fung, Huang, & Liu, 2014). Structural changes in the host cells due to virus overload may also contribute to the high infectivity in male (Schurz et al., 2019). A recent study has revealed the role gender plays in morbidity and mortality of SARS-CoV-2 infection (Drosten et al., 2003). Studies pondering the mechanistic aspect for infectivity suggest that males have high concentration of circulating angiotensin-converting enzyme 2 (ACE2) than in their female counterpart (Patel, Velkoska, & Burrell, 2013; Ullah, 2020a). ACE2 is the targeting receptor site for the (SARS-CoV) and the associated human respiratory coronavirus NL63, that exhibit in human airway epithelia and lung parenchyma (Jia et al., 2005). High-throughput sequencing has shown that (SARS-CoV-2) looks like (SARS-CoV) (Jia et al., 2005).

Severe acute respiratory syndrome coronavirus preferentially attack the (ACE2) receptors due to sequencing similarity. Hence, males are more likely to be affected by (SARS-CoV-2) in contrast to females. Researchers sequenced the genome of the virus and established numerous auspicious vaccine candidates for experimental testing (Grifoni et al., 2020). The recovered antibodies from COVID-19 individuals might be considered to treat persons with initial signs and stop the spread of infection (Casadevall and Pirofski, 2020; Jin et al., 2020; Wu et al., 2020).

The role of transmembrane protease serine 2 (TMPRSS2) in coronavirus infections, and modulation of COVID-19 severity is still

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unknown (Cheng et al., 2015). Some reports suggest its involvement in influenza severity in humans and animals (Cheng et al., 2015). TMPRSS2 (testosterone regulated gene) is higher in men than women. However, TMPRSS2 expression levels and their role are also regulated by estrogen-dependent signaling (Cheng et al., 2015; Penna, Mercurio, Tocchetti, & Pagliaro, 2020; Sakai et al., 2015).

The higher mortality of COVID-19 in men may be due to sex-specific responses, as the immune cells obtained from women usually show a greater response compared to those isolated from men (Scotland, Stables, Madalli, Watson, & Gilroy, 2011). Male has lower basal immunoglobulin levels and a smaller number of circulating and resident CD4/CD8 T-lymphocytes ratio than females (Amadori et al., 1995; Li, Jerkic, Slutsky, & Zhang, 2020).

So far, no vaccine has been approved by the Food and Drug Administration (FDA) for COVID-19 treatment. However, some potential drugs have been reported which might help to reduce the severity of COVID-19. Upon intravenous or subcutaneous administration of Tocilizumab helps in reducing the mortality as well as the risk of invasive mechanical ventilator in severe COVID-19 (Guaraldi et al., 2020).

Angiotensin receptor blockers (ARBs) have effects that are parallel to angiotensin converting enzyme (ACE) inhibitors, however ACE inhibitors act by inhibiting the development of angiotensin II instead of blocking the binding of angiotensin II to muscles on blood vessels (Jia et al., 2005; Ullah, 2020b). ARBs are used for regulating high blood pressure, to treat heart failure, and restrain kidney failure in individuals with diabetes (Ullah, 2020a; Xie et al., 2020). Hence, angiotensin receptor blockers (ARBs such as losartan, valsartan, telmisartan, etc.) can be a novel therapeutic approach to block the binding and therefore, attachment of SARS-CoV-2 RBD to ACE2-expressing cells, thus inhibiting their infection to the host cells.

Apart from antivirals, immunotherapeutic strategies have been proposed with emphasis on the immune response of the host defense against the virus, and the fact that SARS-CoV-2 suppresses interferon induction as an immune evasion approach (Drosten et al., 2003; Ullah, 2020a). Active immunization via vaccines, interferon administration, passive immunotherapy by convalescent plasma or synthesized monoclonal and polyclonal antibodies, as well as immunomodulatory drugs, are different immunotherapeutic approaches against the (SARS-CoV-2) (Owji, Negahdaripour, & Hajighahramani, 2020; Ullah, 2020b). Some of these vaccines are in advanced human clinical trials. Convalescent plasma therapy is already exercised in several countries to help save the lives of severely ill patients (Sharun et al., 2020). Diverse antibodies that target several phases of SARS-CoV-2 pathogenesis or the related immune responses are also suggested. To treat the cytokine storm, induced at a later stage of the disease in some patients, immune modulation through JAK inhibitors, corticosteroids, and other cognate classes are assessed (Owji et al., 2020).

2. Conclusion

The sex and gender discrepancies seen in COVID-19 vulnerability underline the need to comprehend the influence of sex and gender on prevalence and case mortality of the disease and to modify treatment conferring to sex and gender. Understanding from previous outbreaks and pandemics has shown the significance of integrating sex and gender evaluation into preparation and response efforts for health interventions. These differences may be due to known sex differences in genes, chromosomes, and hormones that lead to very different responses to many diseases, including COVID-19.

There is a dire need to establish develop efficient platforms that can develop effective vaccines and antiviral medicines robustly for such outbreaks. Globally, health systems and drugs manufacturing companies have been progressing sluggishly compared to speedy pathogens partly due to technical, political, and investment barriers.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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