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Sex differences in COVID-19 case fatality: do we know enough?



Global data indicate higher COVID-19 case fatality rates among men than women. Most countries with available data indicate a male to female case fatality ratio higher than 1.0, ranging up to 3.5 in some cases (appendix).¹ However, the COVID-19 case fatality rate is higher in women than men in a few countries, such as India, which is one of the worst-affected countries. As of Sept 30, 2020, India had more than 6.4 million recorded COVID-19 cases.² In India, the COVID-19 case fatality rate among men is 2.9% and 3.3% among women.³ Case fatality rates in Nepal, Vietnam, and Slovenia are also higher among women than men.¹ These findings are surprising since global data have indicated that both biological factors (stronger immune responses) and behavioural risk factors (eg, smoking, and other lifestyle habits) place men at a greater risk for health complications and death as a consequence of COVID-19.^{4,5} Such differential findings on the association between sex and COVID-19 case fatality between countries might reflect incomplete COVID-19 data across geographies, biases in case identification by sex, or higher risks for women in certain countries due to demographic factors or countries' health profiles.

In India, the case fatality rate for COVID-19 is lower than that observed in high-income countries, such as the USA.¹ This difference might be due to the age structure of the Indian population, which has a larger proportion of younger individuals than the US population.⁶ The observed differences in India might also be indicative of the populations who are potentially being exposed to the virus, and who is being tested. India does not have national surveillance testing available due to the large population size. Tests are thus prioritised for individuals who have symptoms, or traced contacts of positive cases; these contacts are often exposed in institutional environments such as workplaces and schools, where older (age >65 years) and other susceptible populations are possibly less common. Consequently, the case fatality rate reported by the Indian Government, and the overall case rate have been questioned.⁷ Disproportionate access to testing for certain population subgroups, and the reliance on hospital-level information for the estimation of fatality rates is likely to result in sex biases in our understanding of the impact of COVID-19. Previous research from India

indicates marked sex differences in access to health services, with women being less likely to be admitted to hospital than men.⁸ These differences might result in more severe cases of COVID-19 among women than men in hospital settings.

Interaction between sex and age could be a key factor in explaining the observed sex differences in case fatality. An analysis of COVID-19 cases from India found that the mortality ratio between men and women was non-uniform across different age groups: risk of mortality was significantly higher among women than men, particularly in the 40–49 year age group.³ Socioeconomic status is another important factor, but little is known about how different socioeconomic groups in India are being affected by the pandemic. Data from other national contexts have found that marginalised groups are at higher risk of infection and death. Such an association has been reported in the USA, although data double disaggregated by sex and race or ethnicity were not available, impeding the ability to determine whether sex differences persist across racial and ethnic groups—eg, are Black women more at risk of poor COVID-19 health outcomes and mortality than White men? These intersectional analyses are needed to guide understanding of observed sex differences in COVID-19 mortality.

Researchers and policy experts agree that sex-disaggregated data on COVID-19 infection and case fatality rate are needed to develop gender-equitable solutions to this pandemic.^{9,10} Such solutions must include more careful examination of countries such as India, where mortality risk for COVID-19 is higher for women than men. Maintenance of high-quality sex-disaggregated data is required to monitor these differences across countries. To generate high-quality data, testing surveillance should be equitable, and should cover population subgroups of all socioeconomic strata. Such data should also be made accessible from governments. Divergence in COVID-19 case definition is another aspect to be considered; case definitions might vary across geographies and studies, and might be inconsistent with those of other countries, which impedes generalisation of findings. Furthermore, other social factors linked to COVID-19 exposure and mortality need to be identified, to enable exploration

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of intersectional differences. Understanding these factors will enable identification of the most vulnerable populations in this pandemic, to ensure better targeting of prevention and intervention efforts. Without these improvements, sex-disaggregated data will be of no use for the development of gender-equitable solutions for the pandemic.

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