Is the hygiene hypothesis a plausible explanation for the asymmetry in COVID-19 mortality?

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Madam, there is large variation observed in COVID-19 outcomes that indicate the existence of individual and population-based factors influencing the infection course.[1] By the second wave of COVID-19, mortality rates in twenty most affected countries were varying, ranging from 2% in Philippines to 11% in Mexico.[1] A study evaluating WHO's region-wise statistical observation of six regions showed an Infection Fatality Rate (IFR) of 0.02% for the American, European, and Eastern Mediterranean regions while for South-East Asian and the Western Pacific regions, it was 0.01%.[2] Case Fatality Ratio (CFR) was highest in Europe of 7.3%, 5.3% in American region and a lowest of 1.1% in South-East Asian region.[2] Pre-existing health conditions have become decisive feature in assessing disease progression, and aligned with this discourse, the Hygiene Hypothesis can be a plausible explanation for this pattern of COVID-19 infection and mortality. The theory states that the reduced pathogen exposure in high-income regions during important development phases leads to a decreased stimulation by evolutionary relevant pathogens resulting in immune dysregulation and increase in chronic inflammation, allergy, autoimmunity.[2] The hyper-hygienic practice wards off potential problems before they progress into clinical condition and disturbs the balance of commensal organisms in surface locations such as gastrointestinal tract, skin and increasing COVID-19 susceptibility.[3] Contrarily, extensive exposure to multiple microbes that express pathogen associated molecular patterns activates innate immunity. In this "trained immunity", ascribed to many cell types, a response generated against one set of microbes can have bystander immune protection against other infections.[3] In Ethiopia, the IFR obtained was 0.55% in urban neighbourhoods and 0.78% in remote settlements respectively, an estimate lower than that deduced for higher income countries.[4] Further, background immunity against SARS-CoV-2: TCD4 cells observed in some individuals not exposed to SARS-CoV-2 was found to cross react to SARS-CoV-2 proteins.[5]

However, the hypothesis cannot be over generalized as the number of COVID-19 deaths might be unascertained in low-income countries due to inadequate reporting. Climatic conditions, age, gender, the type of spread of disease also account for differences.[4] On the contrary, we can suspect a positive relation between Social Vulnerability Index and COVID-19 incidence as results from Brazil exhibit.[5]

The Hygiene Hypothesis, albeit cannot be heavily relied upon, offers new perspective in studying the effect of the environment and innate immunity on disease severity and progression. It also provides insights for augmenting standard hygiene practices.

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