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CORRESPONDENCE

Severity of SARS-CoV-2 Reinfections as Compared with Primary Infections

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TO THE EDITOR:

Qatar had a first wave of infections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from March through June 2020, after which approximately 40% of the population had detectable antibodies against SARS-CoV-2. The country subsequently had two back-to-back waves from January through May 2021, triggered by the introduction of the B.1.1.7 (or alpha) and B.1.351 (or beta) variants.[1] This created an epidemiologic opportunity to assess reinfections.

Using national, federated databases that have captured all SARS-CoV-2–related data since the onset of the pandemic (Section S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org), we investigated the risk of severe disease (leading to acute care hospitalization), critical disease (leading to hospitalization in an intensive care unit [ICU]), and fatal disease caused by reinfections as compared with primary infections in the national cohort of 353,326 persons with polymerase-chain-reaction (PCR)–confirmed infection between February 28, 2020, and April 28, 2021, after exclusion of 87,547 persons with a vaccination record. Primary infection was defined as the first PCR-positive swab. Reinfection was defined as the first PCR-positive swab obtained at least 90 days after the primary infection. Persons with reinfection were matched to those with primary infection in a 1:5 ratio according to sex, 5-year age group, nationality, and calendar week of the PCR test date (Fig. S1 and Table S1 in the Supplementary Appendix). Classification of severe, critical, and fatal Covid-19 followed World Health Organization guidelines, and assessments were made by trained medical personnel through individual chart reviews.

Of 1304 identified reinfections, 413 (31.7%) were caused by the B.1.351 variant, 57 (4.4%) by the B.1.1.7 variant, 213 (16.3%) by "wild-type" virus, and 621 (47.6%) were of unknown status (Section S1 in the Supplementary Appendix). For reinfected persons, the median time between first infection and reinfection was 277 days (interquartile range, 179 to 315). The odds of severe disease at reinfection were 0.12 times (95% confidence interval [CI], 0.03 to 0.31) that at primary infection (Table 1). There were no cases of critical disease at reinfection and 28 cases at primary infection (Table S3), for an odds ratio of 0.00 (95% CI, 0.00 to 0.64). There were no cases of death from Covid-19 at reinfection and 7 cases at primary infection, resulting in an odds ratio of 0.00 (95% CI, 0.00 to 2.57). The odds of the composite outcome of severe, critical, or fatal disease at reinfection were 0.10 times (95% CI, 0.03 to 0.25) that at primary infection. Sensitivity analyses were consistent with these results (Table S2).

Table 1.

Severity of SARS-CoV-2 Reinfections as Compared with Primary Infections in the Population of Qatar.

Reinfections had 90% lower odds of resulting in hospitalization or death than primary infections. Four reinfections were severe enough to lead to acute care hospitalization. None led to hospitalization in an ICU, and none ended in death. Reinfections were rare and were generally mild, perhaps because of the primed immune system after primary infection.

In earlier studies, we assessed the efficacy of previous natural infection as protection against reinfection with SARS-CoV-2[2,3] as being 85% or greater. Accordingly, for a person who has already had a primary infection, the risk of having a severe reinfection is only approximately 1% of the risk of a previously uninfected person having a severe primary infection. It needs to be determined whether such protection against severe disease at reinfection lasts for a longer period, analogous to the immunity that develops against other seasonal "common-cold" coronaviruses,[4] which elicit short-term immunity against mild reinfection but longer-term immunity against more severe illness with reinfection. If this were the case with SARS-CoV-2, the virus (or at least the variants studied to date) could adopt a more benign pattern of infection when it becomes endemic.[4]

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Members of the National Study Group for COVID-19 Epidemiology are listed in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

4 References

Supplementary Material

Supplementary Appendix	PDF	511KB
Disclosure Forms	PDF	139KB

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