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NARRATIVE REVIEW

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A mini review of reinfection with the SARS-CoV-2 Omicron variant

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Abstract

Background: COVID-19 has caused severe morbidity and mortality worldwide. After the end of the dynamic zero-COVID policy in China in December, 2022, concerns regarding reinfection were raised while little was known due to the lack of surveillance data in this country.

Aims: This study reviews the probability, risk factors, and severity of severe acute respiratory syndrome coronavirus 2 Omicron variant reinfection, as well as the interval between infections, risk of onward transmission by reinfected cases, and the role of booster vaccination against reinfection.

Sources: References for this review were identified through searches of PubMed and Web of Science up to September 24, 2023.

Results: The rate of reinfection ranges from 3.1% to 13.0%. Factors associated with a higher risk of reinfection include being female, having comorbidities, and being unvaccinated. Reinfection with the BA.4 or BA.5 variant occurs approximately 180 days after the initial infection. Reinfections are less clinically severe than primary infections, and there is evidence of lower transmissibility. The debate surrounding the effectiveness and feasibility of booster vaccinations in preventing reinfection continues.

Conclusions: The reinfection rate during the Omicron epidemic is significantly higher than in previous epidemic periods. However, the symptoms and infectivity of reinfection were weaker than those of the prior infection. Medical staff and individuals at high risk of reinfection should be vigilant. The efficacy of booster vaccinations in reducing reinfection is currently under debate.

KEYWORDS

COVID-19, infectiousness, interval, Omicron variant, reinfection, SARS-CoV-2, severity, wane of immunity

1 | INTRODUCTION

Since the first identification of severe pneumonia with COVID-19 in 2019,[1] there have been over 768 million confirmed cases and more than 6.9 million deaths reported (WHO, June 21, 2023). China's stringent lockdown, quarantine policy, and mass testing before December 2022[2,3] resulted in a lower prevalence of confirmed and asymptomatic cases compared to other countries.[4,5] Following the end of the dynamic zero-COVID policy, the incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has soared, and concerns about reinfection have arisen.[6,7] From the Alpha to the latest Omicron variant, the virulence, transmissibility, and immune evasion of SARS-CoV-2 strains have evolved dramatically.[8,9] Therefore, it is important to study reinfection with the Omicron variant and guide policy-making. This review summarizes the most pressing questions regarding reinfection during the Omicron variant epidemic.

2 | METHODS

We conducted electronic searches for studies using Pubmed and Web of Science until September 24th, 2023, with the search terms "SARS-CoV-2," "COVID-19," "reinfection," "Omicron," "risk," "transmission," "Infectiousness," "severity," "medical staff," "booster vaccination," and "mRNA booster vaccine." To summarize the reinfection rate, we extracted the study population size, study period, and reinfection rate. The inclusion criteria included: reinfection was defined as a positive SARS-CoV-2 test occurring at least 90 days after the initial infection; and reinfection with Omicron variants. The exclusion criteria for assessing the reinfection rate were non-Omicron variants and a sample size of less than 3000 individuals.

3 | HOW OFTEN DOES REINFECTION OCCUR?

Reinfection after primary infection with SARS-CoV-2 is possible, but the rate varies depending on the studied populations and time periods. A study conducted in the United States during the early period of the epidemic in 2020, which included 130,000 SARS-CoV-2 cases, showed a reinfection rate of 0.2%.[10] Between 2019 and 2022, the overall incidence of COVID-19 reinfection was 4.2%, with the highest prevalence observed in Africa (4.7%).[11] Denmark experienced two waves of SARS-CoV-2 pandemics in March to May and September of 2020. An observational study of nearly 4 million people and approximately 12,000 cases showed that the incidence of reinfection was 0.67%, and the protective effect of primary infection against reinfection was 80.5%.[12] However, due to viral variation and the enhanced transmissibility of novel strains, the probability of reinfection is increasing. The Omicron variant is highly transmissible and exhibits strong immune evasiveness, leading to rapid spread. However, it is associated with less severe symptoms than any previous variants.[13]

A retrospective study conducted in Turkey found that reinfection occurred in 26 (0.46%) out of 5554 Alpha cases, 209 (1.16%) out of 17,941 Delta cases, and 520 (13.0%) out of 3992 Omicron cases.[14] The reinfection rate was approximately 30 and 10 times higher in Omicron cases than in Alpha and Delta cases, respectively.[14] During the Omicron period, the Italian population had an incidence rate of 73.02/100,000 person-days.[15] During the Omicron period, 251 (4.2%) symptomatic reinfections were identified in health care workers with previous infections. There was a significant increase in the SARS-CoV-2 reinfection rate before and during the Omicron variant period (0.8% vs. 4.3%; $p < 0.001$).[16] Another study conducted in Mexico identified a reinfection rate of 3.1% during the Omicron predominance period.[17] According to the latest national surveillance data in Singapore, the incidence of Omicron BA.4 or BA.5 was 7.7–78.3/million PD, while the incidence of Omicron XBB reinfection ranged from 509 to 1854/million PD, depending on the individual's vaccination status and previous infected lineage (Table 1).[18] It is worth noting that Ciuffreda's study did not report the specific incidence, but found that BA.5 had the highest reinfection rate compared to other lineages, including BA.1, BA.2, and BA.4.[19] It is important to consider that the reinfection rates of COVID-19 may be underestimated due to the milder symptoms experienced by those who have been reinfected and their reluctance to seek medical attention or testing. Following the relaxation of pandemic restrictions, there has been a decrease in people's willingness to undergo COVID-19 testing. This has made it challenging to conduct population-based surveillance and obtain accurate data on reinfection rates.

TABLE 1 The reinfection rate of COVID-19 during Omicron period in various studies.

Country	Reinfection rate	Study period	Sample size	Reference
Turkey	13.0%	1 January to January 26, 2022	3992	[14]
Italy	73.02/100,000 PD	3 January to March 6, 2022	249,121	[15]
Brazil	4.2%	1 January to March 10, 2022	5976	[16]
Mexico	3.1%	March 3, 2020 to August 13, 2022	6,553,099	[17]
Singapore	7.7–78.3/million PD for Omicron BA.4 or BA.5; 509–1854/million PD for Omicron XBB	October 1, 2022, to November 1, 2022	2,456,791	[18]

Abbreviation: PD, person-days.

All of the aforementioned studies have shown the probability of reinfection within 90 days after the primary infection. The rate of second infection in a short period after recovery was low due to the high titer of neutralizing antibodies and the fact that the virus had not yet undergone mutation. A study conducted in Turkey in 2022 on 520 patients with Omicron reinfection found that 16.5% of cases occurred within 3-6 months, while 83.5% of cases occurred 6 months after the primary infection. The rate of reinfection within 6–12 months and 12 months after the previous infection was 36.7% and 46.8%, respectively.[14]

4 | WHO IS AT HIGHER RISK OF REINFECTION?

The risk of SARS-CoV-2 reinfection is primarily associated with age, gender, lack of vaccination, time since initial infection, infrequent mask use, and underlying medical conditions.[20,21] A retrospective study conducted in Spain from March to November 2020, which included nearly 30,000 patients with SARS-CoV-2, revealed that the average age of reinfected cases was 41.5 years old. Of the 14 cases, 85.7% were female.[22] However, it is important to note that the high reinfection rate in females may be influenced by the small sample size. In Italy, a transition from the Delta to Omicron epidemic occurred between August 2021 and March 2022. A retrospective analysis of 8.4 million SARS-CoV-2 patients during this period revealed that being unvaccinated was the most significant risk factor for reinfection, regardless of the prevalent virus variant. Compared to individuals vaccinated within 120 days, the risks of reinfection were 2.9 and 1.5 times higher among unvaccinated individuals and those vaccinated for more than 120 days, respectively.[15]

The study found that individuals over the age of 60 had a lower risk of reinfection. Additionally, women had a 1.2 times higher risk of reinfection compared to men.[15] The UK also observed a lower reinfection rate among individuals aged 70-80 years, which may be due to the high vaccination rate in this age group[15] or increased immune protection from previous infection.[23] Adolescents who had been vaccinated and infected with Omicron showed the highest protective effect against reinfection, with a 96.4% protection rate after 15–24 weeks of the second dose of vaccination.[24] According to surveillance data from 18 US jurisdictions, adults aged 18–49 years accounted for 72.4%, 66.9%, 63.9%, and 56.9% of reinfections during the periods of Omicron BA.1, BA.2, BA.4/BA.5, and BQ.1/BQ.1.1 predominance, respectively.[25] The higher percentage in this age group may be due to several factors, including later eligibility for vaccination, lower vaccination coverage, increased exposure risk, and possible survival bias.[25]

It is important to acknowledge that various factors, such as age, underlying health conditions, and occupation, may act as confounding variables in different study populations. This can lead to bias and make it challenging to compare research findings. In general, the risk of reinfection is higher for females, patients with comorbidities, those who lack anti-nucleocapsid IgG after the first infection, and those who are unvaccinated.[26] Additionally, individuals with chronic renal failure, cardiovascular disease, bronchopulmonary disease, neuropathy, and autoimmune diseases are at an increased risk of reinfection.[20] Individuals with these underlying conditions should take extra care to strengthen their personal protection and get vaccinated to prevent reinfection.

5 | HOW HIGH IS THE RISK OF REINFECTION AMONG THE MEDICAL STAFF?

The reinfection of medical staff is a matter of concern. Research conducted in Italy found that among the 335,000 patients with SARS-CoV-2 and 157,000 cases of reinfection between September 2021 and May 2022, the risk of reinfection among medical staff was 2.38 times higher than that of nonmedical staff.[20] Similarly, a high reinfection rate among health care workers was observed during England's second wave.[27] This was due to the increased likelihood of exposure to the virus among medical staff while at work.

A study conducted during the Omicron epidemic in India from December 1, 2021 to February 25, 2022, which included over 11,000 medical staff, found that the rate of reinfection was 28.4%. The risk of reinfection was associated with age, gender, and type of work.[28] Individuals over 45 years old had a 40% lower risk of reinfection compared to those under 25 years old. The risk ratio of reinfection for females compared to males was 1.6. The reinfection rates were highest among nursing staff and junior or senior residents (40.8% and 38.6%, respectively), while students/administrators had a rate of 15.4%. The hazard ratio (HR) of residents, nursing, and researchers were 3.0, 3.0, and 1.7, respectively, compared to students/administrators.[28]

Determining a precise value for the risk ratio of reinfection to health care workers may be challenging. However, these data showed that the risk of reinfection was greater for health care workers than for the general population. The most effective measures for preventing SARS-CoV-2 infection among medical staff are appropriate personal protection and hand hygiene.[20] Additionally, a high rate of mask wearing can reduce the risk of reinfection. Medical institutions should also provide more manpower and protective equipment, and reduce work pressure to further decrease the risk of reinfection in this group.

6 | HOW SOON DO REINFECTIONS TAKE PLACE AFTER A PREVIOUS INFECTION?

The duration and efficacy of immune protection, as well as the rate of viral mutation, influence the time between initial and subsequent infections. According to a retrospective cohort study conducted in Switzerland during the early stages of the SARS-CoV-2 epidemic in 2020, antibodies reduced the risk of reinfection by 94% among 498 antibody-positive individuals and 996 antibody-negative individuals. This protective effect lasted for at least 8 months. The study conducted in the United States found that antibodies provided a protective effect of over

80% after 7 months of primary infection.[29] However, the protective effect of primary infection gradually weakens due to the variation of viral strains, enhancement of immune escape capacity, and decrease of antibody titers in recovered patients.

A survey conducted in the United States between December 2021 and August 2022 found that SARS-CoV-2 infection provided limited protection against reinfection with Omicron variants.[30] Additionally, four Indian patients who had received the SARS-CoV-2 vaccine were infected with the Delta/Kappa and Omicron BA.2 variants. In the early stage of reinfection, the neutralizing antibody titer against B.1, Delta, and BA.1 variants decreased by 14, 12, and 117 times, respectively, compared to the breakthrough infection stage.[31] A recent study conducted in Qatar found that the interval between infection with the Omicron variant and reinfection with BA.4 or BA.5 variant was approximately 180 days.[32]

The US surveillance data from September 2021 to December 2022 showed a decrease in the median interval between infections, from 411 days in mid-February 2022 (near the end of the BA.1 period) to 335 days in mid-June 2022 (after the start of the BA.4/BA.5 period).[25] The median time to reinfection remained between 330 and 350 days for the remainder of the BA.4/BA.5 predominance and increased to 367 days by the week ending December 31, 2022 (the BQ.1/BQ.1.1 period).[25] The interval between prior infection and reinfection was primarily influenced by the circulating virus strain and the patient's willingness to undergo detection. Population-based surveillance and continuous case follow-up were crucial for determining this data. The Qatar study offers a more precise estimate of the reinfection interval during the Omicron epidemic.[32]

7 | THE SEVERITY OF REINFECTIONS COMPARED WITH INITIAL INFECTIONS

In general, reinfections are reported to be less clinically severe than primary infections,[26,33] although some severe outcomes have been reported, particularly among individuals who were hospitalized with a previous infection.[34,35] The mean pooled effectiveness from past infection was greater than 78% against severe reinfection (hospitalization and death) for all variants, including Omicron BA.1.[36] Both infection-induced and hybrid immunities could reduce the rates of hospitalizations, intensive care unit admissions, and deaths associated with reinfection, compared to those without pre-existing immunity.[37]

The initial infection or vaccination produces protective antibodies, which should reduce the probability of severe symptoms upon reinfection. Surveillance data from January 2020 to May 2021 in the United Kingdom during the early stage of the SARS-CoV-2 epidemic showed a 61% lower mortality rate for reinfection compared to primary infection. The study found that among individuals aged 50-65 who did not receive the SARS-CoV-2 vaccine, the rate of hospitalization due to reinfection was 34–49% lower than that of primary infection. The main risk factors for severe symptoms of reinfection were being an older adult, being female, and having underlying diseases.[38]

A study conducted in India found that 99.3% of 1007 patients with Omicron reinfection were asymptomatic or experienced mild symptoms such as fever (76.2%), cough (64.0%), muscle pain (63.2%), and sore throat (59.3%).[28] Case reports from India also showed that in patients with multiple episodes of infections with different variants, clinical symptoms gradually improved from fever, sore throat, limb pain, and fatigue to only headache in the last infection.[39] In addition to the protective effect of previous infections, the reduced pathogenicity of the Omicron variant may also contribute to the alleviation of symptoms.

The reduced severity of reinfection could be partially attributed to hybrid immunity, which provides the highest magnitude and durability of protection. In a systematic review that included 11 studies reporting the protective effectiveness of previous SARS-CoV-2 infection and 15 studies reporting the protective effectiveness of hybrid immunity, the effectiveness against reinfection of hybrid immunity following primary series vaccination decreased to 41.8% (95% confidence interval [CI] 31.5–52.8) at 12 months. Similarly, the effectiveness of hybrid immunity following the first booster vaccination decreased to 46.5% (36.0–57.3) at 6 months.[40] Protection from a previous infection against reinfection with a BA.4 or BA.5 subvariant was lower than that against reinfection with a BA.1 or BA.2 subvariant due to their greater capacity for immune evasion.[32] Previous post-Omicron subvariant (including BA.1 or BA.2) infection still provided strong protection against BA.4 or BA.5 reinfection, with 76.2% and 78.0% against symptomatic and any BA.4 or BA.5 reinfection, respectively.[32] A nationwide population-based study in Denmark found that a previous Omicron infection provided high levels of protection against BA.5 (92.7%) and BA.2 (97.1%) infections in triple-vaccinated individuals.[41] Research suggests that individuals who have had a previous Omicron infection and have received triple vaccination are highly protected against BA.5 and BA.2 infections. However, it is important to note that individuals with a previous infection were more likely to get tested for reasons other than suspicion of COVID-19, which may have led to an overestimation of the level of protection.[41]

8 | THE RISK OF TRANSMISSION TO OTHERS AFTER REINFECTION

The risk of transmission following reinfection is dependent on the viral load in the body and the level of immunity within the population. A study conducted in Qatar from February 2020 to July 2021, which included 380,000 SARS-CoV-2 cases, found that the Ct value of breakthrough infections and reinfections in unvaccinated individuals was 1.3–3.2 and 4.0 cycles higher, respectively, compared to primary infections in unvaccinated individuals.[42] urveillance data from December 2021 to May 2022 across 35 California state prisons showed that the risk of transmitting infection to close contacts was 28% for vaccinated Omicron cases, which is lower than the risk of 36% for unvaccinated cases.[43] The study found that during the Omicron epidemic, the infectiousness of reinfections decreased by 23% and 40% in unvaccinated and vaccinated populations, respectively.[43] This reduction in infectiousness was observed in individuals with both vaccine-derived and naturally acquired immunity.[43] The lower transmissibility of reinfection may be due to the

low viral load carried by cases and the protective effect of high levels of immunity in the population.

A household cohort study conducted in Managua, Nicaragua from March 2020 to November 2022 found that prior infection was associated with decreased infectivity in adults and adolescents. The secondary attack risk was 12.3 (95% CI: 10.3–14.8) for those with prior infection compared to 17.5 (95% CI: 14.8–20.7) for naive individuals.[44] Additionally, participants with prior infection were half as likely to be infected compared to those who were naive (RR 0.52, 95% CI: 0.38–0.70).[44]

The reduced infectivity in reinfection may be due to antibodies neutralizing a portion of the virus during the second infection. However, it is unclear whether this remains less infectious against the enhanced immune escape function of new mutant strains.

9 | DO WE NEED BOOSTER VACCINATION TO PREVENT REINFECTION

The evaluation of the effectiveness of vaccines and boosters against reinfections has been conducted. It is known that the titer of neutralizing antibodies gradually decreases after recovery. For instance, in six Indian patients who were re-infected with the Omicron variant after receiving two doses of the Covishield vaccine, the titer of IgG antibody decreased by 2.8 times 7 months after the second dose of the vaccine. Additionally, the titer of neutralizing antibodies against B.1, Delta, and Omicron variants decreased by 3.3, 5.9, and 17.3 times, respectively. After reinfection, the average titer of neutralizing antibodies significantly increased from 1.9 to 2262.[45] Therefore, it has been suggested that inoculation of booster shots may stimulate the immune system to produce new neutralizing antibodies.

An investigation of 76,000 people in the California prison system from December 24, 2021 to April 14, 2022 showed that a third dose of mRNA vaccine increased protection against Omicron by 25.0–57.9% in individuals without primary infections or who were infected before the Delta epidemic.[46] Hybrid immunity and booster vaccination were also associated with a reduced risk and fewer symptoms of SARS-CoV-2 infection during both Delta- and Omicron-dominant periods.[47] However, a prospective cohort study in Mexico found that 30.1% of the 73 medical staff who were reinfected had received a booster immunization within 0–33 days before reinfection.[48] It has been reported that vaccination of individuals previously infected with COVID-19 does not provide additional protection for several months. However, after that period, it does provide significant protection against symptomatic COVID-19, likely by boosting waning natural immunity.[49]

Research has demonstrated that receiving 2 or 3 doses of mRNA vaccine after a heterologous SARS-CoV-2 infection provides the highest level of protection against hospitalization due to Omicron.[50] Additionally, booster doses may decrease the spread of infection among vaccinated individuals who contract the virus.[43] For those who have not previously been infected, booster vaccinations may reduce the risk of symptomatic Omicron infection.[47] It has been demonstrated that a third BNT162b2 booster vaccination provides additional protection against Omicron BA.4 or BA.5 and XBB variants in previously infected children and adolescents, compared to those who remained unvaccinated.[51] This finding suggests that a third booster shot may be beneficial for this population.

It has been reported that a third dose of mRNA vaccine may provide limited protection for individuals who have been vaccinated twice and previously infected with SARS-CoV-2.[50] A test-negative case-control study was conducted among health care workers aged 18 years or older in Quebec, Canada, between March 27 and June 4, 2022, when BA.2 was the predominant variant.[52] The study found that primary infection with Omicron BA.1 provided greater protection against BA.2 infection, with a risk reduction of 72%. Among those who had received two doses of mRNA vaccine, protection was increased to 96%, but a third dose did not improve protection (96%). According to the study, individuals who have received two doses of mRNA vaccine and have had previous BA.1 infection are well protected against BA.2 reinfection for an extended period. The study found that a third vaccine dose did not provide any additional improvement to this hybrid protection.[52] Therefore, it is suggested that there may be limited benefit from administering additional vaccine doses to individuals with hybrid immunity. The study found that nasal IgA responses decline 9 months after infection and subsequent vaccination has minimal impact. This may explain the lack of long-lasting nasal defense against reinfection and the limited effects of booster vaccination on transmission.[53]

The effectiveness of Omicron-adapted mRNA vaccines against reinfection has been reported. The administration of bivalent mRNA vaccines as a fourth dose was safe and did not result in an elevated risk of 27 different adverse events in individuals aged ≧ 50 years.[54] The mRNA booster significantly enhances both humoral and cellular immune responses against the virus, including the Omicron variant.[55] Additional doses of mRNA vaccine have been shown to expand neutralizing antibody responses against highly divergent SARS-CoV-2 variants.[56] A recent SARS-CoV-2 Infection following of a fourth mRNA vaccine dose showed enhanced antibody-dependent cellular cytotoxicity against multiple Omicron subvariants.[57] However, a nonrandomized clinical study with an open-label design demonstrated that administering a fourth dose of either BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) to healthy young health care workers may only provide marginal benefits.[58] The control group had an infection rate of 25.0% with the Omicron variant, while the BNT162b2 group had a rate of 18.3% and the mRNA-1273 group had a rate of 20.7%.[58]

The effectiveness and feasibility of booster vaccination in preventing reinfection is still under debate. Surveillance data is needed to assess the effectiveness of the fourth dose of Omicron-adapted mRNA booster vaccination in preventing reinfection with the Omicron variant, particularly in older and vulnerable populations. However, as the focus on COVID-19 diminishes and group immunity strengthens, individuals may become less inclined to receive a booster vaccine.

10 | THE NEW THREAT OF REINFECTION

Two national matched, retrospective cohort studies were conducted in Qatar during the period of December 19, 2021 to March 21, 2022, which coincided with a large BA.1 and BA.2 Omicron wave. The studies investigated the immune protection of infection with one sub-lineage against reinfection with the other sub-lineage.[59] The effectiveness of BA.1 infection against reinfection with BA.2 was estimated to be 94.2%, while the effectiveness of BA.2 infection against BA.1 reinfection was estimated to be 80.9%.[59] However, the continuous evolution of the Omicron variant has led to the rapid emergence of numerous subvariants with increased immune escape capacity and decreased antibody diversity. Since the emergence of the Omicron variant, its progeny variants, including BQ.1 and XBB strain, have emerged.[60] As of the week ending January 21, 2023, the XBB.1.5 subvariant caused 49.1% of COVID-19 cases in the United States.[61] A new subvariant of XBB is prevalent in several countries, including Singapore, Bangladesh, and India.[61–64] The mutant strains resulting from convergent evolution have evaded all current neutralizing antibody drugs, vaccines, and convalescent plasma, including those from the BA.5 breakthrough.[60]

It has been confirmed that the Omicron BQ.1, BQ.1.1, XBB, and XBB.1 subtypes have an extraordinary ability to evade neutralizing antibodies due to mutations in their spike protein.[60] Individuals who received the WA1/BA.5 bivalent mRNA vaccine or who were previously infected showed significantly reduced neutralizing ability against BQ.1, BQ.1.1, XBB, and XBB.1.[60] The titers of neutralizing antibodies against BQ and XBB were reduced by 13−81 times and 66−155 times, respectively.[60] The reduction was significantly higher compared to any previously prevalent mutants. The monoclonal antibodies that neutralized the early Omicron subvariants were ineffective against these variants. The plasma neutralization data indicated that the XBB, CH.1.1, and BQ.1.10 strains not only evaded the immune response of individuals who received three doses of the vaccine but also those who experienced breakthrough infections with Omicron BA.1/BA.2/BA.5 sublineages, demonstrating a significant property of immune evasion.[60]

The evasion of the viral immune system may have accelerated to overcome high immunity in the population, which could have also accelerated the waning of natural immunity and increased the risk of reinfection against novel variants.[65] Despite high rates of vaccination and infection, populations remain vulnerable to future waves of reinfection from emerging SARS-CoV-2 variants. This vulnerability is reflected by substantially higher reinfection rates during Singapore's XBB wave than during the previous BA.5-driven wave.[18]

11 | CONCLUSION

Due to the emergence of novel variants with increased transmissibility and immune escape, and the gradual waning of neutralizing antibodies, there is a risk of reinfection after 90 days of prior infection during the Omicron wave. The reinfection rate during the Omicron epidemic is significantly higher than in previous epidemic periods. Although the symptoms and infectivity of reinfection were weaker than those of the initial infection, medical staff and individuals at high risk of reinfection, such as those with underlying medical conditions, should remain vigilant. The extent to which booster vaccinations can reduce reinfection with novel predominant sublineages and the characteristics of such reinfection are currently unclear. To address these concerns, more surveillance data is needed.

AUTHOR CONTRIBUTIONS

Hongwei Shen: Writing—original draft. **Dingqiang Chen**: Writing—review and editing; funding acquisition. **Chenglin Li**: Data curation. **Tingting Huang**: Data curation. **Wen Ma**: Project administration; funding acquisition.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no data sets were generated or analyzed during the current study.

ETHICS STATEMENT

All authors have read and approved the final version of the manuscript. Hongwei Shen had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

The lead author Hongwei Shen, Wen Ma affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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