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Infection of healthcare workers despite a high vaccination rate during the fifth wave of COVID-19 due to Omicron variant in Hong Kong

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SUMMARY

Background: No nosocomial infection was recorded in our healthcare workers (HCWs) during the early phase of the coronavirus disease 2019 (COVID-19) pandemic. With the emergence of the Omicron variant of increased transmissibility, infection in HCWs occurred as expected. We aimed to study the epidemiology of infection in HCWs and to describe the infection control measures during the outbreak of the Omicron variant.

Methods: With daily rapid antigen testing and molecular confirmation test for COVID-19, infected HCWs were interviewed by infection control nurses (ICNs) to investigate the potential source of infection. The epidemiology of COVID-19 in Hong Kong served as reference.

Results: During the fifth wave of COVID-19 (31 December 2021 to 31 May 2022), 1,200,068 cases were reported (incidence 95 times higher than in preceding waves in Hong Kong; 162,103 vs 1,707 per million population respectively, $P < 0.001$). The proportion of infected HCWs was significantly higher than that of the general population (24.9%, 1,607/6,452 vs 16.2%, 1,200,068/7,403,100 respectively; $P < 0.01$). The proportion of infected non-clinical staff was significantly higher than that of clinical staff (31.8%, 536/1,687 vs 22.5%, 1,071/4,765 respectively; $P < 0.001$). Of 82.8% (1,330/1,607) infected HCWs interviewed by ICNs, 99.5% (1,324/1,330) had been fully vaccinated; 49.5% (659/1,330) had no identifiable

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source; 40.7% (541/1,330) were probably infected from household members; 9.8% (130/1,330) had possible exposure to confirmed patients or HCWs, but no lapse in infection control measures or inappropriate use of personal protective equipment was recalled.

Conclusion: Omicron variant is highly transmissible such that breakthrough infection occurred despite high level of vaccination.

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Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was described as the first Disease X on the World Health Organization list of priority diseases requiring urgent research and development attention [1,2]. As of 18 September 2022, over 609 million confirmed cases and over 6.5 million deaths have been reported globally [3]. Infection and death among healthcare workers (HCWs) were not unusual, especially during the early phase of the pandemic [4]. In a systemic review of COVID-19 infection among HCWs, 152,888 infections and 1,413 deaths were reported globally as of 8 May 2020. Deaths among HCWs constituted 0.52% of total population of COVID-19 deaths [5].

In Hong Kong, infection control and public health response was immediately activated following the official announcement of the community-acquired pneumonia outbreak in Wuhan, Hubei Province by the National Health Commission of the People's Republic of China on 31 December 2019 [6,7]. Protection of HCWs from nosocomial acquisition of SARS-CoV-2 was considered paramount because 8 HCWs died during the outbreak of severe acute respiratory syndrome (SARS) in 2003. With stringent infection control measures, there was no nosocomial infection with SARS-CoV-2 among HCWs up till the pre-Omicron phase [8–10].

The emergence of Omicron sublineages (BA.1, BA.2 to BA.4 and BA.5) of increasing transmissibility [11] has resulted in explosive outbreaks in the community [12–15]. Models simulating the household setting underscored the contribution of airborne transmission of the Omicron variant, especially during asymptomatic or pre-symptomatic infection, as compared with the ancestral strain [16]. HCWs could also be infected with SARS-CoV-2 in the community, especially during the Omicron wave. Here, we reported the epidemiology of COVID-19 infection among our HCWs and described our infection control measures during the outbreak of the SARS-CoV-2 Omicron variant.

Material and methods

Epidemiology of the fifth wave of COVID-19 Hong Kong

From the outset, the daily number of laboratory-confirmed COVID-19 cases was reported in the public domain of the Centre for Health Protection (CHP), Department of Health, the Government of Hong Kong Special Administrative Region, China [17]. The evolution of the COVID-19 epidemic from the first to the fourth wave in Hong Kong has been summarized previously [14]. The epidemic curve and public health responses were described.

Control of COVID-19 and burden of COVID-19 patients in the hospital

Infection control measures have evolved to minimize the risk of nosocomial outbreaks during the COVID-19 pandemic [8–10]. Briefly, the measures included staff training, directly observed donning and doffing of personal protective equipment (PPE), enforcement of hand hygiene and environmental disinfection, as well as proactive screening and isolation of COVID-19 patients in airborne infection isolation rooms (AIIRs). In the fifth wave, some of the general wards were temporarily converted into negative pressure wards (NPWs) for COVID-19 patients in view of the high occupancy of the AIIRs in Queen Mary Hospital (QMH), a 1,700-bed university-affiliated hospital. COVID-19 patients with clinical improvement were transferred to four extended-care hospitals in our healthcare network. For hospitalized patients, universal admission screening by real-time reverse transcription polymerase chain reaction (RT-PCR) using deep throat saliva (DTS) or nasopharyngeal swab (NPS) specimens was performed. While awaiting RT-PCR results upon admission, patients were managed in designated cubicles, namely surveillance cubicles, in general wards with 6 air changes per hour. Portable air purifiers were placed inside the surveillance cubicles to improve air dilution. Patients with positive RT-PCR results for SARS-CoV-2 were immediately transferred to AIIRs or NPWs which were designated for COVID-19 patients. Patients with negative SARS-CoV-2 results were transferred to other cubicles in general wards. In general wards, repeated testing was undertaken if the patient had clinical features suggestive of COVID-19. The extent of contact tracing for potential secondary cases would depend on risk assessment by the infection control team. For the purpose of the current study, patients with positive SARS-CoV-2 RNA detection 3 or more days after hospitalization were defined as nosocomial cases, so as to include as many nosocomial cases as possible for analysis. For nosocomial COVID-19 cases, sporadic cases referred to isolated cases, whereas clusters referred to ≥ 2 cases. The number of COVID-19 patient admissions and bed occupancy in our network during the fifth wave were recorded.

COVID-19 testing among HCWs

HCWs were encouraged to refrain from work if they had fever or respiratory symptoms. Self-collected DTS specimens were sent to the hospital microbiology laboratory for SARS-CoV-2 RNA detection by RT-PCR if HCWs had symptoms or any epidemiological exposure to COVID-19. Since 21 February 2022, all HCWs were required to perform a rapid antigen test (GLINE-2019-nCoV Ag, BGI, China) by self-collected nasal swabs before work. If the rapid antigen test result was positive, HCWs were required to perform another rapid antigen test to ensure a

consistent positive result. HCWs with immediately repeated positive rapid antigen test results were required to refrain from work and to proceed with a confirmatory test by RT-PCR using DTS. Infected HCWs would be interviewed by an infection control nurse (ICN) to assess the potential source of infection. Possible exposure to COVID-19 was defined as HCWs having contacted a COVID-19 case in either hospital or community setting, regardless of appropriateness of PPE, in the past 5 days. Nosocomial COVID-19 infection among HCWs was defined as staff who had inappropriate PPE when caring for a COVID-19 patient in the past 5 days. Appropriate PPE included the use of a surgical respirator, cap, face shield, gown, and gloves.

COVID-19 vaccination among HCWs

Two formulations of COVID-19 vaccines were available for HCWs since March 2021: CoronaVac, inactivated whole cell vaccine, Sinovac Biotech (Hong Kong) Limited, and BNT162b2 mRNA vaccine, BioNTech, Fosun Pharma in collaboration with the German drug manufacturer. HCWs with direct patient care were required to complete the second dose of COVID-19 vaccination by 16 February 2022. All uninfected HCWs were required to complete the second dose by 1 April 2022. The deadline of receiving the third dose was 16 May 2022, or within 150 calendar days from the second dose, whichever later. HCWs who recovered from COVID-19 were required to complete 2 doses of COVID-19 vaccination unless they had already completed the second or third dose of vaccination before infection. Exemption of vaccination was provided to staff with medical contraindication.

Viral load assessment of respiratory specimens

For clinical specimens, total nucleic acid extraction was performed using 250 μ L of the specimen by the eMAG extraction system (bioMérieux, Marcy-l'Etoile, France) following the manufacturer's instructions. Quantification of SARS-CoV-2 RNA was performed by RT-PCR as previously described [18].

This study was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Hospital Cluster.

Statistical analysis

The Chi-Square test was used to compare independent categorical variables between groups. All reported *P* values were two-sided. A *P* value of <0.05 was considered statistically significant. Computation was performed using the SPSS Version 15.0 for Windows.

Results

Epidemiology of the fifth wave of COVID-19 in Hong Kong

Soon after the importation of the SARS-CoV-2 Omicron variant [19], the fifth wave of COVID-19 in Hong Kong commenced on 31 December 2021, which was the second anniversary of the official announcement of community-acquired pneumonia of unknown etiology in Wuhan, Hubei Province [6]. During the fifth wave (defined as 31 December 2021 to 31 May 2022 in the

current study), a total of 1,200,068 COVID-19 cases were reported to CHP. The incidence of COVID-19 during the fifth wave was 95 times higher than the total from the first to fourth wave ($n=12,636$) in Hong Kong (162,103 vs 1,707 per million population respectively, $P<0.001$). The daily number of new cases exceeded 10,000 on 25 February 2022 and reached a peak of $>50,000$ on 3 March 2022, amounting to 1,352 and $>7,676$ per million population respectively. As of 31 May 2022, there were 9,165 deaths within the fifth wave (1,238 per million population), of which 6,507 (71.0%) and 1,534 (16.7%) were aged ≥ 80 and 70–79 years respectively. Among the fatal cases, 6,923 out of 9,165 (75.5%) had not received any COVID-19 vaccine, while the vaccination coverage of the first, second, and third dose in the Hong Kong population was 6,700,406 (90.5%), 6,332,041 (85.5%), and 3,876,310 (52.4%) respectively [20]. The epidemic curve and public health responses by managing cases in community isolation facilities in the Asia World-Expo ($\sim 1,000$ beds), public rental buildings ($\sim 3,000$ residential flats), fangcang shelters ($\sim 20,000$ beds), and Kai Tak cruise terminal ($\sim 1,000$ beds) are shown in Figure 1.

Control of COVID-19 and burden of COVID-19 in the hospital

With increasing COVID-19 patient admissions during the fifth wave, up to 50% of beds in the general wards were temporarily converted into NPWs caring for COVID-19 patients. Mobile Modular High Efficiency Particulate Arrestance Filter Units (MMHUs) and exhaust fans were installed in each cubicle to increase air changes per hour from 6 to 10. Negative pressure was established with airflow from the corridor to the cubicles. Of 2,320 COVID-19 patients admitted to QMH, 1,284 were male and 1,036 female, with a median age of 73 years (range: 8 days to 107 years). The daily numbers of COVID-19 patient admissions and bed occupancy during the fifth wave are shown in Figure 2.

During the study period, 37 nosocomial COVID-19 patients were diagnosed at a median of 12 days (range, 3–158 days) after hospitalization in 16 general wards without conversion to NPWs. There were 10 sporadic cases in 10 different general wards. The remaining 27 patients comprised 6 clusters in 6 different general wards, including 12 cases in 1 cluster. ICNs coordinated infection control measures when a nosocomial COVID-19 patient was diagnosed. Nosocomial COVID-19 patients were immediately transferred to AIIRs to reduce the risk of further transmission in the general wards. Terminal disinfection of the general ward was performed. Hand hygiene among HCWs and patients were enforced based on our previous experience on outbreak prevention and control [21–25]. All exposed patients and HCWs in the general ward were tested for SARS-CoV-2 by RT-PCR daily for 7 days for early recognition of secondary cases.

COVID-19 infection among HCWs

During the fifth wave, a total of 1,607 (24.9%) of 6,452 HCWs in QMH were tested positive for COVID-19 till 31 May 2022 (Figure 3). The proportion of infected HCWs was significantly higher than that of the general population in Hong Kong (24.9%, 1,607/6,452 vs 16.2%, 1,200,068/7,403,100 respectively; $P<0.001$). The proportion of infected non-clinical staff was

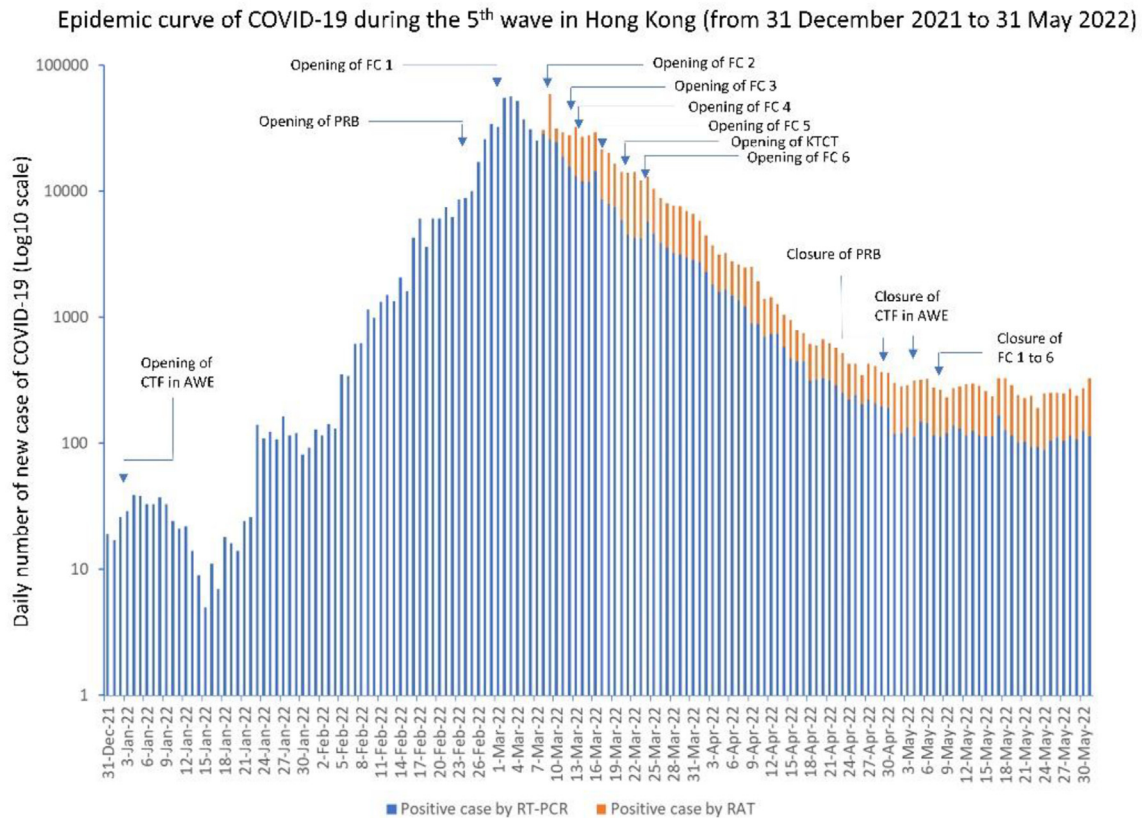


Figure 1. Epidemic curve of COVID-19 during the fifth wave in Hong Kong (31 December 2021 to 31 May 2022). Note. CTF in AWE, community treatment facility of around 1,000 beds in Asia World-Expo which was re-opened on 2 January 2022; FC, fangcang shelter for the purpose of community isolation facility. FC1 denotes fangcang shelter located in Tsing Yi which was opened on 1 March 2022; FC2 denotes fangcang shelter located in San Tin which was opened on 9 March 2022; FC3 denotes fangcang shelter located in Hong Kong-Zhuhai-Macao Bridge which was opened on 12 March 2022; FC4 denotes fangcang shelter located in Fanling which was opened on 13 March 2022; FC5 denotes fangcang shelter located in Hung Shui Kiu which was opened on 17 March 2022; FC6 denotes fangcang shelter located in Tam Mi which was opened on 24 March 2022. All six fangcang shelters were purposely built as community isolation facilities to provide a total of 20,000 beds; KTCT denotes Kai Tak cruise terminal which was converted into community isolation facility and opened on 21 March 2022 to provide around 1,000 beds; PRB denotes public rental buildings, Queens Hill Estate, located in Fanling, and Heng King House of Lai King Estate, located in Kwai Chung, which were converted into community isolation facility and opened on 24 February 2022 to provide around 3,000 residential flats; RAT, rapid antigen test; RT-PCR, reverse transcription polymerase chain reaction.

significantly higher than that of clinical staff (31.8%, 536/1,687 vs 22.5%, 1,071/4,765 respectively; $P < 0.001$). Among 1,607 infected HCWs, 1,330 (82.8%) were interviewed by an ICN by phone. None had history of past infection of COVID-19. Symptomatic infection was reported in 1,050 (78.9%) HCWs. Symptoms included sore throat (53.8%, 565), cough (27.1%, 285), fever (19.9%, 209), runny nose (12.8%, 134) and headache (7.0%, 74). Among the 1,330 interviewees, 659 (49.5%) did not report any exposure to cases in the household or hospital. Another 541 (40.7%) reported contact with infected household members. The remaining 130 (9.8%) recalled possible exposure in the past 5 days to patients or staff within or outside the hospital, who were subsequently diagnosed to have COVID-19. Among this group of 130 HCWs, 113 were clinical staff, with 22 (19.5%) having performed aerosol generating procedures (AGPs) for COVID-19 patients with full PPE (Figure 4). Six (0.5%) out of 1,330 infected HCWs had not received any COVID-19 vaccine. Only 1% of the staff was exempted from COVID-19 vaccination in our healthcare network as of 31 May 2022.

Discussion

During the fifth wave of COVID-19 predominantly caused by Omicron subvariant BA.2 in Hong Kong, an unprecedented number of COVID-19 infections was reported among our HCWs even though infection control practices in the healthcare setting remained stringently enforced throughout the COVID-19 pandemic. Our finding of HCWs infection was in contrast with the observation in the early phase of the COVID-19 pandemic in Hong Kong that nosocomial infection among HCWs was not recorded in hospitals [9,10], temporary test centers [26], and community isolation and treatment facilities [27]. Nosocomial infection of nine HCWs was only reported in a COVID-19 outbreak in late 2020 [18]. In this study, about one-fourth of HCWs were infected in our hospital and the proportion was comparable to a private hospital of 600-bed in Hong Kong [28]. It is important to explore if the infection control measures remained appropriate to protect our HCWs.

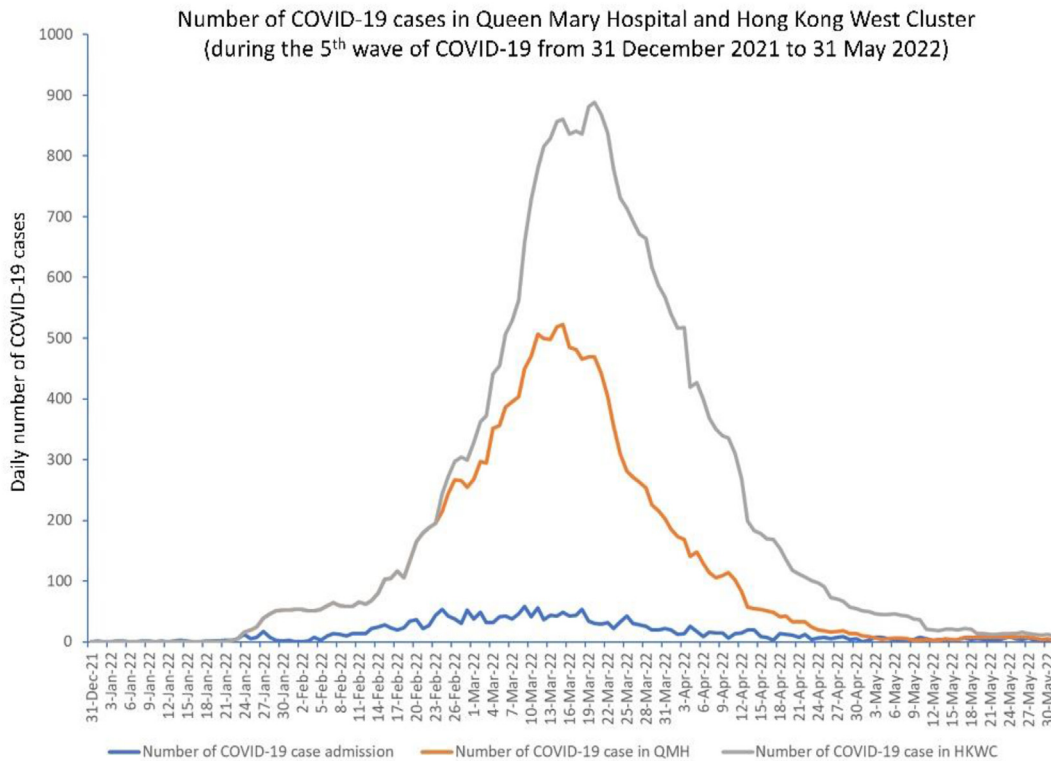


Figure 2. Number of COVID-19 cases in Queen Mary Hospital and Hong Kong West Cluster during the fifth wave of COVID-19. Note. HKWC, Hong Kong West Cluster; QMH, Queen Mary Hospital. Hong Kong West Cluster is a healthcare network comprising Queen Mary Hospital, a 1,700-bed university-affiliated tertiary referral center, and another 5 extended-care hospitals with a total of 1,700 beds. During the fifth wave of COVID-19, four out of 5 extended-care hospitals received clinically stable COVID-19 from Queen Mary Hospital.

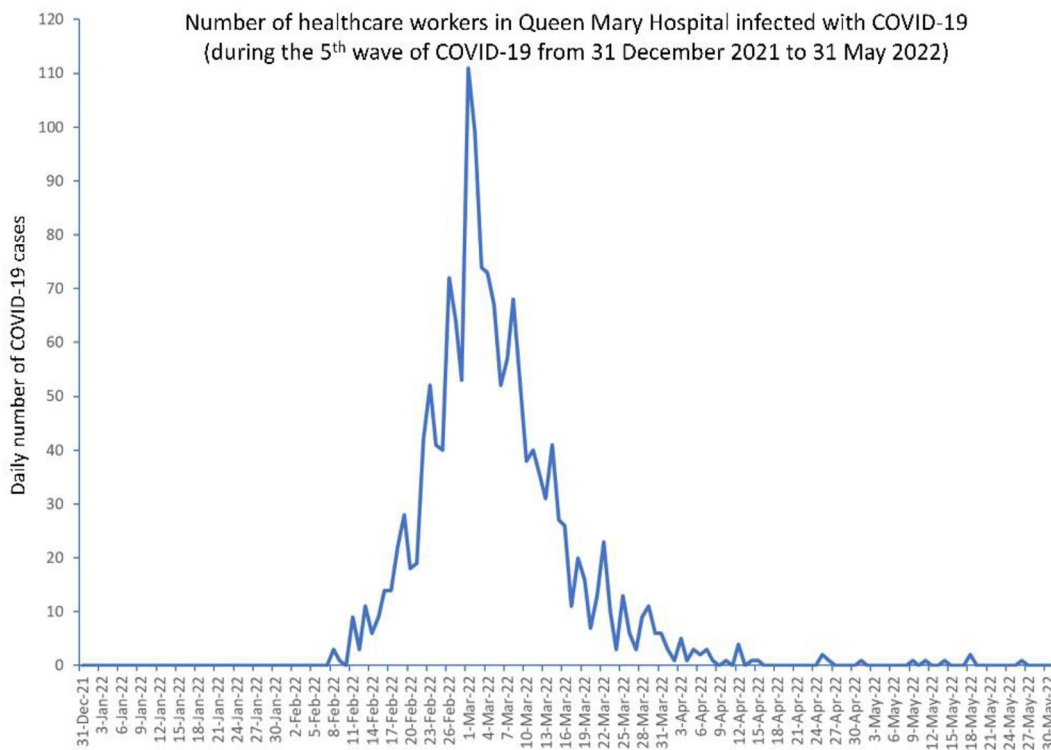


Figure 3. Number of healthcare workers in Queen Mary Hospital infected with COVID-19. Note. The peak of healthcare worker infection occurred earlier than the peak of COVID-19 cases in the community and the hospital. It was the result of effort of infection control nurses to remind healthcare workers to avoid social gathering and obey social distancing when there was increasing HCW infection.

Analysis of COVID-19 infected healthcare workers in Queen Mary Hospital (31 December 2021 to 31 May 2022)

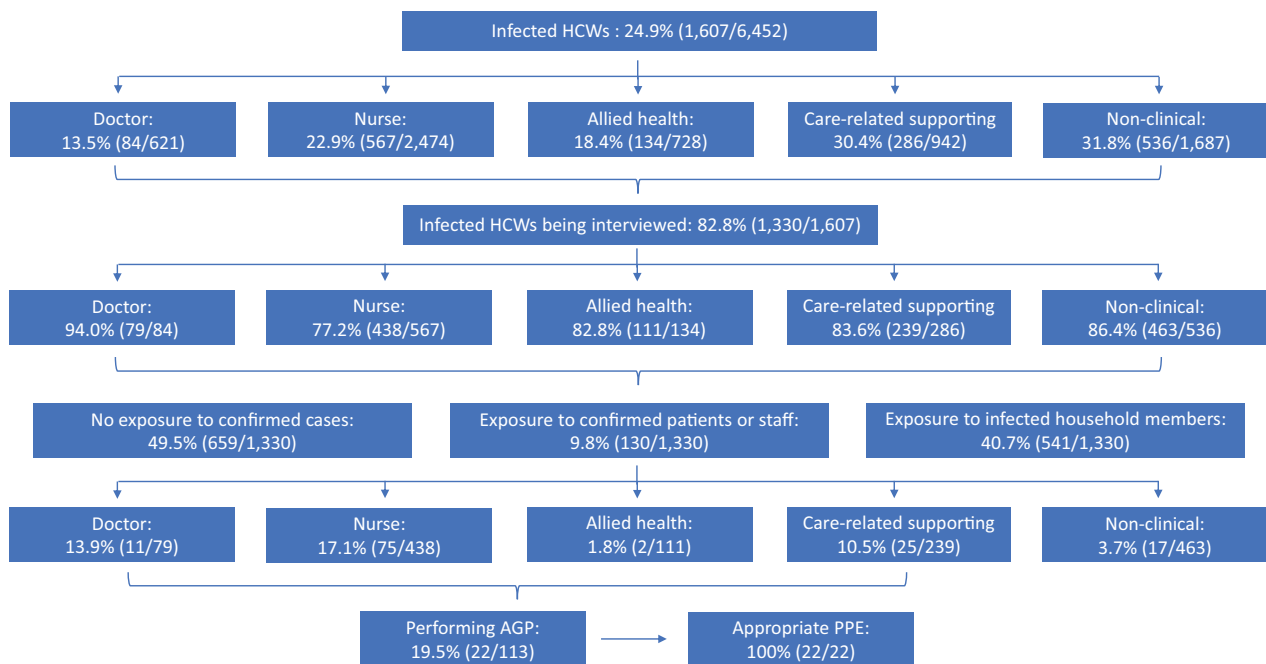


Figure 4. Analysis of COVID-19 infected healthcare workers in Queen Mary Hospital (31 December 2021 to 31 May 2022). Non-clinical staff includes administrative, clerical, and non-care related supporting staff. AGP, aerosol generating procedures; PPE, personal protective equipment.

Before the onset of the fifth wave of COVID-19, we adopted a hospital-based approach that all suspected or confirmed COVID-19 patients were isolated in healthcare facilities, including AIIRs in the hospitals or community treatment facilities. This approach of institutionalization for containment could have minimized community transmission of COVID-19. In the healthcare facilities, HCWs were provided with full PPE including a surgical respirator, cap, face shield, gown, and gloves during patient care. Directly observed donning and doffing was enforced to maximize staff protection and minimize the risk of self-contamination upon removal of PPE. With the evolution of SARS-CoV-2, RNA of the virus has been increasingly detected in air samples collected in AIIRs with 12 air changes per hour [29,30]. However, the quantitation of viral RNA was as low as 0.005 genome copies per litre of air [30]. The provision of full PPE should be sufficient to protect HCWs from inhalation of SARS-CoV-2.

With the emergence of SARS-CoV-2 Omicron subvariant BA.2 in the fifth wave, there were explosive outbreaks in the community, especially during mask-off activities in restaurants [31] as well as vertical transmission in high-rise residential buildings [13,14]. Although the operation of community isolation facilities in the Asia World-Expo, public rental buildings, fangcang shelters, and Kai Tak cruise terminal had provided some 25,000 additional beds to manage patients with mild or asymptomatic COVID-19 infection, this was still insufficient to cope with the approach of institutionalization for containment during the peak of the fifth wave, with more than 10,000 confirmed cases per day. HCWs thus could also have acquired infection in the community. In fact, about 50% of HCWs had no identifiable source of infection in the household or the hospital setting

based on our epidemiological analysis, suggesting widespread transmission of COVID-19 in the community.

The proportion of infected HCWs was significantly higher than that of our general population. It may be related to the policy of daily COVID-19 testing among the HCWs that the number of tests per HCW was significantly higher than that of the general population during the study period (unpublished data) according to the statistics on testing for COVID-19 in Hong Kong [32]. In fact, daily COVID-19 testing detected an additional 19% of asymptomatic cases among our HCWs in this study. In a systemic analysis of COVID-19 infection, frontline HCWs were more likely to report a positive COVID-19 test when compared with community individuals in the United Kingdom and the United States [33]. In our study, it is interesting to observe that the proportion of infected non-clinical staff was significantly higher than that of clinical staff. The alertness of clinical staff may be higher as a result of on-going infection control training. Hand hygiene among our clinical staff remained highly compliant during the COVID-19 pandemic [34].

Nosocomial acquisition of SARS-CoV-2 remains difficult to ascertain because our HCWs, especially clinical staff, were not under closed-loop management in the hospital as in mainland China [35]. Clinical staff who had performed AGP for COVID-19 patients reported having donned full PPE during patient care. None of our clinical staff fulfilled the case definition of nosocomial COVID-19 infection. However, about 10% of HCWs, including clinical and non-clinical staff, recalled possible exposure to patients in the general wards or infected HCWs. The possibility of COVID-19 transmission from patient to HCWs or HCWs to HCWs could not be excluded. In fact, 80% of air samples collected in NPWs caring for COVID-19 patients were

positive for SARS-CoV-2 RNA [36]. Based on the results, air dispersal of SARS-CoV-2 in general wards with unrecognized COVID-19 patients would be possible. This may also explain the presence of 37 hospitalized patients with nosocomial acquisition of SARS-CoV-2 in general wards during our study period.

Universal masking has been adopted in our community and healthcare settings even before the announcement of the COVID-19 pandemic [37,38]. Universal masking was also recommended by the Centers for Disease Control and Prevention of the United States [39], and maximizing the fitness of the mask was further emphasized [40]. Experimental studies demonstrated that surgical masks were effective at preventing virus spread under conditions of low virus load, whereas more advanced masks were required in potentially virus-rich indoor environments including medical centers and hospitals [41]. Recent studies showed that the universal use of surgical respirators as an additional infection preventive measure contributed to the rapid control of Omicron transmission in the hospital [42]. Use of the surgical respirator by an infected HCW may be one of the reasons for the lack of Omicron transmission in a cohort of immunosuppressed patients [43]. These preliminary findings may provide indirect epidemiological evidence of airborne transmission of the Omicron variant in the clinical areas. The use of surgical masks or surgical respirators to minimize the risk of Omicron transmission in the healthcare setting deserves further investigation.

There are several limitations in this study. Firstly, we did not perform case-control analysis to investigate the risk factors for COVID-19 infection among HCWs, because 50% of them could not identify the source of infection during overwhelming transmission of COVID-19 in the community. Secondly, we were not able to perform detailed epidemiological analysis for HCWs who recalled possible exposure to infected patients or staff within or outside the hospital. The route of transmission thus could not be definitively ascertained. Thirdly, we did not perform whole genome sequencing analysis to establish the transmission relationships, as the predominant virus circulating in both the community and hospitals was already known to be subvariant BA.2 during the study period [13,36]. Fourthly, we defined nosocomial COVID-19 cases as patients with positive SARS-CoV-2 RNA detection 3 or more days after hospitalization. As the mean incubation period of COVID-19 was 3.42 days for the Omicron variant [44], misclassification of a small proportion of nosocomial cases might have occurred. Finally, we did not analyze the relationship between the regimen of COVID-19 vaccination and the risk of infection. The impact of COVID-19 vaccination on HCW infections during circulation of the SARS-CoV-2 Omicron variant has been reported previously. Using the two-dose BNT162b2 regimen as reference, two-dose CoronaVac recipients had a significantly higher risk of infection, whereas three-dose BNT162b2 and two-dose CoronaVac plus BNT162b2 booster regimens were associated with a lower risk of infection [28].

Conclusions

SARS-CoV-2 Omicron variant is highly transmissible such that breakthrough infection might occur despite a high level of vaccination coverage in the population. Although a significant proportion of HCWs were infected, none had severe infection, underpinned by a high vaccination rate. Nosocomial

transmission of COVID-19 from patients to HCWs could not be ascertained by epidemiological analysis in view of the component of airborne transmission.

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Conflicts of interest statement

All authors report no conflicts of interest relevant to this article.

Credit Author Statement

Shuk-Ching Wong: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing - original draft, Writing - review and editing. Veronica Wing-Man Chan: Investigation. Lithia Lai-Ha Yuen: Investigation. Christine Ho-Yan AuYeung: Investigation. Jessica Oi-Yan Leung: Investigation. Chi-Kuen Li: Investigation. Monica Oi-Tung Kwok: Investigation. Simon Yung-Chun So: Data curation, Formal analysis. Jonathan Hon-Kwan Chen: Resources. Kelvin Hei-Yeung Chiu: Resources. Anthony Raymond Tam: Resources. Ivan Fan-Ngai Hung: Resources. Kelvin Kai-Wang To: Resources. Janice Yee-Chi Lo: Writing - review and editing. Kwok-Yung Yuen: Funding acquisition, Supervision. Vincent Chi-Chung Cheng: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing - original draft, Writing - review and editing. All authors have read and agreed to the published version of the manuscript.

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