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The time serial distribution and influencing factors of asymptomatic COVID-19 cases in Hong Kong

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1. Background

The COVID-19 pandemic is an ongoing global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of 13 August 2020, over 20.6 million cases and 749,000 deaths of COVID-19 have been reported in more than 188 countries and territories around the globe [1]. As an international city with high population mobility, Hong Kong has reported 4313 confirmed cases and 65 deaths as of 13 August, and is now experiencing a third wave of COVID-19 outbreak with more than 3000 confirmed cases recorded since 1 July [2]. As a newly emerging infectious disease worldwide, the containment of the COVID-19 needs the One Health approach recognizing the interrelationship between animals, humans and the environment and encourages collaborative efforts to improve the global health [3]. Common symptoms of people with SARS-CoV-2 include fever, cough, and tiredness while most cases are mild or even with no symptoms, which is defined as asymptomatic cases [4]. Chinese authorities' daily figures showed that 80% of coronavirus infections were asymptomatic

and health experts believe that the asymptomatic cases of coronavirus infection could be an important source of contagion [5]. According to a recent report [6], Hong Kong was at a higher risk of asymptomatic case importing compared with local transmission.

This study aims to analyse the time serial distribution and influencing factors of asymptomatic cases in Hong Kong with the updated information in the third wave of COVID-19 outbreak, which is highly indicative to mitigating the one health issue of SARS-CoV-2 global transmission.

2. Methods

The study used the publicly released COVID-19 surveillance data from the Centre for Health Protection (CHP) in Hong Kong [7]. By 12 August 2020, a total of 4244 confirmed cases of COVID-19 has been reported, 49.8% of them were men, and their mean (\pm standard deviation) age was 44.0 years (\pm 20.3). Among all confirmed cases, 894 (21.1%) of them were asymptomatic at the time of detection. To visualize the serial distribution of cases, we plotted the asymptomatic ratio (the number of asymptomatic cases divided by the total cases) and

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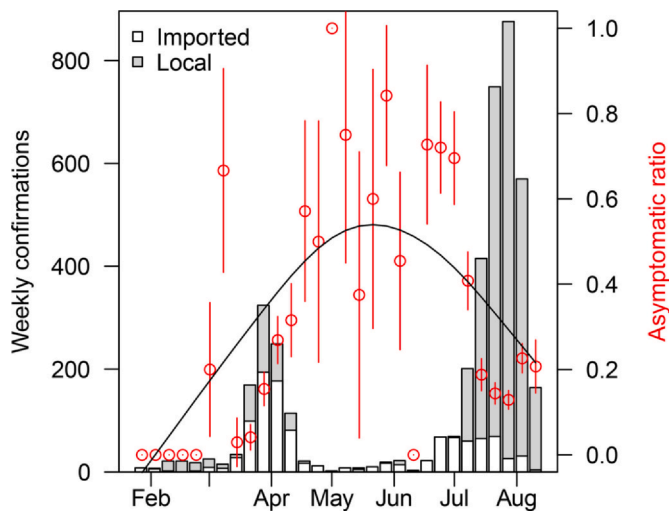


Fig. 1. The time serial distribution of weekly confirmation and asymptomatic ratio. The proportion of asymptomatic COVID-19 cases were plotted in red dots with 95% confidence interval indicated by the vertical red lines and the corresponding serial trend was simulated in the black smooth curve. The classification was shown in the bars with the grey representing the local cases and the white representing imported cases. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

the proportion of imported and local cases by week in Fig. 1. In addition, we plotted the daily time serial distribution of confirmed cases in the third wave in Supplementary Fig. 1.

To determine the relative contributions (%) of explanatory variables on asymptomatic cases, we applied the boosted regression tree (BRT) model using “gbm” package in R statistical software (version 3.6.1). The explanatory variables included gender, age, the time interval between the index case to new cases identified, as well as case classification (including local, imported, possibly local case, epidemiologically linked with imported case, epidemiologically linked with possibly local case, and epidemiologically linked with local case). Local-related cases were classified as local cases, and imported-related cases as imported cases. Three main model parameters in the model included number of interactions, shrinkage (learning rate) and tree complexity. The actual number of interactions was determined by minimizing the estimated deviance with a 10-fold cross-validation. We set the shrinkage of 0.005 to achieve a trade-off. Tree complexity was tested from 1 to 8 and the optimal tree complexity of 2 was selected. For boosting, a bagging factor of 0.5 was set. To explore the association between each predictor and the asymptomatic ratio, the multivariable logistic regression model was then used to estimate the effect size. The adjusted odds ratio (AOR) and their 95% confidence intervals (95% CI) were estimated.

3. Results

Over 50% were imported cases in April while local cases dominated in the current wave in July and August in Fig. 1. There were no asymptomatic cases reported in February. The proportion of asymptomatic cases experienced a steady escalation and reached the summit in June.

The contribution of each explanatory variable for the asymptomatic cases is presented in Table 1. The results showed that the time interval between the index case and the newly identified case was the dominating attributive factor (48.56%) for asymptomatic cases, followed by classification of imported or local cases (34.87%), age (15.94%) and gender (0.63%). Despite the fact that age contributed 15.94% of relative importance to the BRT model, no significant association was reported between age or gender and the proportion of symptomatic cases

Table 1
Summary of the relative contributions (%) of explanatory variables by boosted regression tree model, and the adjust odds ratio (AOR) of explanatory variables by logistic regression model.

Predictors	Contribution (%)	AOR (95% CI)
Time interval	48.56	1.01 (1.01–1.02) ***
Case classification	34.87	0.09 (0.07–0.11) ***
Age (year)	15.94	1.00 (0.99–1.00)
Gender	0.63	1.10 (0.94–1.29)

in the Logistic regression. Besides, local cases were less likely to be asymptomatic compared with imported cases (OR: 0.09, 95% CI: 0.07–0.11). Additionally, the proportion of asymptomatic cases increased with the time interval between the index case and the newly identified case (OR:1.01, 95% CI: 1.01–1.02).

4. Discussion

Amidst the third wave of COVID-19 outbreak in Hong Kong, the asymptomatic cases were more likely to be imported cases. The proportion of asymptomatic cases rose with the time approaching near the current wave. This result suggests it might be necessary to overhaul the quarantine exemption policy under the high importing risk of asymptomatic cases in Hong Kong.

However, the study has some limitations. Firstly, the asymptomatic cases were not identified from a random sample of the total population in the city because the testing resources need to be assigned in priority to people with symptoms, which will inevitably lead to the underestimation of the proportion of asymptomatic cases. In addition, a study on the Diamond Princess cruise found that the mean incubation period might influence the estimates of the true proportion of asymptomatic cases [8]. Second, the effects of time-varying control measures were not considered while it should not exert a big impact on the proportion of asymptomatic cases.

Scientific evidence has suggested that the transmissibility of asymptomatic case might be smaller than that of the symptomatic cases [6]. Nevertheless, a study in Hong Kong estimated that 44% (95% CI, 25–69) of secondary cases were infected during the first cases' pre-symptomatic stage, which highlighted the necessity to adjust control measures for probable asymptomatic transmission [9].

Since a high proportion of asymptomatic cases were imported cases in Hong Kong, strict quarantine and travel policy need to be considered and massive testing on viral shedding needs to be carried out. With experts' agreement on the SARS-CoV-2 as a one health issue [10], protective measures by the WHO including community-wide mask wearing and social distancing should be effective in reducing the global transmission of asymptomatic cases [11].

Overall, the current pandemic caused by the pathogen SARS-CoV-2 requires some One Health-based control strategies for containing the virus including rising hygienic standards for the supply chain in animal slaughter houses, regular surveillance of SARS-CoV-2 among various species of animals, regular testing and decontamination of air and surfaces in public places, minimizing human-to-human transmission such as social distancing, monitoring travel restrictions to minimizing imported cases and early identification and quarantine of both symptomatic and asymptomatic cases [12]. Further studies on the COVID-19 asymptomatic cases are warranted by the One Health approach.

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Ethics approval and consent to participate

The ethical approval or individual consent was not applicable.

Availability of data and materials

All data and materials used in this work were publicly available via source of data.

Consent for publication

Not applicable.

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Disclaimer

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Authors' contributions

DH, SZ, LY, and HL conceived the study; JT, XZ (Xiaoyu), XZ (Xingyue) carried out the analysis, discussed the results, drafted the first manuscript. All authors critically read and revised the manuscript, and gave final approval for publication.

Declaration of Competing Interest

DH was supported by Alibaba (China) Co. Ltd. Collaborative Research project. Other authors declare no competing interests.

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