

UWL REPOSITORY

repository.uwl.ac.uk

Epidemiological characteristics of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China: an overview of vaccine breakthrough infection events

He, Z, Xiang, HB, Manyande, Anne ORCID: https://orcid.org/0000-0002-8257-0722, Xu, W, Fan, I and Xiang, B (2021) Epidemiological characteristics of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China: an overview of vaccine breakthrough infection events. Frontiers in Medicine, 8.

http://dx.doi.org/10.3389/fmed.2021.736060

This is the Accepted Version of the final output.

UWL repository link: https://repository.uwl.ac.uk/id/eprint/8279/

Alternative formats: If you require this document in an alternative format, please contact: <u>open.research@uwl.ac.uk</u>

Copyright: Creative Commons: Attribution 4.0

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy: If you believe that this document breaches copyright, please contact us at <u>open.research@uwl.ac.uk</u> providing details, and we will remove access to the work immediately and investigate your claim.



Epidemiological characteristics of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China: An overview of vaccine breakthrough infection events

Zhigang He¹, Hong-bing Xiang¹, Anne Manyande², Weiguo Xu¹, Li Fan³, Boqi Xiang^{4*}

¹Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, China, ²University of West London, United Kingdom, ³Department of Orthopedics, Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, China, ⁴Rutgers University, United States

Submitted to Journal: Frontiers in Medicine

Specialty Section: Infectious Diseases - Surveillance, Prevention and Treatment

Article type: Brief Research Report Article

Manuscript ID: 736060

Received on: 04 Jul 2021

Revised on: 21 Sep 2021

Journal website link: www.frontiersin.org



Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

Author contribution statement

All the authors contributed to the paper presented methodology and conceptualization. They all contributed to data analysis and paper writing.

Keywords

COVID-19 disease, Asymptomatic carrier, Nosocomial infection, Scientific protective strategy, vaccine breakthrough infection

Abstract

Word count: 108

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has wreaked havoc to human beings around the world. Although China quickly brought the Coronavirus disease (COVID-19) pandemic under control, there have been several sporadic outbreaks in different regions of China since then. This article describes the chronological nosocomial COVID-19 infection events that related to several sporadic outbreaks of SARS-CoV-2 in different regions of China. We reported epidemiological characteristics and management measures of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China, specially focused on domestic COVID-19 breakthrough infection in China – a vaccinated healthcare professional working in the isolation ward of a designated COVID-19 hospital.

Contribution to the field

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has wreaked havoc to human beings around the world. Although China quickly brought the Coronavirus disease (COVID-19) pandemic under control, there have been several sporadic outbreaks in different regions of China since then. This article describes the chronological nosocomial COVID-19 infection events that related to several sporadic outbreaks of SARS-CoV-2 in different regions of China. We reported epidemiological characteristics and management measures of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China, specially focused on domestic COVID-19 breakthrough infection in China – a vaccinated healthcare professional working in the isolation ward of a designated COVID-19 hospital.

Funding statement

This work is funded by the National Natural Science Foundation of China (81873467, 81670240, and 81271766).

Ethics statements

Studies involving animal subjects Generated Statement: No animal studies are presented in this manuscript.

Studies involving human subjects

Generated Statement: No human studies are presented in this manuscript.

Inclusion of identifiable human data

Generated Statement: No potentially identifiable human images or data is presented in this study.

Data availability statement

Generated Statement: The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Epidemiological characteristics of sporadic nosocomial COVID-19 infections from 1

- 2 June 2020 to June 2021 in China: An overview of vaccine breakthrough infection 3 events
- Zhigang He¹, Hongbing Xiang¹, Anne Manyande², Weiguo Xu³, Li Fan^{4,*}, Boqi Xiang^{5,*} 5
- 6 7

4

¹ Department of Anesthesiology, Tongji Hospital of Tongji Medical College, Huazhong University

- 8 of Science and Technology, Wuhan, 430030 Hubei, PR China;
- 9 ² School of Human and Social Sciences, University of West London, London, United Kingdom;

³ Department of Orthopedics, Tongji Hospital of Tongji Medical College, Huazhong University of 10

- Science and Technology, Wuhan 430030, PR China; 11
- 12 ⁴ Department of Orthopedics, Union Hospital of Tongji Medical College, Huazhong University of
- 13Science and Technology, Wuhan 430030, PR China;
- 14 ⁵ School of Public Health, Rutgers University, New Brunswick, NJ 08854, USA.
- 15
- 16
- *Correspondence: Boqi Xiang, E-mail: bx67@sph.rutgers.edu; Li Fan, E-mail: fanleeeee@163.com. 17reviev
- 18

19 Abstract

- 20 The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has wreaked
- 21 havoc to millions of people around the world. Although China quickly brought the Coronavirus
- 22 disease (COVID-19) under control, there have been several sporadic outbreaks in different regions
- 23 of China since June 2020. This article describes the chronological nosocomial COVID-19
- 24 infection events related to several sporadic outbreaks of SARS-CoV-2 in different regions of
- 25 China. We report epidemiological characteristics and management measures of sporadic
- 26 nosocomial COVID-19 infections from June 2020 to June 2021, and specially focused on the
- 27 domestic COVID-19 breakthrough infection in China including domestic COVID-19
- 28 breakthrough infection a vaccinated healthcare professional working in the isolation ward of a
- 29 designated COVID-19 hospital.
- 30 Keywords: COVID-19 disease; asymptomatic carrier; nosocomial infection; Scientific protective
- 31 strategy; vaccine breakthrough infection
- 32

33 Introduction

The outbreak of the COVID-19 virus was first reported in Wuhan, China, in December 2019. The COVID-19 pandemic led China to quarantine the population in order to protect them ¹. Chinese authorities decided to adopt extraordinary measures to contain and limit the spread of the SARS-CoV-2 virus. From 1 January to 8 April 2020, >8,000 patients with COVID-19 were hospitalized and the Chinese government imposed the Wuhan lockdown on January 23, which ended on April 8, 2020.

40

41 With the COVID-19 epidemic quickly under control in the early stages of 2020, importing the 42 SARS-CoV-2 virus could pose great challenges to the control and prevention of nosocomial 43 COVID-19 infection in healthcare settings. Our previous report showed the impact of the novel 44 coronavirus SARS-CoV-2 among healthcare workers in hospitals during the early phase of the 45 COVID-19 epidemic², and suggested that local authorities need to be extremely cautious and 46 implement stringent protective measures to safeguard healthcare workers in order to counteract the threats brought by the pandemic³⁻⁵. Though medical staff belong to the susceptible population to a 47 48 certain extent, hospitals have practiced cohorting in accordance with recommendations from 49 COVID-19 infection prevention and control professional societies, which has reduced the risk of 50 hospital-acquired COVID-19. Because healthcare workers are at the interface between hospitals and 51 the community, where there is significant COVID-19 transmission, they may be infected by 52 asymptomatic carriers with COVID-19 or COVID-19 patients. Furthermore, in the designated 53 hospital admitting COVID-19 patients or asymptomatic carriers, medical staff are highly exposed 54 to nosocomial COVID-19 acquisition and SARS-CoV-2 transmission. Therefore, healthcare staff 55 may play a key role in initiating or amplifying sporadic COVID-19 outbreaks in healthcare settings 56 including hospitals and other care facilities.

57

The importing of the SARS-CoV-2 virus from overseas, induced sporadic outbreaks with COVID-19 from June 2020 to June 2021 in China^{6, 7}. This article describes the chronological events that led to several sporadic nosocomial COVID-19 infections in different regions of China from June 2020 to June 2021, including domestic COVID-19 breakthrough infection — a vaccinated healthcare professional working in the isolation ward of a designated COVID-19 hospital⁸. Lastly, we provide an overview of local COVID-19 outbreak induced by the B.1.617.2 (Delta) variant of the COVID-19 virus in China.

65

66 Methods

From the beginning of June 1, 2020, every day, we prospectively focused on the COVID-19 epidemic data from the Chinese Center for Disease Control and Prevention. Once we had the new report of nosocomial COVID-19 infection in China, we tracked this epidemic and collected its epidemiological characteristics from announcements by the local Health Commission and presented a narrative research for geographical and epidemiological characteristics of nosocomial COVID-19 infection from June 2020 to June 2021.

73

We searched epidemiologic data published on the website of WHO, the China Center for Disease Control and Prevention, National Health Commission, the Health Commission of Qingdao, Shenyang, Shijiazhuang, and Dalian city, Jilin, Shaanxi, and Guangdong Province from June 2020 to January 2021. Using the keywords "nosocomial infection", "COVID-19 variant", "SARS-CoV-

2", "B1.617.2 (Delta) lineage", and Boolean operator 'AND', we periodically searched the

published medical literature using the PubMed service maintained by the U.S. National Library of

- 80 Medicine of NIH. Confirmed COVID-19 cases are defined as persons who tested positive for SARS-
- 81 CoV-2 and had clinical symptoms. Asymptomatic carriers refer to persons without clinical
- 82 symptoms who tested positive for SARS-CoV-2.
- 83
- 84 **Results**

85 Regional distribution of nosocomial COVID-19 infections from June 2020 to June 2021

From June 2020 to June 2021, regional distribution of the sporadic nosocomial COVID-19
infections is shown in Figure 1, 2 and Table 1. Most of these cities are located in coastal or airline
hub areas, for example, Dalian, Qingdao, Shanghai are coastal cities, and Xi'an, Shenyang,
Shijiazhuang, and Guangzhou are airline hub cities.

90

91 Occupational distribution of nosocomial COVID-19 infections from June 2020 to June 2021

From June 2020 to June 2021, six cities in China had reported over 45 cases with nosocomial COVID-19 infections, including 39 confirmed cases and 6 asymptomatic cases (Table 2). Among them, nursing staff (3), doctors (6), patients (12), accompanying staff (22), and laboratorian (2) were diagnosed. The route of these nosocomial infections mainly included workplace accidental exposure to COVID-19, cross infection among healthcare workers, patients, and accompanying staff.

97

98 SARS-CoV-2 gene sequencing results of nosocomial COVID-19 infections from June 2020 to 99 June 2021

SARS-CoV-2 gene sequencing is crucial work for nosocomial COVID-19 infections in new sporadic outbreak regions. The virus strain of nosocomial COVID-19 infection found in Qingdao city is the virus strain lineage B.1.1 imported from overseas (Table 2). Gene sequencing results showed that the coronavirus found in Dalian, Shenyang, and Shijiazhuang cities is similar to the strain imported from Europe; The virus strain found in Xi'an city is a COVID-19 variant B.1.1.7 lineage; SARS-CoV-2 strain found in Guangzhou city is the imported virus strain B1.617.2 (Delta) lineage (Table 2).

107 A report from Fang et al⁹ showed that the strains associated with specific outbreak in Dalian City 108 as follows: LNDL-BHQ-0722-Y S12 L001 R1 001, were LNDL-SFL-0722-109 Y S9 L001 R1 001, LNDL-WY-0722-Y S11 L001 R1 001, LNDL-XY-0722and 110 Y S10 L001 R1 001; The parent strain from Wuhan was 111 NC 045512.2 Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu-

112 1_complete_genome. After accessing the public database GISAID and GenBank, 3 Russian strains

113 detected in July were found to share the 10 variation sites with the 2 Hebei strains (GISAID IDs:

EPI_ISL_596266, EPI_ISL_569792, and EPI_ISL_569793)¹⁰. Evidence indicates that these the
 Shijiazhuang strains may have originated from these Russian strains¹⁰.

116

117 **Discussion**

- 118 This paper provides us with an inspiring vision regarding the current COVID-19 pandemic. The
- 119 main findings of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 are listed
- 120 below: (1) the importance of rolling out an overall nucleic acid test campaign to all staff in healthcare

settings, is a crucial part of the COVID-19 surveillance; (2) The case of coronavirus transported onto the workplace warns us that the current hospital disinfection concept urgently requires updating, especially in designated hospitals, and there is an urgent demand of the management of staff accompanying patients in non-designated hospitals; (3) The phenomenon about COVID-19 vaccine breakthrough infection deserves our great attention.

126 For healthcare workers, patients/accompanying staff, and cleaner, their COVID-19 infection may 127 be from hospital (hospital-acquired infection, also nosocomial infection) or community 128 (community-acquired infection). Distinguishing nosocomial infection and community-acquired 129 infection is an important base to control the epidemic in nosocomial COVID-19 infections. Because 130 healthcare workers are at the interface between hospitals and the community, where there is 131 significant COVID-19 transmission, they may be infected by asymptomatic carriers from the 132 community with COVID-19 or COVID-19 patients. These healthcare workers (infected in the 133community) do not belong to nosocomial infection (also called hospital-acquired infection). For 134 example, in Figure 1, the infected cases (including healthcare workers, cleaner, etc.) in Beijing, 135Dalian (27 Dec. 2020) and Shanghai were community-acquired infection, not nosocomial infection. For nosocomial infection of healthcare workers, patients/accompanying staff, and cleaner, as the 136 137 effective control measures taken by the local government must include: (1) these hospitals imposed 138 lockdown, especially in the designated COVID-19 hospital; (2) rolling out an overall nucleic acid 139 test campaign to all staff is key in healthcare settings.

140

155

141 Among 9 sporadic nosocomial COVID-19 infections, our results showed that 8 series cases were 142 found by rolling out overall a nucleic acid test campaign to all hospital staff, suggesting the 143 importance of regular screening for all staff in healthcare settings. As part of efforts to control the 144 COVID-19 infections, one of the effective prevention measures taken by local authorities is that all 145 hospital personnel labeled a key population are closely monitored⁷. Whether the epidemic in 146 nosocomial COVID-19 infections can be brought under control depends on how many new 147 infections emerge of their close contacts and secondary close contacts in the next two weeks. If 148 these hospitals imposed lockdown as the effective control measures taken by the local government, 149 then ideally, new confirmed cases with COVID-19 infections will see a downward trend within two 150 weeks. Cases such as hospital-acquired infection in the designated hospital of Qingdao city are a 151warning that workplace storage and transport could be a hotbed for the coronavirus, or other 152pathogens. There is an urgent demand for workplace disinfection to protect the health safety of 153medical staff, patients, and accompanying staff in the current pandemic or into another worse 154 outbreak.

156 Our data also showed that a vaccinated healthcare professional who received inactivated vaccine 157 was infected with COVID-19 while working in the isolation ward of a designated COVID-19 158 hospital, and the coronavirus strain was determined to be the imported COVID-19 variant strain 159 B.1.1.7⁸, suggesting that there exists the domestic COVID-19 vaccine breakthrough infection in 160 China, and this phenomenon deserves our serious attention. Vaccination is well-known to be key to stopping the virus from circulating and more variants from popping up¹¹⁻¹³. The vaccine 161 162 breakthrough infection case was defined as an individual with positive SARS-CoV-2 nucleic acid 163 amplification tested after receiving at least one dose of a SARS-CoV-2 vaccine¹⁴⁻¹⁶. Jacobson et al¹⁷ 164 addressed post-vaccination SARS-CoV-2 infections and the incidence of the B.1.427/B.1.429 variant among healthcare personnel at a northern California academic medical center. Hacisuleyman et al¹⁸ reported two women with vaccine breakthrough infection in a cohort of 417 persons who had received the second dose of BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) vaccine at least two weeks previously, and the viral sequencing showed that they were infected with the new variant virus including E484K in 1 woman and three mutations (T95I, del142–144, and D614G) in both. These observations revealed a potential risk of COVID infection with the variant virus after successful vaccination.

Vaccine breakthrough cases with SARS-CoV-2 were reported in many countries¹⁹⁻²¹. An analysis 172173 from Israel's vaccination campaign showed that COVID-19-related hospitalizations, severe disease, 174and death were reduced in infected cases with SARS-CoV-2 after vaccination, including symptomatic and asymptomatic infections²¹. Antonelli et al²² identified risk factors for post-175176 vaccination SARS-CoV-2 infection and describe the characteristics of post-vaccination illness, and 177found that Almost all symptoms were reported less frequently in infected vaccinated individuals 178than in infected unvaccinated individuals, and vaccinated participants were more likely to be 179 completely asymptomatic, especially if they were 60 years or older. Our vaccine breakthrough case 180 from Xi'an supported vaccine effectiveness and cautioned around relaxing physical distancing and 181 other personal protective measures in the post-vaccination era.

182

183 SARS-CoV-2 virus delta variants have drawn worldwide attention. The WHO proposed three labels 184 for global SARS-CoV-2 variants, including variant of concern (VOC), variant of interest (VOI), and 185 variant under monitoring, to be used alongside the scientific nomenclature in communications about 186 variants to the public²³. The B.1.617 variant of the COVID-19 virus has been called a triple mutant 187 variant since it splits into three lineages including the B.1.617.1 (Kappa) variant, the B.1.617.2 188 (Delta) variant, and the B.1.617.3 variant²⁴. The delta COVID-19 variant, which was first detected 189 in India in October 2020, had been reported in more than 80 countries on June 20, 2021²⁵. The WHO 190 declared the delta variant a "variant of concern" on May 10, 2021. In Mid-June 2021, the US Centers 191 for Disease Control and Prevention upgraded its classification of the delta from a "variant of 192 interest" to a "variant of concern."²⁶ Our results showed that two medical staff (1 laboratorian and 193 1 emergency doctor), infected with COVID-19 in the designated hospital, occurred due to workplace 194 accidental exposure to COVID-19, and the coronavirus strain was determined to be the imported 195 B.1.617.2 (Delta) variant.

196

197To conclude, our findings add to the accumulating evidence regarding the importance of regular198screening for all staff in healthcare settings. Furthermore, our study highlights the need for an update199of the current hospital disinfection procedures in designated hospitals to prevent the nosocomial200spread of SARS-CoV-2 infection. Finally, the epidemiological exposure of vaccinated medical staff201should draw concern in order to minimize the impact of a new outbreak induced by virus mutants.

202

203 Table 1: Epidemiological characteristics of sporadic nosocomial COVID-19 infections

Date	City	Number of	Hospital type	Profession	Classification of	Route of infection	Database
		hospital/ cases			infection		
19 Jun.	Beijing	1/1	Designated	nurse	Community-	family member	Link 1
2020			hospital		acquired	exposure with	
					infection	COVID-19	

11 Oct.	Qingdao	1/12	Designated	Patients and	hospital-	nosocomial	Link 2
2020			hospital	accompanying	acquired	infection	
				staff	infection		
29 Oct.	Qingdao	1/1	Designated	nurse	hospital-	workplace	Link 3
2020			hospital		acquired	accidental	
					infection	exposure to	
						COVID-19	
18 Dec.	Dalian	1/3	Non-	Patients	hospital-	nosocomial	Link 4
2020			designated		acquired	infection	
			hospital		infection		
27 Dec.	Dalian	1/1	Non-	Cleaner	Community-	cold-chain	Link 5
2020			designated		acquired	environment-to-	
			hospital		infection	human	
						transmission	
3 Jan.	Shenyang	1/12	Non-	Medical staff,	hospital-	nosocomial	Link 6
2021			designated	patients and	acquired	infection	
			hospital	accompanying	infection		
				staff			
14 Jan.	Shijiazhuang	2/14	Non-	Medical staff,	hospital-	nosocomial	Link 7
2021			designated	patients and	acquired	infection	
			hospital	accompanying	infection		
				staff			
20 Jan.	Shanghai	2/2	Non-	Logistics	Community-	imported from	Link 8
2021			designated	support staff	acquired	overseas	
			hospital		infection		
17 Mar.	Xi'an	1/1	Designated	laboratorian	hospital-	Mild	Link 9
2021			hospital		acquired	Breakthrough	
					infection	Infection	
14 Jun.	Guangzhou	1/2	Designated	Laboratorian	hospital-	nosocomial	Link 10
2021			hospital	and	acquired	infection	
				Emergency	infection		
				doctor			
27 Jul.	Nanjing	1/4	Non-	accompanying	hospital-	nosocomial	Link 11
2021			designated	staff	acquired	infection	
			hospital		infection		
10 Aug.	Yangzhou	1/3	Non-	Doctor	hospital-	nosocomial	Link 12
2021			designated		acquired	infection	
			hospital		infection		

204

Designated hospital: a hospital designated for treatment of imported COVID-19 cases

205

206 Link 1: https://finance.sina.com.cn/china/gncj/2020-06-19/doc-iircuyvi9385332.shtml?r=9&tj=none&tr=9

207 Link 2: https://www.zhihu.com/question/425220159

208 Link 3: https://new.qq.com/omn/20201030/20201030A05GXU00.html

209 Link 4: http://www.xinhuanet.com/politics/2021-01/06/c_1126953634.htm

- 210 Link 5: <u>https://new.qq.com/omn/20201229/20201229A0259M00.html</u>
- 211 Link 6: https://new.qq.com/omn/20210111/20210111A0DFD500.html
- 212 Link 7: https://news.sina.com.cn/c/2021-01-20/doc-ikftpnnx9631142.shtml
- 213 Link 8: https://new.qq.com/omn/20210131/20210131A0071200.html
- 214 Link 9: https://news.sina.com.cn/c/2021-03-18/doc-ikkntiam4831560.shtml
- 215 Link 10: https://news.sina.com.cn/c/2021-06-14/doc-ikqcfnca0979774.shtml
- 216 Link 11: http://med.china.com.cn/content/pid/281087/tid/1026
- 217 Link 12: http://news.hexun.com/2021-08-18/204179459.html
- 218
- 219

220 Table 2: Epidemiological characteristics of sporadic nosocomial COVID-19 infections

Date	City	Confirmed/	How to discover the	Virus type	Database
		asymptomatic	source of infection		
		cases			
19 Jun.	Beijing	1/0	Nucleic acid testing for	One ancestral virus strain	Link 1
2020			close contacts of people	(XFDM strain) 27	
			with infection cases		
11 Oct.	Qingdao	6/6	Regular screening for	Imported virus strain	Link 2
2020			medical staff	Lineage B.1.1 ²⁸	
29 Oct.	Qingdao	1/0	Regular screening for	Imported virus strain	Link 3
2020			medical staff	Lineage B.1.1 ²⁸	
18 Dec.	Dalian	3/0	Regular screening for	European family branch 1	Link 4
2020			medical staff	of the L genotype	
27 Dec.	Dalian	1/0	Regular screening for	European family branch 1	Link 5
2020			medical staff	of the L genotype	
3 Jan.	Shenyang	12/0	Regular screening for	Imported virus strain	Link 6
2021			medical staff		
14 Jan.	Shijiazhuang	14/0	Regular screening for	the strain imported from	Link 7
2021			medical staff	Europe ²⁹	
20 Jan.	Shanghai	2/0	Nucleic acid testing for	Imported virus strain	Link 8
2021			close contacts of people		
			with infection cases		
17 Mar.	Xi'an	1/0	Regular screening for	Imported virus strain	Link 9
2021			medical staff	B.1.1.7 ⁸	
14 Jun.	Guangzhou	2/0	Regular screening for	Imported virus strain	Link 10
2021			medical staff	B1.617.2 (Delta) Lineage	
27 Jul.	Nanjing	4/0	Regular screening for	Imported virus strain	Link 11
2021			medical staff	B1.617.2 (Delta) Lineage	
10Aug.	Yangzhou	3/0	Regular screening for	Imported virus strain	Link 12
2021			medical staff	B1.617.2 (Delta) Lineage	

221

Delta Lineage: the highly contagious Covid-19 variant first identified in India

222

223 Link 1: http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2020.246

Link 2: http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2020.224

- 225 Link 3: <u>https://new.qq.com/omn/20201030/20201030A05GXU00.html</u>
- 226 Link 4: http://www.xinhuanet.com/politics/2021-01/06/c_1126953634.htm
- 227 Link 5: https://new.qq.com/omn/20201229/20201229A0259M00.html
- 228 Link 6: https://new.qq.com/omn/20210111/20210111A0DFD500.html
- 229 Link 7: http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2021.006
- 230 Link 8: https://new.qq.com/omn/20210131/20210131A0071200.html
- 231 Link 9: http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2021.094
- 232 Link 10: https://news.sina.com.cn/c/2021-06-14/doc-ikqcfnca0979774.shtml
- 233 Link 11: http://med.china.com.cn/content/pid/281087/tid/1026
- 234 Link 12: http://news.hexun.com/2021-08-18/204179459.html
- 235

239

236 Authors contribution

All the authors contributed to the paper presented methodology and conceptualization. They allcontributed to data analysis and paper writing.

240 Funding

This work is funded by the National Natural Science Foundation of China (81873467, 81670240,and 81271766).

243

244 **Declaration of competing interest**

245 The authors declare that they have no known competing financial interests or personal relationships 246 that could have appeared to influence the work reported in this paper

247

248 **References**

249 1. Feng M, Li Z, Xiong J, Xu W and Xiang B. Geographical and Epidemiological
250 Characteristics of 3,487 Confirmed Cases With COVID-19 Among Healthcare Workers in
251 China. *Frontiers in Public Health.* 2021;8.

252 2. Xiang B, Li P, Yang X, Zhong S, Manyande A and Feng M. The impact of novel
253 coronavirus SARS-CoV-2 among healthcare workers in hospitals: An aerial overview.
254 American Journal of Infection Control. 2020;48:915-917.

3. Abbas M, Nunes TR, Martischang R, Zingg W, Iten A, Pittet D and Harbarth S.
Nosocomial transmission and outbreaks of coronavirus disease 2019: the need to
protect both patients and healthcare workers. *Antimicrobial Resistance and Infection Control.* 2021;10.

4. O'Leary N, Kingston L, Griffin A, Morrissey A-m, Noonan M, Kelly D, Doody O,
Niranjan V, Gallagher A, O'Riordan C and Lynch A. COVID-19 healthcare policies in
Ireland: A rapid review of the initial pandemic response. Scandinavian Journal of
Public Health. 2021.

263 5. Ran L, Chen X, Wang Y, Wu W, Zhang L and Tan X. Risk Factors of Healthcare
264 Workers With Coronavirus Disease 2019: A Retrospective Cohort Study in a Designated
265 Hospital of Wuhan in China. *Clinical Infectious Diseases*. 2020;71:2218-2221.

6. Feng M, Ling Q, Xiong J, Manyande A, Xu W and Xiang B. Geographical and
Epidemiological Characteristics of Sporadic Coronavirus Disease 2019 Outbreaks From
June to December 2020 in China: An Overview of Environment-To-Human Transmission

269 Events. Front Med. 2021;8: 654422.

- 7. Feng M, Ling Q, Xiong J, Manyande A, Xu W and Xiang B. Occupational
 Characteristics and Management Measures of Sporadic COVID-19 Outbreaks From June
 2020 to January 2021 in China: The Importance of Tracking Down "Patient Zero". *Frontiers in Public Health.* 2021;9.
- 8. Outbreak Reports: Mild Breakthrough Infection in a Healthcare Professional
 Working in the Isolation Area of a Hospital Designated for Treating COVID-19 Patients
 Shaanxi Province, China, March, 2021. China CDC Weekly. 2021, 3(19): 397-400.
 http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2021.094.
- 278 9. Fang FH, Song Y, Hao LP, Nie K and Sun XD. A Case of COVID-19 Detected in a
 279 Cargo Worker at Pudong Airport Shanghai Municipality, China, November 8, 2020.
 280 China Cdc Weekly. 2020;2:910-911.
- 10. Qi S, Zhao X, Hao P, Liu N, Gao GF, Song Y, Xu W and Li Q. Two Reemergent Cases
 of COVID-19-Hebei Province, China, January 2, 2021. *China Cdc Weekly*. 2021;3:25-27.
 11. Kashte S, Gulbake A, El-Amin Iii SF and Gupta A. COVID-19 vaccines: rapid
 development, implications, challenges and future prospects. *Hum Cell*. 2021.
- 12. Inchingolo AD, Inchingolo AM, Bordea IR, Malcangi G, Xhajanka E, Scarano A,
 Lorusso F, Farronato M, Tartaglia GM, Isacco CG, Marinelli G, D'Oria MT, Hazballa D,
 Santacroce L, Ballini A, Contaldo M, Inchingolo F and Dipalma G. SARS-CoV-2 Disease
 through Viral Genomic and Receptor Implications: An Overview of Diagnostic and
 Immunology Breakthroughs. *Microorganisms*. 2021;9.
- 13. van der Lubbe JEM, Huber SKR, Vijayan A, Dekking L, van Huizen E, Vreugdenhil J,
 Choi Y, Baert MRM, Feddes-de Boer K, Gil AI, van Heerden M, Dalebout TJ, Myeni SK,
 Kikkert M, Snijder EJ, de Waal L, Stittelaar KJ, Tolboom J, Serroyen J, Muchene L,
 van der Fits L, Rutten L, Langedijk JPM, Barouch DH, Schuitemaker H, Zahn RC and
 Wegmann F. Ad26. COV2. S protects Syrian hamsters against G614 spike variant SARS-CoV2 and does not enhance respiratory disease. *npj Vaccines*. 2021;6:12.
- 14. Ioannou P, Karakonstantis S, Astrinaki E, Saplamidou S, Vitsaxaki E, Hamilos G,
 Sourvinos G and Kofteridis DP. Transmission of SARS-CoV-2 variant B.1.1.7 among
 vaccinated health care workers. *Infectious diseases (London, England)*. 2021:1-4.
- 15. Blachere NE, Hacisuleyman E and Darnell RB. Vaccine Breakthrough Infections with
 SARS-CoV-2 Variants REPLY. *New England Journal of Medicine*. 2021.
- 16. Kustin T, Harel N, Finkel U, Perchik S, Harari S, Tahor M, Caspi I, Levy R,
 Leshchinsky M, Ken Dror S, Bergerzon G, Gadban H, Gadban F, Eliassian E, Shimron O,
 Saleh L, Ben-Zvi H, Keren Taraday E, Amichay D, Ben-Dor A, Sagas D, Strauss M, Shemer
 Avni Y, Huppert A, Kepten E, Balicer RD, Netzer D, Ben-Shachar S and Stern A. Evidence
 for increased breakthrough rates of SARS-CoV-2 variants of concern in BNT162b2-mRNAvaccinated individuals. *Nature Medicine*. 2021.
- 307 17. Jacobson KB, Pinsky BA, Rath MEM, Wang H, Miller JA, Skhiri M, Shepard J, Mathew
 308 R, Lee G, Bohman B, Parsonnet J and Holubar M. Post-vaccination SARS-CoV-2 infections
 309 and incidence of the B. 1. 427/B. 1. 429 variant among healthcare personnel at a northern
 310 California academic medical center. *medRxiv : the preprint server for health sciences*.
 311 2021.
- 312 18. Hacisuleyman E, Hale C, Saito Y, Blachere NE, Bergh M, Conlon EG, Schaefer-

- Babajew DJ, DaSilva J, Muecksch F, Gaebler C, Lifton R, Nussenzweig MC, Hatziioannou
 T, Bieniasz PD and Darnell RB. Vaccine Breakthrough Infections with SARS-CoV-2
 Variants. New England Journal of Medicine. 2021;384:2212-2218.
- 19. Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P, Sudre CH, Nguyen LH,
 Drew DA, Merino J, Hu C, Selvachandran S, Antonelli M, Murray B, Canas LS, Molteni
 E, Graham MS, Modat M, Joshi AD, Mangino M, Hammers A, Goodman AL, Chan AT, Wolf J,
 Steves CJ, Valdes AM, Ourselin S and Spector TD. Vaccine side-effects and SARS-CoV2 infection after vaccination in users of the COVID Symptom Study app in the UK: a
 prospective observational study. *Lancet Infectious Diseases*. 2021;21:939-949.
- 20. Bernal JL, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, Simmons R, Cottrell S, Roberts R, O'Doherty M, Brown K, Cameron C, Stockton D, McMenamin J and Ramsay M. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. *BMJ-British Medical Journal*. 2021;373.
- 21. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, Brooks N, Smaja M,
 Mircus G, Pan K, Southern J, Swerdlow DL, Jodar L, Levy Y and Alroy-Preis S. Impact
 and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID19 cases, hospitalisations, and deaths following a nationwide vaccination campaign
 in Israel: an observational study using national surveillance data. *Lancet*.
 2021;397:1819-1829.
- 22. Antonelli M, Penfold RS, Merino J, Sudre CH, Molteni E, Berry S, Canas LS, Graham MS, Klaser K, Modat M, Murray B, Kerfoot E, Chen L, Deng J, Osterdahl MF, Cheetham NJ, Drew DA, Nguyen LH, Pujol JC, Hu C, Selvachandran S, Polidori L, May A, Wolf J, Chan AT, Hammers A, Duncan EL, Spector TD, Ourselin S and Steves CJ. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. *The Lancet Infectious diseases.* 2021.
- 340 23. Hao Y, Guan XH, Liu TT, He ZG and Xiang HB. Hypothesis: the central medial
 341 amygdala may be implicated in sudden unexpected death in epilepsy by
 342 melanocortinergic-sympathetic signaling. *Epilepsy Behav.* 2014;41:30-2.
- 24. Liu TT, He ZG, Tian XB and Xiang HB. Neural mechanisms and potential treatment
 of epilepsy and its complications. *Am J Transl Res.* 2014;6:625-30.
- 25. Liu TT, He ZG, Tian XB, Liu C, Xiang HB and Zhang JG. Hypothesis: Astrocytes in
 the central medial amygdala may be implicated in sudden unexpected death in epilepsy
 by melanocortinergic signaling. *Epilepsy Behav.* 2015;42:41-3.
- 348 26. Xiang HB, Liu C, Liu TT and Xiong J. Central circuits regulating the sympathetic
 349 outflow to lumbar muscles in spinally transected mice by retrograde transsynaptic
 350 transport. *Int J Clin Exp Pathol.* 2014;7:2987-97.
- 27. Pang X, Ren L, Wu S, Ma W, Yang J, Di L, Li J, Xiao Y, Kang L, Du S, Du J, Wang
 J, Li G, Zhai S, Chen L, Zhou W, Lai S, Gao L, Pan Y, Wang Q, Li M, Wang J, Huang Y,
 Wang J, Grp C-FR and Grp C-LT. Cold-chain food contamination as the possible origin
 of COVID-19 resurgence in Beijing. *National Science Review.* 2020;7:1861-1864.
- 28. Liu P, Yang M, Zhao X, Guo Y, Wang L, Zhang J, Lei W, Han W, Jiang F, Liu WJ,
 Gao GF and Wu G. Cold-chain transportation in the frozen food industry may have

357 caused a recurrence of COVID-19 cases in destination: Successful isolation of SARS-358 CoV-2 virus from the imported frozen cod package surface. Biosafety and health. 359 2020;2:199-201. 360 29. Liu C, Liu TT, He ZG, Shu B and Xiang HB. Inhibition of itch-related responses 361 by selectively ablated serotonergic signals at the rostral ventromedial medulla in 362 mice. Int J Clin Exp Pathol. 2014;7:8917-21. 363 364 365 366 367 Figure 1: Geographical distribution of sporadic nosocomial COVID-19 infections from June 368 2020 to June 2021 in China. Seven cities (Dalian, Beijing, Qingdao, Shijiazhuang, Xi'an, 369 Guangzhou, and Shanghai) reported the nosocomial COVID-19 infections. Medical staff, patients 370 and accompanying staff (12) in Shenyang (Jan 3, 2021), patients (3) in Dalian (Dec 18, 2020), 371 patients and accompanying staff (6) in Qingdao (Oct 11, 2020), laboratory personnel (1) in Xi'an 372 (Mar 17, 2021), medical staff, patients and accompanying staff (14) in Shijiazhuang (Jan 14, 2021), 373 and Medical staff (2) in Guangzhou (Jun 14, 2021) were diagnosed as infected cases. 374 375 376 Figure 2: The graph's left-right axis is used as a timeline of the key events and dynamic profile 377 of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China. 378 From June 2020 to June 2021, five cities in China had reported 10 series cases with nosocomial 379 COVID-19 infections, including 39 confirmed cases and 6 asymptomatic cases. 380 The delta COVID-19 variant was first detected in India in October 2020. The World Health 381 Organization designated Delta as a variant of interest in April and a variant of concern on 11 May 382 2021. In Mid-June 2021, the US Centers for Disease Control and Prevention upgraded its 383 classification of delta from a "variant of interest" to a "variant of concern." 384 385

Figure 1.TIF



