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Cover Photo: China has become the first country to promise vaccines as a global public product. As of February 23, 2021, China has overcome domestic needs and has provided free vaccine assistance to 53 countries in need, as well as agreeing to supply an additional 27 countries willing to purchase vaccines.

Nankun Liu

Preplanned Studies

Clinical Effects of the COVID-19 Pandemic Among the Uninfected Pregnant Women — 6 PLADs, China, 2019–2020

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Summary

What is already known about this topic?

The coronavirus disease 2019 (COVID-19) pandemic potentially affected prenatal care quality and maternal and fetal outcomes globally.

What is added by this report?

During COVID-19 pandemic period, the rates of caesarean sections (CS) and preterm birth for uninfected pregnant women increased slightly in areas that were relatively severely impacted by the pandemic in China. The overall number of prenatal examinations did not dramatically decrease, while the eligible examinations significantly decreased in Hubei Province.

What are the implications for public health practice?

Routine prenatal examinations had been well maintained during the pandemic period in China. In the future, in-time prenatal examinations should be provided to improve the quality of screening and management of high-risk pregnancy under pandemic-affected circumstances. Psychological counseling and transfer treatment channels should be strengthened for pregnant women during lockdown period.

The impact of the coronavirus disease 2019 (COVID-19) pandemic on pregnant women have been of considerable concern. Uninfected pregnant women may be affected by generalized social panic, reduced number of prenatal examinations (NPE)*, and delayed medical treatment. During the COVID-19 pandemic in China, most pregnant women stayed at home unless an urgent prenatal examination or treatment was required. It was reported that

COVID-19 pandemic resulted in approximately 1/3 of pregnant women having inadequate antenatal visits and 44.7% of pregnancies with complications due to their fear of contracting infections (1). This study examined the impact of the COVID-19 pandemic on the clinical characteristics of uninfected pregnant women and their neonates by using two ongoing programs conducted by the Maternal and Newborn Health Monitoring Program (MNHMP) and a birth cohort of the Haidian Maternal and Child Care Hospital (HMCCH) in Beijing, China. The results suggested that the rates of caesarean section (CS) and preterm birth[†] increased slightly in areas that were more affected by the pandemic. NPE were not significantly interrupted, and most maternal and neonatal clinical characteristics were within the normal ranges. The rate of the number of prenatal eligible examinations exceeding 5 times (PEE5) with blood pressure and blood routine examinations during the regulated prenatal care according to the National Standards for Basic Public Health Services in China was significantly reduced in Hubei. We concluded that the frequency of routine prenatal care had been well maintained in China during the pandemic period in 2020. However, special in-time prenatal examination should be provided to improve the quality of care for pregnant women, and screening and management of high-risk pregnancies should be strengthened when pandemic-like circumstances occur in the future.

This prospective cohort study was based on two ongoing multicenter programs including: 1) the MNHMP established in 2013 by the National Center for Women and Children's Health (NCWCH) of China CDC, of which the detailed information had been described previously (2); and 2) a birth cohort in

^{*} The times of examinations which women took from their first antenatal care examination to childbirth.

[†] Live infants born before 37 gestational weeks.

[§] The regulated prenatal care in standards for the management and service of maternal health is issued in the National Standards for Basic Public Health Services (Third Edition) by National Health Commission in China. There are routine prenatal cares for five times at <13rd, 16th–20th, 21st–24th, 28th–36th, and 37st–40th. The details can be found on the website: http://www.nhc.gov.cn/.

HMCCH in Beijing in China. For all areas, pregnant women were recruited with delivery or termination from January 1, 2019 to May 31, 2019 (pre-pandemic period: P-2019) and from January 1, 2020 to May 31, 2020 (pandemic period: P-2020). Finally, 32,277 pregnant women were included from 6 Provincial Administration Level Divisions(PLADs), including 6,449 in Hubei Province, 5,878 in Guangdong Province, 3,641 in Hebei Province, 6,328 in Shandong Province, 2,920 in Yunnan Province, and 7,061 in Beijing Municipality. The main outcomes, including the NPE, PEE5, preterm birth, stillbirth, large for gestational age (LGA)**, small for gestational age $(SGA)^{\dagger\dagger}$, macrosomia §§, and low birth weight (LBW) ¶¶ status were recorded or calculated. Means ± standard deviations (SDs) or medians (25%-75% percentile ranges) were used to describe distributions. SGA and LGA status were assessed from gestational week 24-42. COVID-19 pandemic status served as a categorical variable. Three regression models were used to estimate the effects of the pandemic depending on the data distribution, i.e., Poisson, linear, and log-binomial regressions. The confounders included body mass index (BMI, categorical), age (categorical), parity, gravidity, ethnicity, and educational level. The study protocol was approved by the institutional review board of Peking University.

The demographic characteristics of all women were listed in Table 1. The mean ages differed between the two periods (P-2019 *vs.* P-2020) for Hubei (29.1 *vs.* 28.7), Guangdong (28.4 *vs.* 27.9), Beijing (31.6 *vs.* 31.4), and Hebei (29.8 *vs.* 29.4). However, the differences were negligible (maximum 1.7% in Guangdong). Parity distribution varied by location but did not differ between the two periods. The average BMI (kg/m²) ranged from 22.2 (Hubei) to 23.2 (Hebei). For Hebei alone, the average BMI increased slightly from 23.1 (P-2019) to 23.5 (P-2020). Educational levels differed greatly; although significant differences between the two periods were evident in Hubei and Guangdong, the overall pattern remained similar.

The maternal and neonatal clinical characteristics

were listed in Table 2. The NPE varied by locations. The average NPE in Hubei and Beijing decreased slightly from P-2019 to P-2020 but increased in Guangdong and Hebei. Comparatively speaking, the ratio of PEE5 significantly decreased from 5.4% (P2019) to 2.6% (P2020) in Hubei. No betweenperiod changes in maternal death, stillbirth, neonatal gender, or normal weight or LBW status were evident. The maternal death and stillbirth rates rarely occurred. Guangdong (28%) and Yunnan (27%) exhibited lower CS rates than the other regions. The CS rates increased significantly between the two periods for Hubei and Guangdong only. Most Apgar scores ranged from 9 to 10 except for Hubei monitored at 1 min, but the differences were negligible. The preterm birth rate increased between the two periods for Hubei and Guangdong only. The macrosomia rate in Beijing only increased by about 2%. The SGA rates decreased for Hubei and Guangdong only. The LGA rate in Hubei only increased from 8% to 10%.

The adjusted regression parameters of the clinical manifestations of the two periods are listed in Table 3, which were consistent with those without adjustment for confounders. For Hubei, the NPE, delivery gestational weeks(DGW)***, and SGA were negatively associated with the pandemic, and the CS and preterm birth rates were positively associated. Guangdong was similar, but the NPE change lacked significance. The PEE5 in Hubei were negatively associated with the pandemic, while not for others. The effect of the pandemic on preterm birth in Hubei and Guangdong change substantially with additional did not adjustment for CS. In contrast, we only found the positive associations for the macrosomia risk in Beijing and the NPE in Hebei, and a negative association for the DGW in Yunnan.

DISCUSSION

This study explored the effects of the pandemic on pregnancy-related clinical manifestations in uninfected women. Overall, the effects were minor. However, the significantly increased rates of CS and preterm birth in

[¶] Late fetal deaths weighing more than 1,000 g or occurring after 28 weeks gestation.

^{**} Live infants born at gestational weeks 24–42 without major birth defects and with birthweight above the 90th percentile for gestational age of the reference population mean for birthweight and gestational age.

^{††} Live infants born at gestational weeks 24–42 without major birth defects and with birthweight below the 10th percentile for gestational age of the reference population mean for birthweight and gestational age.

^{§§} Live infants with weight at birth not less than 4,000 g.

Live infants with weight at birth less than 2,500 g.

^{***} Duration from the last menstrual period reported by the women and the time of delivery.

Hubei and Guangdong with relatively high COVID-19 prevalence level requires attention, as the increased risk of macrosomia in Beijing. Thus, our hypothesis is only partly supported.

Many reports on the pregnancy complications and neonatal birth outcomes of infected women have appeared; the preterm birth and CS rates increased significantly in countries with high COVID-19 burdens (3–4). However, the effects on uninfected pregnant women have been rarely reported. In the United Kingdom, it has been proposed that the stillbirth increase was caused by a reluctance to visit hospitals for fear of contracting COVID-19 (5). The medical facility experienced a major decline in all aspects of routine obstetric activities during pandemic period (6). In China, strict prevention and control policies ensured social distancing. Even in areas with

low infection rates, all nonessential examinations were to be postponed or reduced.

In our study, the NPE decreased only in Hubei by 5%. In the other five areas, the NPE did not decrease and even increased in Hebei. The pandemic did not increase the stillbirth or LBW rates. Beijing (only) exhibited a slightly increased rate of macrosomia. Similar results were found in Wuhan City in Hubei Province suggesting that most of the clinical manifestations did not increase except for the weight of newborns being significantly heavier during the pandemic period (7). All health services worked well, despite the fact that the pandemic consumed a great deal of medical resources. Since the outbreak, medical resources have been rationally allocated using a Joint Prevention and Control Mechanism prepared by the State Council of China to protect pregnant women (8).

TABLE 1. Demographic characteristics of the participants in the 2 periods of 2019 and 2020 in 6 provincial-level administrative divisions (PLADs) of China.

Demographic characteristic	- · H		ıbei Guangdong		Beijing	
County or district	Huangm	ei, Luotian	Longchuan, Zijin		Haidian	
Year	P-2019	P-2020	P-2019	P-2020	P-2019	P-2020
No. of subjects	3,300	3,149	3,328	2,550	3,902	3,159
Age (years)	28.7 ± 4.2**	29.1 ± 4.3 ^{§, §§}	27.9 ± 5.0	28.4 ± 5.0 ^{§, §§}	31.4 ± 4.0	31.6 ± 4.0*, §§
	28.0 (26.0, 31.0)††	29.0 (27.0, 32.0) ^{§,} ¶	¹ 27.0 (24.0, 31.0)	28.0 (25.0, 31.0) ^{§,} ¶¶	31.0 (29.0, 34.0)	31.0 (29.0, 34.0) ^{†,} ¶¶
Missing	0 (0)	2 (0)	0 (0)	2 (0)	0 (0)	0 (0)
Gravidity						
1 time	1,276 (39)	1,220 (39)	884 (27)	698 (27)	1,785 (46)	1,422 (45)
≥2 times	2,024 (61)	1,929 (61)	2,444 (73)	1,852 (73)	2,117 (54)	1,737 (55)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Parity						
Nulliparous	_ †††	_	1,255 (38)	960 (38)	2,517 (65)	2,058 (65)
Multiparous	_	_	2,073 (62)	1,590 (62)	1,385 (35)	1,101 (35)
Missing	-	_	0 (0)	0 (0)	0 (0)	0 (0)
BMI (kg/m²)	22.2 ± 3.1**	22.3 ± 3.2	22.0 ± 3.3	22.1 ± 3.5	_	_
	21.7 (20.1, 23.8)††	21.9 (20, 24)		21.7 (19.5, 24.1)	_	_
Missing	116 (4)	167 (5)	84 (3)	87 (3)	-	-
Education						
Primary or lower	26 (1)	15 (0) ^{§, ***}	58 (2)	53 (2) ^{†, ***}	-	-
Junior high	558 (17)	424 (14)	1,865 (56)	1,351 (53)	-	-
Senior high	2,295 (72)	2,377 (78)	760 (23)	566 (22)	-	-
College or higher	316 (10)	242 (8)	645 (19)	580 (23)	-	-
Missing	105 (3)	91 (3)	0 (0)	0 (0)	-	-
Ethnicity						
Han	3,248 (100)	3,086 (100)	3,233 (98)	2,483 (98)	-	-
Others	10 (0)	12 (0)	51 (2)	47 (2)	-	-
Missing	42 (1)	51 (2)	44 (1)	20 (1)	_	_

TABLE 1. (Continued)

Demographic characteristic	Shandong Shizhong, Huaiyin		Hebei Zhengding, Xingtai		Yunnan Huaning, Tonghai	
County or district						
Year	P-2019	P-2020	P-2019	P-2020	P-2019	P-2020
No. of subjects	3,879	2,449	2,280	1,361	1,952	968
Age (years)	31.3 ± 4.3	31.3 ± 4.2	29.4 ± 3.9	$29.8 \pm 3.9^{\dagger, \S\S}$	27.9 ± 4.8	28.0 ± 4.6
	31.0 (29.0, 34.0)	31.0 (29.0, 34.0)	29.0 (27.0, 32.0)	30.0 (27.0, 32.0) ^{†,} ¶¶	28.0 (24.0, 31.0)	28.0 (25.0, 31.0)
Missing	0 (0)	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)
Gravidity						
1 time	1,353 (35)	832 (34)	562 (25)	317 (23)	537 (28)	227 (23)*, ***
≥2 times	2,526 (65)	1,617 (66)	1,718 (75)	1,044 (77)	1,415 (72)	741 (77)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Parity						
Nulliparous	1,968 (51)	1,182 (48)	764 (34)	465 (34)	772 (40)	390 (40)
Multiparous	1,911 (49)	1,267 (52)	1,516 (66)	896 (66)	1,180 (60)	578 (60)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
BMI (kg/m²)	22.9 ± 3.6	22.8 ± 3.6	23.1 ± 4.0	23.5 ± 4.2	22.1 ± 3.7	22.1 ± 3.8
	22.3 (20.2, 24.8)	22.3 (20.3, 24.6)	22.4 (20.2, 25.3)	22.8 (20.4, 26.1) ^{†,} ¶¶	21.4 (19.4, 24.1)	21.4 (19.2, 24.2)
Missing	36 (1)	9 (0)	1 (0)	0 (0)	0 (0)	0 (0)
Education						
Primary or lower	9 (0)	9 (0)	19 (1)	4 (0)	199 (10)	86 (9)
Junior high	237 (7)	138 (7)	457 (25)	277 (24)	700 (36)	372 (39)
Senior high	477 (14)	240 (12)	479 (26)	310 (27)	564 (29)	289 (30)
College or higher	2,687 (79)	1,675 (81)	895 (48)	551 (48)	475 (25)	211 (22)
Missing	469 (12)	387 (16)	430 (19)	219 (16)	14 (1)	10 (1)
Ethnicity						
Han	3,740 (98)	2,375 (98)	1,819 (98)	1,124 (99)	1,514 (78)	744 (78)
Others	79 (2)	54 (2)	31 (2)	17 (1)	419 (22)	216 (22)
Missing	60 (2)	20 (1)	430 (19)	220 (16)	19 (1)	8 (1)

Notes: The COVID-19 pandemic level of the 6 PLADs are: Hubei, level IV; Guangdong, level III; Beijing, level II; Shandong, level II; Hebei, level I; and Yunnan, level I.

Abbreviations: P-2019, January 1–May 31, 2019 as the pre-pandemic period; P-2020, January 1–May 31, 2020 as the pandemic period. *P<0.05:

Overall, the pandemic did not compromise routine prenatal examinations in China.

Notably, the CS rate increased in Hubei and Guangdong during the pandemic period. One possible explanation is that the number of high-risk pregnant women with pregnancy complications may increase due to delayed prenatal examinations and in-time interventions during the pandemic. This viewpoint was supported by the decreased PEE5 in Hubei. In India, delayed health-seeking behaviors during pandemic period resulted in 44.7% of pregnancies having

complications, roughly 1/3 of women having an inadequate number of antenatal visits, and a 2.5-fold rise in admission to the intensive care unit of pregnant women (*I*). Another possible explanation is that the pandemic increased stress and anxiety. In China, a study conducted in 25 hospitals across China during January 1–February 9, 2020 found that the pandemic increased the risk of depressive and anxiety symptoms (*9*). Perhaps more women requested CS to ensure a live birth. In Wuhan, maternal requested CS significantly increased during the lockdown period (*7*). For the risk

[†] *P*<0.01;

[§] P<0.001;

¹ The COVID-19 pandemic levels were classified according to the provincial overall prevalence rate compared to Hubei Province;;

^{**} Mean value ± standard deviation;

^{††} Median value (25%–75% percentile);

^{§§} Compared by *t* test;

Tompared by Mann-Whitney U test;

^{***} Compared by Chi-square test;

^{†††} Data was unavailable.

TABLE 2. Maternal and neonatal clinical characteristics in the two periods of 2019 and 2020 in 6 provincial-level administrative divisions (PLADs) of China.

Characteristic		lubei		ngdong		eijing
N1 [¶]	P-2019	P-2020	P-2019	P-2020	P-2019	P-2020
l1 " lo. of prenatal exa		3,149	3,328	2,550	3,902	3,159
Mean (SD)	5.3 ± 2.5**	5.0 ± 2.0 ^{§, §§}	5.2 ± 2.5	5.4 ± 2.5 ^{§, §§}	15.0 ± 2.8	14.0 ± 3.1 ^{§, §§}
Median (IQR)	5 (4, 6.8) ^{††}	5 (4, 6) ^{§, ¶¶}	5 (3, 7)	5 (3, 7) ^{§, ¶¶}	15 (13, 17)	14 (13, 16) ^{§, ¶¶}
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
renatal eligible ex	aminations (> 5 times					
No	3,123 (94.6)	3,067 (97.4) ^{§, ***}	3,270 (98.3)	2,494 (97.8)	-	-
Yes	177 (5.4)	82 (2.6)	58 (1.7)	56 (2.2)	-	-
Missing	0 (0)	0 (0)	0 (0)	0 (0)	-	-
Delivery gestationa	l weeks					
Mean±SD	39.0 ± 1.3**	38.9 ± 1.3 ^{§, §§}	39.2 ± 1.4 **	39.0 ± 1.4 ^{§, §§}	39.11 ± 1.3	39.10 ± 1.4
Median (IQR)	39.0 (38.0, 40.0) ^{††}	39.0 (38.0, 40.0) ^{§,} ¶¶	39.3 (38.4, 40.1) ^{††}	39.1 (38.4, 40.0) ^{§,} ¶¶	39.3 (38.6, 39.9)	39.1 (38.6, 40.0
Missing `	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Caesarean section	(CS)					
No	1,738 (53)	1,449 (46) ^{§, ***}	2,483 (75)	1,761 (69) ^{§, ***}	2,273 (58)	1,804 (57)
Yes	1,562 (47)	1,700 (54)	845 (25)	789 (31)	1,629 (42)	1,355 (43)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Maternal death	. ,	• •	. ,		• •	` '
No	_†††	_	3,328 (100)	2,550 (100)	3,902 (100)	3,159 (100)
Yes	_	_	0 (0)	0 (0)	0 (0)	0 (0)
Missing	_	_	0 (0)	0 (0)	0 (0)	0 (0)
Stillbirth (%)			- (=/	- 1-/	- \=/	→ \ - /
No	3,293 (100)	3,143 (100)	3,326 (100)	2,549 (100)	3,900 (100)	3,155 (100)
Yes	7 (0)	6 (0)	2 (0)	1 (0)	2 (0)	4 (0)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
N2 [¶]				· ·		
N2 " Neonatal gender	3,293	3,143	3,326	2,549	3,900	3,155
Female	1,548 (47)	1,434 (46)	1,561 (47)	1,192 (47)	1,886 (48)	1,547 (49)
Male	1,745 (53)	1,709 (54)	1,765 (53)	1,356 (53)	2,014 (52)	1,608 (51)
Unknown	0 (0)	0 (0)	0 (0)	1,000 (00)	0 (0)	0 (0)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Neonatal weight (k		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mean±SD	9) 3.32 ± 0.4	3.33 ± 0.4	3.16 ± 0.4	3.17 ± 0.4	3.33 ± 0.4	3.32 ± 0.4
	3.30 (3.00, 3.60)	3.30 (3.00, 3.60)	3.10 (2.90, 3.40)	3.20 (2.90, 3.50)	3.35 ± 0.4 3.35 (3.08, 3.60)	3.32 ± 0.4 3.32 (3.08 3.60)
Median (IQR)		• • •	, ,	, ,		,
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Apgar score		88 80 . 0 08		24 . 22* 88		
1 min (SD)	8.7 ± 0.8	8.9 ± 0.6 ^{§, §§}	9.4 ± 0.6	9.4 ± 0.6*, §§	10 ± 0.4	9.9 ± 0.5
Missing	454 (14)	586 (19)	0 (0)	0 (0)	2 (0)	2 (0)
5 min (SD)	9.5 ± 0.6	9.4 ± 0.6 ^{§, §§}	10 ± 0.2	10 ± 0.2	10 ± 0.3	10 ± 0.3
Missing	447 (14)	583 (19)	0 (0)	0 (0)	2 (0)	2 (0)
10 min (SD)	9.5 ± 0.5	9.9 ± 0.4 ^{§, §§}	10 ± 0.1	10 ± 0.1	10 ± 0.4	10 ± 0.4
Missing	992 (30)	672 (21)	0 (0)	0 (0)	13 (0)	15 (1)
Preterm birth						
No	3,212 (98)	3,036 (97)*,***	3,180 (96)	2,399 (94) ^{†,***}	3,729 (96)	3,011 (95)
Yes	81 (2)	107 (3)	146 (4)	150 (6)	171 (4)	144 (5)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
ow birth weight						
No	3,235 (98)	3,083 (98)	3,194 (96)	2,434 (96)	3,788 (97)	3,049 (97)
Yes	58 (2)	60 (2)	132 (4)	115 (4)	112 (3)	106 (3)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Macrosomia						
No	3,093 (94)	2,923 (93)	3,239 (97)	2,467 (97)	3,728 (96)	2,977 (94)*, ***
Yes	200 (6)	220 (7)	87 (3)	82 (3)	172 (4)	178 (6)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
N3 [¶]	3,269	3,118	3,322	2,529	3,857	3,105
Small for gestation		-,	-,	_,	3,00.	5,.50
No	3,029 (93)	2,929 (94)*,***	2,898 (87)	2,310 (91) ^{§,***}	3,688 (96)	2,967 (96)
Yes	240 (7)	189 (6)	424 (13)	219 (9)	169 (4)	138 (4)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
_arge for gestation		- (-)	- (-)	- (-/	· (-)	- \-/
No	3,007 (92)	2,817 (90)*,***	3,179 (96)	2 404 (05)	3,531 (919)	2,811 (91)
No Yes	3,007 (92) 262 (8)	301 (10)	3,179 (96) 143 (4)	2,404 (95) 125 (5)	3,531 (919) 326 (9)	2,811 (91) 294 (9)
						, ,
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

TABLE 2. (Continued)

Characteristic	Shandong P 2020		Hebei Passa		Yunnan	
	P-2019	P-2020	P-2019	P-2020	P-2019	2020
N1 [¶] Number of prenatal e	3,879 examinations	2,449	2,280	1,361	1,952	968
Mean±SD	_	_	5.5 ± 3.0**	6.3 ± 2.8 ^{§, §§}	11.5 ± 2.6	11.6 ± 2.4
Median (IQR)	_		6 (2, 8) ^{††}	7 (4, 8) ^{§, ¶¶}	11 (10, 13)	12 (10, 13)
Missing	_	_	0 (0)	0 (0)	0 (0)	0 (0)
Prenatal eligible exar	minations (>5 times)		0 (0)	0 (0)	0 (0)	
No	-	-	1,606 (70.4)	960 (70.5)	779 (39.9)	249 (25.7) ^{§, ***}
Yes	-	-	674 (29.6)	401 (29.5)	1,173 (60.1)	719 (74.3)
Missing	-	-	0 (0)	0 (0)	0 (0)	0 (0)
Delivery gestational v						
Mean±SD	39.2 ± 1.3	39.2 ± 1.3	39.1 ± 1.4	39.2 ± 1.5	39.0 ± 1.4	38.9 ± 1.4
Median (IQR)	39.3 (38.6, 40.1)	39.3 (38.6, 40.1)	39.3 (38.6, 40.0)	39.3 (38.6, 40.0)	39.0 (38.3, 40.0)	39.0 (38.0, 40.0)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Caesarean section	4.047 (50)	4.050 (54)	4 004 (00)	000 (00)	4 400 (74)	000 (70)
No Yes	1,947 (50)	1,256 (51)	1,381 (60)	808 (60)	1,439 (74)	693 (72)
res Missing	1,932 (50) 0 (0)	1,193 (49) 0 (0)	899 (40) 0 (0)	552 (40) 1 (0)	512 (26) 1 (0)	274 (28) 1 (0)
Maternal death	0 (0)	0 (0)	0 (0)	i (U)	1 (0)	1 (0)
No	3,879 (100)	2,449 (100)	2,280 (100)	1,359 (100)	1,748 (100)	909 (100)
Yes	0 (0)	0 (0)	0 (0)	2 (0)	1,740 (100)	1 (0)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	203 (10)	58 (6)
Stillbirth (%)	- (=/	- (-/	- (-/	- (-/	(/	\-/
No	3,879 (100)	2,449 (100)	2,277 (100)	1,360 (100)	1,946 (100)	965 (100)
Yes	0 (0)	0 (0)	3 (0)	1 (0)	6 (0)	3 (0)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
N2 [¶]						
Neonatal gender	3879	2449	2277	1360	1946	965
Female	1,889 (49)	1,166 (48)	1,096 (48)	658 (48)	930 (48)	450 (47)
Male	1,988 (51)	1,282 (52)	1,181 (52)	702 (52)	1,016 (52)	515 (53)
Unknown	2 (0)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
leonatal weight (kg)	· /	· /	()	· /	` '	()
Mean±SD	3.40 ± 0.4	3.40 ± 0.4	3.33 ± 0.5	3.32 ± 0.5	3.23 ± 0.5	3.22 ± 0.4
Median (IQR)	3.40 (3.10, 3.70)	3.40 (3.10, 3.70)	3.30 (3.00, 3.60)	3.30 (3.00, 3.60)	3.20 (3.00, 3.50)	3.20 (3.00, 3.50)
Missing	0 (0)	1 (0)	8 (0)	12 (1)	0 (0)	0 (0)
Apgar score						
1 min	_	_	9.9 ± 0.4	9.9 ± 0.4	9.3 ± 1.4	9.5 ± 1 ^{†, §§}
Missing	-	-	110 (5)	17 (1)	1 (0)	0 (0)
5 min	_	_	10 ± 0.3	10 ± 0.3	9.8 ± 1.2	9.9 ± 0.7 ^{†, §§}
Missing	-	-	110 (5)	17 (1)	1 (0)	0 (0)
10 min	_	_	10 ± 0.3	10 ± 0.1	9.8 ± 1.2	9.9 ± 0.8*, §§
Missing	_	_	110 ± 0.3	17 (1)	1 (0)	0 (0)
Preterm birth			(-/	,	. (-/	- (-/
No	3,710 (96)	2,359 (96)	2,174 (95)	1,293 (95)	1,845 (95)	929 (96)
Yes	169 (4)	90 (4)	103 (5)	67 (5)	101 (5)	36 (4)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
ow birth weight						
No	3,790 (98)	2,397 (98)	2,199 (97)	1,312 (97)	1,863 (96)	934 (97)
Yes	89 (2)	51 (2)	70 (3)	36 (3)	83 (4)	31 (3)
Missing	0 (0)	1 (0)	8 (0)	12 (1)	0 (0)	0 (0)
Macrosomia				4.000 (0.1)	4 00 4 (00)	
No	3,540 (91)	2,252 (92)	2,117 (93)	1,266 (94)	1,864 (96)	932 (97)
Yes	339 (9)	196 (8)	152 (7)	82 (6)	82 (4)	33 (3)
Missing	0 (0)	1 (0)	8 (0)	12 (1)	0 (0)	0 (0)
N3 [¶]	3877	2448	1844	1138	1900	953
Small for gestational		0.054 /05:	4 === 45=:	4.0=0.40=:	. = . =	
No	3,720 (96)	2,351 (96)	1,759 (95)	1,078 (95)	1,717 (90)	875 (92)
Yes	155 (4)	95 (4)	85 (5)	60 (5)	183 (10)	78 (8)
Missing	2 (0)	2 (0)	0 (0)	0 (0)	0 (0)	0 (0)
arge for gestational		2 127 (07)	1 640 (00)	1.020 (04)	1 702 (04)	000 (04)
	3,358 (87)	2,137 (87)	1,648 (89)	1,038 (91)	1,783 (94)	900 (94)
No Yes	517 (13)	309 (13)	196 (11)	100 (9)	117 (6)	53 (6)

Abbreviations: P-2019, January 1-May 31, 2019 as the pre-pandemic period; P-2020, January 1-May 31, 2020 as the pandemic period. P<0.05;

[†] *P*<0.01;

[§] *P*<0.001;

[¶] N1: number of the total subjects, N2: those N1 without delivering stillbirths; and N3: those N2 delivering fetuses at gestational weeks 24-42 and without major birth defects;

^{**} Mean value ± standard deviation (SD);

^{††} Median value (25%–75% percentile);

^{§§} Compared by *t* test;

Compared by Nest,
Compared by Mann-Whitney U test;
Compared by Chi-square test;
Data are unavailable.

TABLE 3. Adjusted relative risk associated with the occurrence of the COVID-19 between 2019 and 2020 in 6 provincial-level administrative divisions (PLADs) of China.

Characteristics	Hubei	Guangdong	Beijing
NPE ^{¶, §§}	0.95 (0.92, 0.99)†	1.03 (1.00, 1.07)	0.99 (0.96, 1.02)
PEE5**, §§	0.49 (0.37, 0.64) [§]	1.22 (0.84, 1.76)	-
DGW ^{††, §§}	-0.15 (-0.22, -0.08) [§]	-0.16 (-0.23, -0.08)§	0 (-0.02, 0.02)
CS**, §§	1.11 (1.06, 1.17) [§]	1.17 (1.08, 1.27) [§]	1.02 (0.97, 1.08)
NW ^{††, §§}	0 (-0.02, 0.02)	0.01 (-0.01, 0.03)	-0.01 (-0.07, 0.05)
Stillbirth**, §§	0.88 (0.30, 2.63)	1.5 (0.09, 24.47)	2.43 (0.44, 13.28)
Preterm birth**, §§	1.37 (1.02, 1.84)*	1.34 (1.07, 1.67)*	1.03 (0.83, 1.28)
LBW ^{**,} §§	1.08 (0.75, 1.58)	1.18 (0.92, 1.51)	1.16 (0.89, 1.50)
Macrosomia**, §§	1.10 (0.91, 1.34)	1.18 (0.87, 1.59)	1.26 (1.03, 1.55)*
SGA**, §§	0.81 (0.67, 0.98)*	0.71 (0.60, 0.83) [§]	1.01 (0.81, 1.25)
LGA**, §§	1.17 (0.99, 1.38)	1.10 (0.87, 1.39)	1.11 (0.96, 1.29)
Characteristics	Shandong	Hebei	Yunnan
NPE ^{¶, §§}	_	1.08 (1.03, 1.13)§	1.0 (0.96, 1.05)
PEE5**, §§	-	0.96 (0.82, 1.12)	1.97 (1.65, 2.34)§
DGW ^{††, §§}	-0.02 (-0.09, 0.05)	0 (-0.11, 0.1)	-0.13 (-0.23, -0.02)
CS**, §§	0.99 (0.94, 1.04)	0.99 (0.92, 1.07)	1.05 (0.93, 1.19)
$NW^{\dagger\dagger,\S\S}$	-0.01 (-0.03, 0.02)	-0.02 (-0.06, 0.01)	-0.01 (-0.04, 0.03)
Stillbirth**, §§	-	0.58 (0.06, 5.55)	0.66 (0.13, 3.31)
Preterm birth**, §§	0.85 (0.64, 1.11)	1.01 (0.72, 1.42)	0.73 (0.50, 1.06)
LBW ^{**,} §§	0.98 (0.67, 1.43)	0.75 (0.48, 1.18)	0.77 (0.51, 1.16)
Macrosomia**, §§	0.88 (0.73, 1.06)	0.86 (0.65, 1.14)	0.83 (0.56, 1.24)
SGA**, §§	0.98 (0.74, 1.30)	1.13 (0.82, 1.55)	0.87 (0.67, 1.12)
LGA**, §§	0.93 (0.81, 1.08)	0.82 (0.65, 1.03)	0.87 (0.63, 1.19)

Abbreviations: NPE, No. of prenatal examinations; PEE5, Prenatal eligible examinations of ≥5 times; DGW, delivery gestational weeks; CS, Caesarean section; NW, Neonatal weight; LBW, low birth weight; SGA, small for gestational age; LGA, large for gestational age.

of preterm birth in Hubei and Guangdong, it increased regardless of their higher CS rates. According to clinical practices, women with preterm birth usually had certain pregnancy complications. Though, the routine NPE had been maintained during the pandemic period in China, the prenatal care quality could not be ensured. It is speculated that certain pregnancy complications, drug misuse, or abnormal syndromes may not be treated as usual, which can trigger preterm birth. Therefore, special in-time prenatal examinations should be provided to improve prenatal care quality with certain pregnancy complications when a pandemic occurs in future.

The results of this study were subject to some limitations. First, this study only included 11 county-level study settings in 6 PLADs to represent a nationwide survey. Second, the asymptomatic infection cases were not excluded by the RNA test. However, we employed a population-based monitoring system by HMCCH with high-quality data. Also, the prevalence rate of asymptomatic infections in China had been at a very low level to 10^{-6} – 10^{-4} (10), which does not affect our statistical results for the non-infected pregnant women. In summary, prenatal examinations proceeded as normal and most maternal and neonatal clinical characteristics were within normal ranges. It should be

^{*} *P*<0.05; † *P*<0.01;

[§] P<0.001;

[¶] Relative risk calculated by Poisson regression model;

^{**} Relative risk calculated by log-binomial regression model;

^{††} Regression coefficient (β value) calculated by linear regression model;

^{§§} Adjusted for BMI (categorical), age (categorical), parity, gravidity, ethnicity, and education. For Hubei Province, parity information is unavailable. For Beijing, the information of BMI, ethnicity, and education is unavailable.

noted that the prenatal care quality may be reduced due to limitations in medical resources. Only specific interventions were additionally required to protect pregnant women with pregnancy complications living in regions with a high burden of COVID-19 pandemic.

Psychological counseling and transfer treatment channel should be strengthened for those at high risk during lockdown. For example, online psychological counseling can be used as a good auxiliary method during severe pandemic conditions.

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Outbreak Reports

An Investigation of a Confirmed Imported Case of COVID-19 Infected Abroad — Qingpu District, Shanghai Municipality, China, November 15, 2020

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Summary

What is already known about this topic?

A passenger who was from the United States was taken to the hotel for the required isolation on November 13, 2020. During the quarantine she was diagnosed as the COVID-19 patient on November 15, 2020. Controlling the importation of COVID-19 remains a major challenge.

What is added by this report?

In this study, an epidemiological investigation was conducted for a confirmed case of COVID-19, including the treatment records in the hospital and 14-day travel trajectory before the onset of disease.

What are the implications for public health practice?

This study described an epidemiological investigation and management process on an imported case of COVID-19 and analyzed the test results, aiming to provide useful warnings to strengthen the capacity of public health system in response to the importation.

It has been nearly 1 year since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, the pathogen of which has been identified as COVID-19 virus (also known as SARS-CoV-2, 2019-nCoV, or HCoV-19) (1–2). The spread of the virus has led to a global health crisis (3). China has taken effective measures to suppress COVID-19. However, it still faces a huge challenge of detecting and dealing with imported cases (4).

This investigation was for an imported case that was detected on November 15, 2020 by Qingpu CDC, Shanghai. With the detection of this case, one of the most important tasks was an epidemiological investigation that could provide key information for screening close contacts of this case. The case was promptly sent for isolation and treatment, and the close contacts were sent to an isolated place for active and effective medical observation. The results of this

investigation might benefit future surveillance efforts and mitigate the risk caused by the imported cases.

INVESTIGATION AND FINDINGS

On November 15, 2020, a Chinese traveler returned to Shanghai Municipality from the United States with symptoms such as cough, sputum, and sore throat. This patient then went to the Qingpu Branch of the Zhongshan Hospital Affiliated to Fudan University Zhongshan Hospital) for (Qingpu consultation. Based on the results of routine test for COVID-19, the nasal swab test was positive. Qingpu CDC subsequently used a fluorescent RT-qPCR (probe method) to verify the results. The ORF1a/b and N gene nucleic acid tests of COVID-19 were all positive in the nasal swab, throat swab, and sputum specimens. The case was then transferred to the Shanghai Public Health Clinical Center (SPHCC) and confirmed again.

This case occurred in an 18-year-old female international student with Chinese nationality, returning to China with her mother by flight. According to her description, she studied at a university in the United States from August 2019 to November 2020. To confirm the accuracy, we conducted separate epidemiological investigations on her and her mother from October 30 to November 13, 2020. The relevant epidemiological history of the case was shown in Figure 1.

According to the description of the patient and her mother, from October 30 to the noon of October 31, they did a yard sale at home and had contact with more than 50 people (some of the customers did not wear masks). During the period, the case only did business alone for about 1 hour (about 15–18 individuals in contact with her, half of whom did not wear masks) in the morning of October 30. Due to about 1.5 hours online lessons at home in the afternoon on the October 30, the patient did not

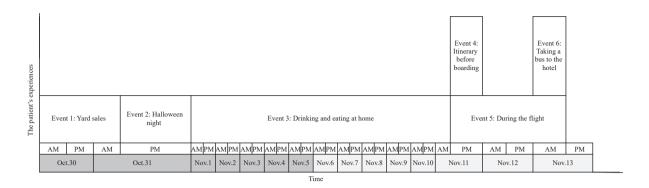


FIGURE 1. The patient's experiences during the two weeks before being detected with COVID-19 infection (according to self-reports from patient).

participate in sales. Except for the above 2 periods, both were selling together (had contact with approximately 20 people). They were close to customers (about 1 meter) every time they made sales including the sales the patient made alone. Because of Halloween, both were at home from noon to night on October 31. During the period, the case received 4 visitors (both the visitors and the patient wore masks and did not have prolonged contact with each other).

From November 1 to 11, except for moving things to the new house, the patient and her mother were at home. Usually, the daily necessities were purchased (once a week) by an American friend who was the only person that had frequent contact during the 14-day investigation. On the afternoon of November 11, the friend drove them to the airport. Before entering the waiting hall, they had a meal at a restaurant near the airport, and there were a few customers and waiters wearing masks in the restaurant. When waiting at the terminal of the airport, the patient sat next to her mother (no people on either side of the seat, and few people around). They wore masks (except drinking water) all the time and did not go to the bathroom. However, the patient spent about 5 minutes to buy two bottles of water at the airport.

From the evening of November 11 (Pacific Standard Time) to the early morning of November 13 (Beijing Time), both the patient and her mother ate three times on the plane and drank water several times with no masks. However, the patient went to the bathroom 7–8 times (the patient reported that the bathroom environment was messy in the middle and late stages of the trip) and washed her face 1–2 times during the flight. Although the plane had stopped in Seoul City, Korea, no passengers boarded or exited. After the plane arrived in Shanghai Municipality, the patient and her mother were tested by PCR assay at the airport and took a bus with 20 other passengers who wore masks to the designated medical observation point for isolation.

The patient and her mother had undergone a series of tests. Before the patient was diagnosed, the antibody test and CT test were performed once (the first antibody test results showed that IgM and IgG were negative and the CT results were normal), and nucleic acid tests were performed four times (the result at airport customs was negative, while the results at Qingpu Zhongshan Hospital, Qingpu CDC, and the SPHCC were all positive). The test results of the patient during the detection period (performed by Qingpu Zhongshan Hospital), the treatment period (performed by SPHCC), and the 14-day isolation period (performed by Qingpu CDC) were shown in Figure 2. However, until the end of the isolation, her mother had been underwent nucleic acid tests three times (November 13, 17, and 25) and all results were negative.

PUBLIC HEALTH RESPONSE

Qingpu CDC immediately reported the case information to Shanghai CDC as soon as confirmed and the corresponding treatment measures for the patient were also actively implemented. The Shanghai CDC tracked the handling of the incident, promptly checked the patient's close contacts on the flight and soon after arriving in Shanghai. According to the rules and requirements for determining and tracking the close contacts established by the China CDC, a total of 25 close contacts (including her mother) were isolated and placed under medical observation. During the 14-day quarantine, all close contacts underwent nucleic acid tests twice, and all showed negative results.

DISCUSSION

There is an incubation period in COVID-19

infection before symptoms appear. The incubation period is normally from 1 to 14 days, mostly 3 to 7 days (5–6). After the incubation period, some infectees will show clinical symptoms. During the incubation period, the infected person has no symptoms but has a certain level of contagiousness. If appropriate isolation is not carried out, the infectee will become a potential reservoir of the infection. Therefore, during the epidemic, in order to counter the spread of COVID-19 infections, the government should require all people with a clear epidemiological contact history to self-quarantine for 14 days (7).

We conducted an epidemiological investigation on the case from November 15 to 16. Based on the self-reported travel experience of the patient and her mother and the isolation status of other passengers, we had made the following inferences about the possibility of the patient being infected with COVID-19, as shown in Table 1. Based on the investigation, we inferred that this case was most likely infected with COVID-19 during the yard sale event in the United States. The guests on Halloween night may also be a possible source of transmission. In addition, the potential risk of being infected while waiting for the

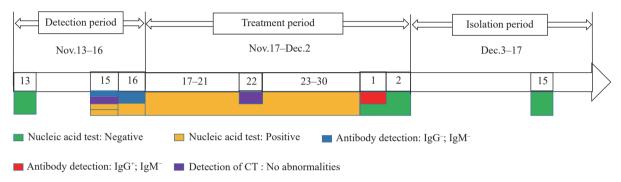


FIGURE 2. The test results of the patient during detection, treatment, and the 14-day isolation observation period in Qingpu District, Shanghai Municipality.

TABLE 1. The potential routes and risk levels of the patient's COVID-19 infection at different events during the transition from US to China.

Investigation	Events	Reason	Risk level
	1	The patient contacted many customers alone for about 3–4 minutes and half of the customers did not wear a mask, but the patient wore a mask.	Extremely high
	2	The patient entertained 4 visitors alone during Halloween and opened the door twice. But the visitors did not enter the door and both the patient and the visitors wore masks.	Medium
	3	Neither the patient's mother nor American friends had symptoms.	Low
First investigation*	4	The patient basically stayed with the mother and wore masks, but she spent about 5 minutes buying 2 bottles of water when waiting for the flight.	Medium
	5	The patient went to the bathroom about 7–8 times and took off the mask 1–2 times in the bathroom to wash her face. The patient reported that the bathroom environment was messy in the later stages of the flight.	High
	6	All passengers had no abnormal symptoms. The patient and other passengers wore masks.	Low
	1	As mentioned in the first investigation.	Extremely high
	2	As mentioned in the first investigation.	Medium
Follow-up	3	End of the 14-day quarantine period, the mother's nucleic acid test was negative. The friend had not shown any signs.	Very low
investigation [†]	4	As mentioned in the first investigation.	Medium
ŭ	5	The nucleic acid tests of other passengers on the flight were negative. After the 14-day quarantine period, no other positive cases of the flight.	Very low
	6	After the 14-day quarantine period, no other positive cases were found among the passengers on the bus	Very low

^{*}The basis for judgment: the epidemiological survey report from November 15 to 16.

[†] The basis for judgment: on November 27, the passengers of this flight had met the 14-day quarantine and were discharged.

flight cannot be ruled out. The risk of infection for other passengers on the flight increased due to the presence of asymptomatic infections. The possibility of infection in the aircraft could also be nonnegligible depending on the flight range, in which a longer period of flight would increase the risk of transmission. For example, the toilets on the aircraft become humid and messy when used by many people, which might create conditions for the transmission. The toilet space on the plane was slightly narrow, which greatly increased the risk of infection during the prolonged flight. The investigator stated that she had visited the bathroom many times during the flight. In this investigation, all the other passengers on the flight were not positive during the 14-day quarantine period, and there had been no reports of related infections since then. However, this reminds us that the "toilet incident" might be a loophole of prevention and control on the airplane that is worth taking appropriate countermeasures for. For example, disinfection supplies should be equipped in the toilets of the aircraft and warning signs should be posted in the corresponding places to remind passengers to disinfect appropriately.

The laboratory diagnosis of this case indicated that comprehensive judgment based on clinical and test results was important. Except for nucleic acid detection, the detection of antibodies (8) and CT scans (9) played an important role in the determination of COVID-19. The first two tests for antibodies (IgG and IgM) of the patient were negative, which suggested that the patient was in an early stage of onset. The results of the first CT scan could also be verified accordingly. However, the positive test results of the ORF1a/b and N genes of COVID-19 in the sputum specimen of this patient indicated that the subject had the ability to spread the virus. On the seventh day in the SPHCC, the results of the CT scan of the patient were also normal, which might be due to early case detection and treatment. In addition, monitoring and management during isolation were also of great importance. The patient recovered after 17 days of treatment. In order to ensure safety, the subject was quarantined for another 14 days. This person has since been discharged from isolation.

So far, COVID-19 is still raging around the world. With the large-scale resumption of work and production of Chinese enterprises, the prevention and control of COVID-19 are still facing huge challenges

from imported cases and locally sporadic cases caused by the imported cases or cold chain transport (10). An efficient multisectoral collaboration mechanism and a sensitive surveillance and response system will greatly contribute to prevention and control of the COVID-19.

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Outbreak Reports

COVID-19 Super Spreading Event Amongst Elderly Individuals — Jilin Province, China, January 2021

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Summary

What is already known on this topic?

Clusters of COVID-19 cases often happened in small settings (e.g., families, offices, school, or workplaces) that facilitate person-to-person virus transmission, especially from a common exposure.

What is added by this report?

On January 10 and 11, 2021, an individual gave three product promotional lectures in Tonghua City, Jilin Province, that ultimately led to a 74-case cluster of COVID-19. Our investigation determined the outbreak to be an import-related COVID-19 superspreading cluster event in which elderly, retired people were exposed to the infected individual during his promotional lectures, which were delivered in a confined space and lasted several hours.

What are the implications for public health practice?

Routine activities, such as attending a lecture in a classroom, can provide an environment conducive to COVID-19 superspreading events because respiratory viruses can spread easily and widely. We suggest local government to strengthen infection management, reduce unnecessary indoor large gathering activities, and promote wearing of masks, especially during wintertime in the north of China. Health education for elderly people should promote use of effective personal protection and emphasize the importance of wearing masks.

On January 10, 2021, 4 people from Wangkui County, Suihua City, Heilongjiang Province returned to Jilin Province. They tested positive for coronavirus disease 2019 (COVID-19) and subsequently caused an outbreak in Tonghua City of Jilin Province (1). On January 11, Jilin Province initiated their COVID-19 prevention and control emergency plan. China CDC and Jilin CDC jointly conducted an epidemiological investigation and traced the outbreak. Based on the findings of the investigation, Dongchang District was

locked down to help stop virus transmission starting from January 20.

INVESTIGATION AND RESULTS

Through January 31, 2021, there have been about 140 cases associated with the same case (called Mr. L in this report), showing Mr. L to be a super spreader.

Mr. L, a 44-year-old male, is a product promotion lecturer who travels often. From December 23, 2020 to January 3, 2021, Mr. L traveled by train and plane in Shandong, Shanxi, Henan, and Heilongjiang provinces; from January 3 to 6, Mr. L traveled by train inside Heilongjiang Province; and on January 7, he traveled through Jilin Province by train to Changchun City. From January 9 to 12, Mr. L lived in Tonghua City and hosted product promotion training courses, dining in small restaurants, and having external contact. Mr. L took the K350 train on January 5, traveling in a seat adjacent to 2 of the aforementioned 4 confirmed cases from Wangkui County. He arrived in Tonghua on January 9 and conducted 3 training activities in the following 2 days. At noon on January 10, due to muscle pain and other symptoms, Mr. L went to a pharmacy (his body temperature was in the normal range when measured at the pharmacy) (Figure 1)

On January 10 and 11, Mr. L gave 3 lectures in Location A of Tonghua City, with each lecture lasting about 2.5 hours. The classroom of Location A was about 30 square meters and had doors and windows closed. Mr. L did not wear a mask during the 3 lectures. A total of 97 (40, 31, and 26) participants took part in the 3 lectures. Most participants were retirees; 61% (59/97) were female; and the median age was 72 years (60 to 87 years). By January 31, 76% (74/97) of the participants were tested positive. The attack rates in the 3 lectures were 90% (36/40), 90% (28/31), and 38% (10/26). In addition, Mr. L infected at least 7 other contacts, including 5 employees at Site A (Ms. D, in an hotel room next to Mr. L's room; and

Ms. E, an employee at the restaurant that Mr. L visited twice). Infected close contacts of Mr. L spread the virus during dinners, other lectures, shopping, and playing mahjong, etc. There were more than 30 infections by the close contacts of Mr. L. In summary, until January 31, Mr. L directly infected 81 close contacts (first-generation cases) and indirectly infected at least 60 close contacts of the contacts (second-generation and

third-generation cases) in Dongchang District of Tonghua (Figure 2).

On January 10, Jilin CDC sequenced the virus isolated from the first batch of pharyngeal swab samples from the original imported cases from Wangkui County, Suihua City, Heilongjiang Province. On January 12, the sequencing data were delivered to China CDC for whole genome sequencing. The 4

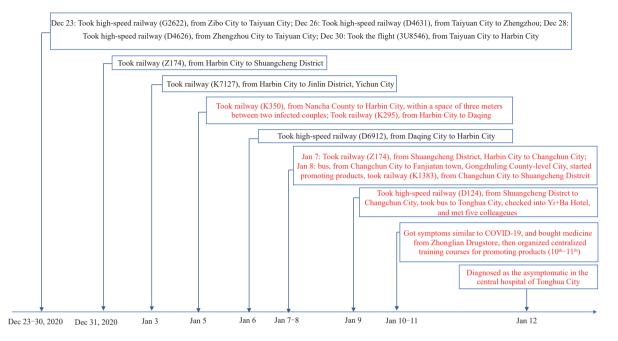


FIGURE 1. Movement of Mr. L from December 23, 2020 to January 12, 2021.

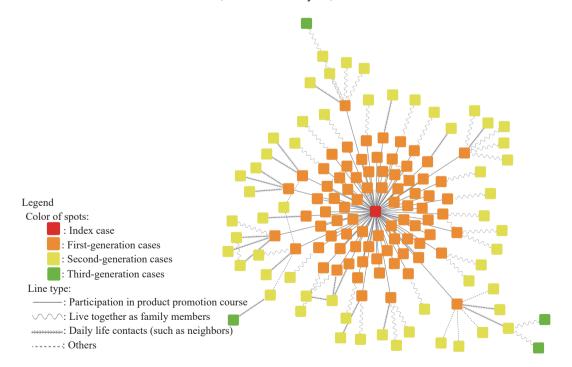


FIGURE 2. Three generations of infection from index case, Mr. L from January 12 to January 31, 2021.

genome samples belonged to the L-genotype of the European I branch (b.1.1) and shared 12 nucleotide mutations with the first case of the December 2020 Dalian outbreak and the January 2021 Wangkui outbreak. On January 16, Jilin CDC provided a second batch of 11 samples (including Mr. L's sample) to China CDC for whole sequencing analysis. The sequences of the two batches were highly homologous and belonged to the same transmission chain.

DISCUSSION

The epidemic in Tonghua City was detected early but developed rapidly. The outbreak was directly related to Mr. L, and had a clear intergenerational transmission relationship.

Most of the individuals in the outbreak were retired elders from small and medium-sized cities. The joint epidemiological investigation found that these individuals lived a somewhat sedate lifestyle, had a similar socioeconomic level, and were eager to participate in external activities. They took free buses to other locations, greatly expanding their geographic range for activities. Because the course participants were elderly, the outbreak had a high proportion of severe and critical cases. By the end of January, 47 severe or critical cases were reported, accounting for 15.2% of the total cases, including 1 death of an 87-year-old person on January 25, 2021.

Three major factors contributed to this outbreak: First, Mr. L had muscle pain and visited a pharmacy on January 10 to obtain medication. This indicated that Mr. L was likely at an early stage of disease when holding lectures on January 10 and January 11. Early stage illness is believed to be most infectious (2). Second, most of the participants in his classes were elderly, with a median age of 72 years. The classes lasted long and were held in a small, confined space. Third, personal protection was not utilized, and social distancing were not maintained. The classroom was crowded, with about 30 people in a 30 square meters space. Mr. L and many participants did not wear masks during class. The outbreak was relatively confined, and no new virus strains were identified through genetic sequencing. This investigation showed, therefore, that there was no evidence of increased virulence or transmission.

In winter, the life of retired people in the north can be sedate and routine. Participating in educational events is an attractive activity. Thus, imported viruses can spread easily and widely. We suggest that local governments strengthen infection control management and reduce unnecessary indoor large gathering activities during wintertime, especially in the north of China. Health education for elderly people should be strengthened to promote use of effective personal protection.

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Outbreak Reports

Local Outbreak of COVID-19 in Shunyi District Attributed to an Asymptomatic Carrier with a History of Stay in Indonesia — Beijing Municipality, China, December 23, 2020

COVID-19 Epidemiology Investigation Team¹; Laboratory Testing Team¹; Wenzeng Zhang^{1,#}

Summary

What is known about this topic?

Patients with coronavirus disease 2019 (COVID-19) infection can be categorized by severity: asymptomatic infection, mild illness, moderate illness, severe illness, and critical illness. The rate of transmission to a specific group of contacts (the secondary attack rate) may be 3–25 times lower from people who are asymptomatically infected than from those with symptoms. The incubation period is 2–14 days.

What is added by this report?

An individual with asymptomatic infection shed live virus that started a 42-case outbreak in Shunyi District of Beijing in December 2020. The individual had been quarantined for 14 days in a designated quarantine hotel in Fuzhou after entering China from Indonesia. During quarantine, he had 5 negative throat swab tests and 2 negative IgM serum tests. The investigation team determined that the incubation periods of 31 confirmed cases ranged from 2 to 23 days.

What are the implications for public health practice?

The frequency of nucleic acid testing should be increased for international entrants and people who are close contacts of confirmed COVID-19 cases. The investigation team recommend expanding sample types for nucleic acid testing to include anal swabs and residential environmental sampling; serum antibody testing can be used as a reference indicator. Parallel testing by two institutions at key points in time, such as the end of isolation, should be implemented.

As of December 22, 2020, no local cases of coronavirus disease 2019 (COVID-19) had been reported from Shunyi District of Beijing for 319 days. On December 23, the Shunyi District CDC received a report of a confirmed COVID-19 case, and another case was reported 2 days later. By January 31, 2021, 42 cases had been reported in Shunyi — a confirmed, local COVID-19 outbreak.

Shunyi CDC immediately launched an epidemiological investigation with laboratory testing to identify the source of infection, determine routes of transmission, assess the scale of the outbreak, and provide recommendations for stopping the outbreak and preventing recurrence. The investigation showed that all confirmed COVID-19 cases were associated with an asymptomatic carrier who was an international traveler from Indonesia. The investigation serves as a reminder that the government should pay attention to asymptomatic infections in our COVID-19 prevention and control strategies, including international entrant screening policies and practices.

INVESTIGATION AND RESULTS

At 05:08 on December 23, 2020, the index case of this local outbreak (Patient A) was reported to Shunyi CDC as a confirmed COVID-19 infection. Shunyi CDC conducted in-person interviews with a detailed questionnaire that used China CDC definitions for suspected and confirmed COVID-19 cases (*1*–2). A series of response measures were implemented but contact tracing did not immediately lead to source identification.

At 05:30 on December 25, 2 days later, a second case (Patient B) was reported to Shunyi CDC. Patient B had nausea, sore throat, and dizziness at 18:00 on December 16, but did not seek medical attention at that time. An investigation found that Patient B had a roommate who was a 28-year old Indonesian man who had returned from Indonesia on November 26. The person from Indonesia had entered China at Fuzhou Airport; en route, he sat in seat 60L; a nearby passenger in seat 60J was later confirmed as a COVID-19 case. Because he was a close contact of a confirmed case, the person from Indonesia was required to be in medical quarantine from November 26 to December 10. During quarantine, five consecutive COVID-19 nucleic acid tests and two consecutive virus-specific

antibodies tests were performed; all tests were negative.

After completing the 14-day quarantine, the individual from Indonesia travelled from Fuzhou to Beijing, arriving at 00:05 on December 11. He rented an apartment that day in a community in Shunyi District through a housing agency; there were four others in the apartment. One of the other four was Patient B.

From December 12 to 20, the person from Indonesia was required to conduct quarantine at the apartment, but he did not strictly abide by the quarantine regulations. During this period, he went to malls, supermarkets, and restaurants. At 15:17 on December 13, he went to Hualian Mall and returned to the rental unit at 16:51. Two people with whom he had close contact in Hualian Shopping Center became Patient C (a salesperson in the mall) and Patient D. Further investigations revealed that Patient A had close contact with Patient C while at Hualian Shopping Center on December 17.

From December 21 to 24, the person from Indonesia took the subway to work at a company in Wangjing, Chaoyang District around 09:00 every day and took the subway back to the apartment after getting off work around 19:00, arriving home around 20:00. He stated that he was wearing a disposable mask during shopping and work. Between December 10 and 24, no throat swabs or serum specimens from this person were obtained.

At 09:28 on December 25, the person from Indonesia was determined to be a close contact of Patient B and was transferred to a hotel designated for

medical quarantine at 15:14. Throat swabs and serum specimens were collected and tested for viral nucleic acids and virus-specific antibodies respectively. Sera tested positive for IgM and negative for IgG specific to the COVID-19 virus.

At 14:30 on December 27, the person from Indonesia was transferred to Beijing Ditan Hospital for further diagnosis and treatment. On December 28, his throat swab and stool specimens were positive for COVID-19, with cycle threshold (Ct) values of 39.0/37.0 (ORF1ab/N), and 24-28/24-28. At 22:00, he was diagnosed as an asymptomatic COVID-19 carrier (Patient E).

Between December 10, 2020 and January 31, 2021, 42 COVID-19 cases were identified and linked to this outbreak. Starting on December 25, the number of cases significantly increased, reaching a peak on December 27 and 28 (Figure 1).

The 42 cases involved 5 generations of infection - 1 case in the first generation (Patient E), 3 in the second generation, 13 in the third generation, 22 in the fourth generation, and 3 in the fifth generation. The second-generation cases were infected when living together or during close contact in a shopping mall with Patient E. Among the second-generation cases, one resided with Patient E and the other two were close contacts of Patient E in the Hualian Mall on December 13. The third-generation cases were infected when living together or traveling in cars, or when in close contact with second-generation cases in the mall. The fourth and fifth generation cases were infected when eating or working with cases.

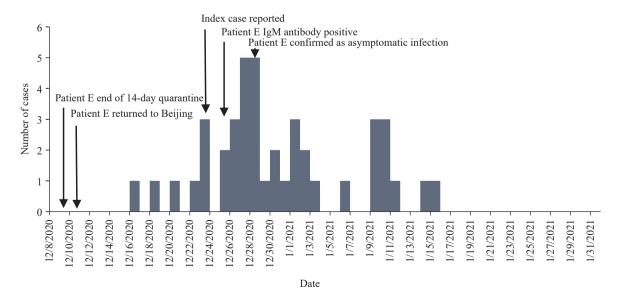


FIGURE 1. Epidemiological curve of a local outbreak of COVID-19 in Shunyi District, Beijing, 2020–2021.

According to our epidemiological investigation, 31 of the 42 outbreak cases had clear last exposure times. Based on data from these 31 cases, we calculated the median incubation period to be 5 days, with a range of 2 to 23 days.

In total, 41 cases were reported from Shunyi District, and 1 was reported from another district in Beijing. The median age was 32 years (8 months – 62 years); the male: female ratio was 1.6:1; 18 (42.9%) were workers, and 8 (19%) were unemployed. There were no severe or critically ill cases. Overall, 24 cases (57.1%) were moderate illness, 10 (23.3%) were mild illness, and 8 (18.2%) were asymptomatic. Except Patient E, the remaining 7 cases of asymptomatic infection were confirmed by the test results of throat swabs or anal swabs for COVID-19 (Table 1).

The investigation for Patient E obtained 203 environmental specimens during December 26 and 27, including 21 samples from the apartment, among which 9 tested positive for COVID-19 virus, and 183 samples from the workplace, among which 5 were positive and 1 was indeterminate.

Full-length genome sequences were determined for 14 specimens from people, including Patient E, and 5 environmental samples (2 were from the apartment and the workplace of Patient E). Sequence alignment and phylogenetic analyses showed that all 19 strains were highly homologous, with similarities over 99.993% and having only 1–2 sites with nucleotide variations. The strain that caused this local outbreak of COVID-19 in Shunyi District belonged to the L-Lineage European Branch 2.3 (B.1.160.3) and has high homology with COVID-19 strains found in Southeast Asia during the same period.

Ultimately, Shunyi CDC identified asymptomatic

Patient E as the source of infection for this outbreak in Shunyi District.

PUBLIC HEALTH RESPONSE

Shunyi CDC conducted face-to-face interviews with all confirmed cases to ascertain and record their activities during the 14 days before onset of symptoms or positive nucleic acid tests. Contact times (exposure times) between cases were evaluated and incubation were calculated. Close contacts had been advised to quarantine themselves at designated hotels for 21 days and at home for 7 days, with daily check-in by medical staff and body temperature readings twice daily. Contacts developing fever or respiratory symptoms were transferred immediately to designated medical institutions for diagnosis and treatment, if needed. Throat swabs, anal swabs, and serum specimens were obtained from all subjects, close contacts, and other key individuals. Environmental samples from the patient's residence, workplace, and points visited during the four days before illness onset or positive nucleic acid testing were obtained and tested (3). Parallel testing of samples by two institutions at key time points were implemented. Social distancing measures, discouragement of mass gatherings, mass testing of the entire population, closed management of the community where the COVID-19 cases were located, and health code scanning and registration of people entering public places had also been strictly implemented.

DISCUSSION

The results of this outbreak investigation remind us

TABLE 1. The first sampling and testing results of 8 cases of asymptomatic infection of a local outbreak of COVID-19 in Shunyi District, Beijing, 2020–2021.

Patient	Throat sw	ab	Anal swa	Serum specimen		
Patient	ORF 1a/b (A lab/B lab)	N (A lab/B lab)	ORF 1a/b (A lab/B lab)	N (A lab/B lab)	IgM	IgG
E	-1-	-1-	-1-	-1-	+	_
F	+/+	+/+	-1-	- <i>I</i> -	-	-
G	+ /n.a.	+ /n.a.	– /n.a.	– /n.a.	-	-
Н	+/+	+/+	+/+	+/+	-	-
1	+/+	+/+	-1-	- <i>I</i> -	-	-
J	- / -	-1-	+/+	+/+	-	-
K	+/+	+/+	+/+	+/+	-	-
L	+/-	-/+	-1-	+ / -	_	

Abbreviation: ORF 1a/b=Open reading frame 1a/b; n.a.=not applicable.

that we must pay attention to asymptomatically infected patients for the prevention and control of COVID-19. If an asymptomatic infected individual is not detected in time, he or she can cause a serious public health event (4-6). Early detection, early reporting, early isolation, and early treatment of asymptomatic patients require a joint effort with policymakers, clinicians, technicians, epidemiologists, virologists, and patients.

The results of this outbreak investigation showed that Patient E went to Shunyi District, Beijing after the 14-day quarantine that is required of international entrants to China. During the next seven days, Patient E went shopping and dining many times and was not strictly quarantining himself at home. Local staff did not manage this individual properly as an international entrant to China. As a result, he had contact with four co-residents including Patient B. On the Day 18 after entry, he had short-term, close contact in the mall with patients C and D. Patients B, C, and D later became confirmed COVID-19 cases. The turn of events revealed gaps in the management of international entrants and showed that the community supervision responsibility had not been thoroughly implemented. We recommend that for international entrants and people in close contact with COVID-19 cases after the 14-day intensive medical quarantine, at least 7 days of home quarantine are necessary. Local staff should tightly implement their responsibilities for infectious disease management and strictly manage home quarantine.

Patient E was asymptomatic and was not detected and isolated in time, enabling virus transmission that started this local COVID-19 outbreak. Unnoticed, asymptomatically infected individuals may accelerate person to person spread of COVID-19. Therefore, effective screening and management of asymptomatic but infected individuals is a key requirement for successfully controlling virus spread in the COVID-19 pandemic. For international entrants and people who are in close contact with COVID-19 cases, the

frequency of nucleic acid testing should be increased. We propose expanding nucleic acid testing and screening and adding anal swabs and residence environmental specimens to the set of tests to perform; serum antibody testing can also be used as a reference indicator. Parallel testing by two institutions at key management time points should be implemented.

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Notes from the Field

A Case of New Variant COVID-19 First Emerging in South Africa Detected in a Security Guard at the Isolation Point — Shenzhen, China, January 23, 2021

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On January 22, 2021, a 34-year-old male, who served as a security guard at the isolation point in Shenzhen, tested positive for coronavirus disease 2019 (COVID-19) during the every-three-day routine test. After the nasopharyngeal swab was further confirmed as positive for COVID-19 by Shenzhen CDC, the patient was transferred to the Third People's Hospital of Shenzhen and was diagnosed as a COVID-19 asymptomatic infection. On January 25, 2021, Shenzhen CDC identified the 20H/501.Y.V2 (B.1.351) variant, which was a variant of COVID-19 virus first emerging in the South Africa.

The epidemiological investigation indicated that the patient (ACC-XG00731) began working as a security guard at the isolation point on July 25, 2020 in Shenzhen. On January 19, his test result was negative. According to his statement, in the last 14 days, he had worked on the isolation floor occasionally but had not been exposed to the individuals who were in quarantine, had no exposure to the household or medical waste generated from the isolation personnel, and did not participate in the sewage treatment of the isolation point. On January 22, 2021, 1 case (ACC-XG00741) of COVID-19 infection in this isolation point was detected in entry isolation personnel from South Africa and was diagnosed on January 22. It was considered possible that case ACC-XG00731 is a descendant of the case ACC-XG00741.

On January 25, 2021, the sample of the 2 cases were sequenced by Shenzhen CDC using the second-generation (MiSeq) and third-generation sequencing technology (Nanopore). Compared with the Wuhan reference (EPI_ISL_402125) (1), these 2 strains exhibited 23 to 24 nucleotide variation sites, belonging to the Pangolin lineage B.1.351 (2), which were all classified as the 20H/501.Y.V2 variant (Figure 1). The genomic sequence of ACC-XG00731 and ACC-XG00741 strains were highly homologous (99.997%), sharing 23 variation sites (G174T, C241T, C1059T, A2692T, C3037T, G5230T, C9808T, A10323G,

C14408T. C21614T. A21801C. A22206G. C23664T, A23403G, G22813T, G25477T, G25563T, C25904T, C26456T, C26645T, C28253T, C28887T, and G29737T). The 2021A-XG00731 strain only had one specific variation site (C16428T). As is characteristic of 501.Y.V2 variant, the ACC-XG00731 strains carried several amino acid mutation sites, including K417N, E484K, and N501Y.

The 501Y.V2 lineage, which was connected to a fast-growing epidemic, emerged in early August in South Africa (3). The 501Y.V2 lineage includes several specific mutations (D80A, LAL242-244del, R246I, K417N, E484K, N501Y, D614G, and A701V) in the spike protein of the COVID-19 virus, also known as severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2). The N501Y mutation had also been identified in the B.1.1.7 variant (also known as 501Y.V1) first emerging in the United Kingdom (4); recently, the B.1.1.7 variant was estimated to be approximately 56% more transmissible than existing viruses in circulation (5). The N501Y mutation may influence the function of spike receptor binding domain that promotes the interaction to ACE2 on the host cells, making infection easier (6).

In the case that the 501Y.V2 variant first emerging from South Africa was detected in returnees and further spread to the security guard at the isolation point in Shenzhen, the management measures of the isolation points should be heightened. The 501Y.V2 and 501Y.V1 variant had been detected in Guangdong (7) and Shanghai in China, respectively (8), and had been identified in tens of countries worldwide, posing a more serious challenge to the global epidemic. Understanding the faster-spreading variants of COVID-19 virus may be beneficial for the policy decisions to contain their spread.

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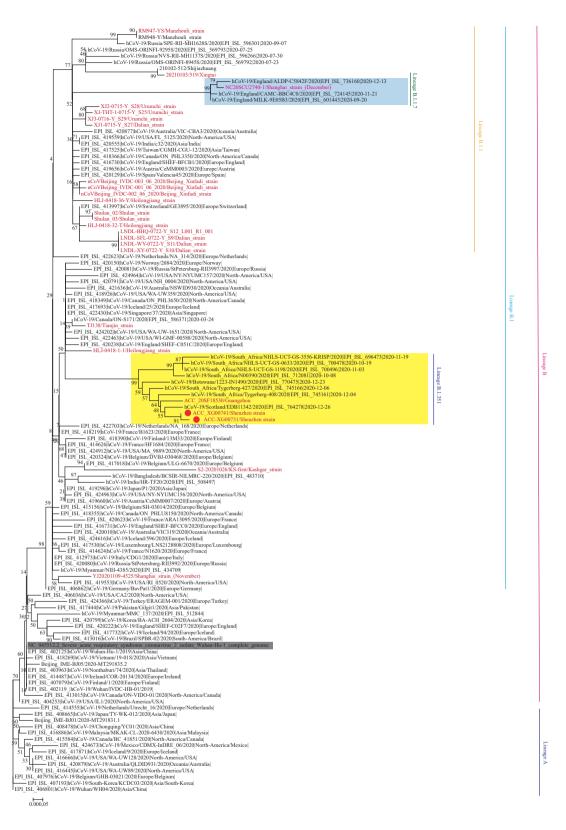


FIGURE 1. Phylogenetic tree based on the full-length genome sequences of the COVID-19 virus.

The strains associated with specific outbreaks in China are marked in red. The South African 501Y.V2 variants are highlighted with yellow color and the Guangdong imported 501Y.V2 variant are marked in red, and the Shenzhen 20H/501.Y.V2 variant are exhibited with the red dots. The UK VUI-202012/01 variants are highlighted in blue. The Wuhan reference strain is marked in gray. The S(A)- or L(B)-lineage and sublineages of the COVID-19 virus were marked and colored on the right.

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