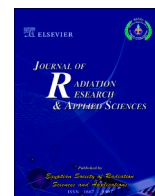




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The comparison of clinical characteristics between imported and native cases of COVID-19 in China

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ARTICLE INFO

Keywords:

COVID-19
Clinical features
Imported case
Native case

ABSTRACT

The study aimed to determine the trends in the manifestations and severity over the epidemic course of imported COVID-19 cases, with comparison to native cases. The clinical characteristics of imported and native Chinese COVID-19 cases included in the study were assessed and compared. The association was analyzed using Mann-Whitney *U* test for categorical variables, Kruskal-Wallis *H* test for continuous variables, and Spearman's correlation test for disease severity. A total of 247 imported patients were enrolled, with an average age of 29 years, and 41.3% were female. The imported patients were younger than the native patients (29 vs 47 years) and included a lower proportion of fever (44.1%), chills (5.3%), fatigue (10.1%), leukopenia (14.6%), lymphopenia (39.3%), elevated C-reactive protein (CRP) (7.3%), elevated D-dimer (16.3%), and pneumonia (65.6%). Among patients with moderate severity, imported cases had a lower proportion of fever (44.2%), dyspnea (8.3%), and increased CRP (7.7%) than native cases. COVID-19 infection was less severe in imported cases than that in native cases.

1. Introduction

In December 2019, a series of pneumonia cases of unknown cause was discovered in Wuhan, Hubei, China (Huang et al., 2020). The clinical and imaging presentation markedly resembled viral pneumonia, including fever, fatigue, cough, dyspnea, normal or decreased white blood cell count, and bilateral ground-glass opacity and consolidation on chest computed tomography (CT). However, the disease could cause severe complications, including acute respiratory distress syndrome, and considerable mortality, even in patients who were previously in a health condition. The causative pathogen was identified as a novel coronavirus (Zhu et al., 2020), which were first named as severe acute

respiratory syndrome coronavirus 2 (SARS-COV-2) by the International Committee on Taxonomy of Viruses, and then formally named as “corona virus disease 2019 (COVID-19)” by the World Health Organization (WHO) (Qu et al., 2020).

The first wave of infection was mainly linked to the Huanan Seafood Market in Wuhan Hubei Province, China in late December 2019. Confirmed of a human-to-human transmission (Li et al., 2020), COVID-19 has formally declared a global pandemic on March 11, 2020 (Qu et al., 2020). By October 19, 2020, a total of 40 million cases were confirmed with COVID-19, including over 1 million deaths in over 200 countries, reported by WHO (World Health Organization). While, the incidence and mortality rates were continuously increasing.

Peer review under responsibility of The Egyptian Society of Radiation Sciences and Applications.

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<https://doi.org/10.1016/j.jrras.2022.04.007>

Received 22 December 2021; Received in revised form 2 April 2022; Accepted 25 April 2022

Available online 16 May 2022

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With rapid response and aggressive public health interventions, the COVID-19 epidemic was largely contained in China (Lancet, 2020), reflected by the reduced number of newly confirmed native cases. Accordingly, a large number of Chinese individuals living abroad returned to China to avoid SARS-COV-2 infection. However, some of them had already been infected before getting back (Chen et al., 2020). Although these imported cases posed new challenges for both China (Chen et al., 2020) and other countries as the global pandemic worsen, little was known about the characteristics of imported COVID-19 cases. This study aimed to determine the trends in the manifestations and

severity over the epidemic course of imported COVID-19 cases, with comparison to native cases.

2. Methods

2.1. Study design and participants

This study was approved by the Ethics Committee of Shanghai Public Health Clinical Center (SPHCC), and informed consent was obtained from all patients.

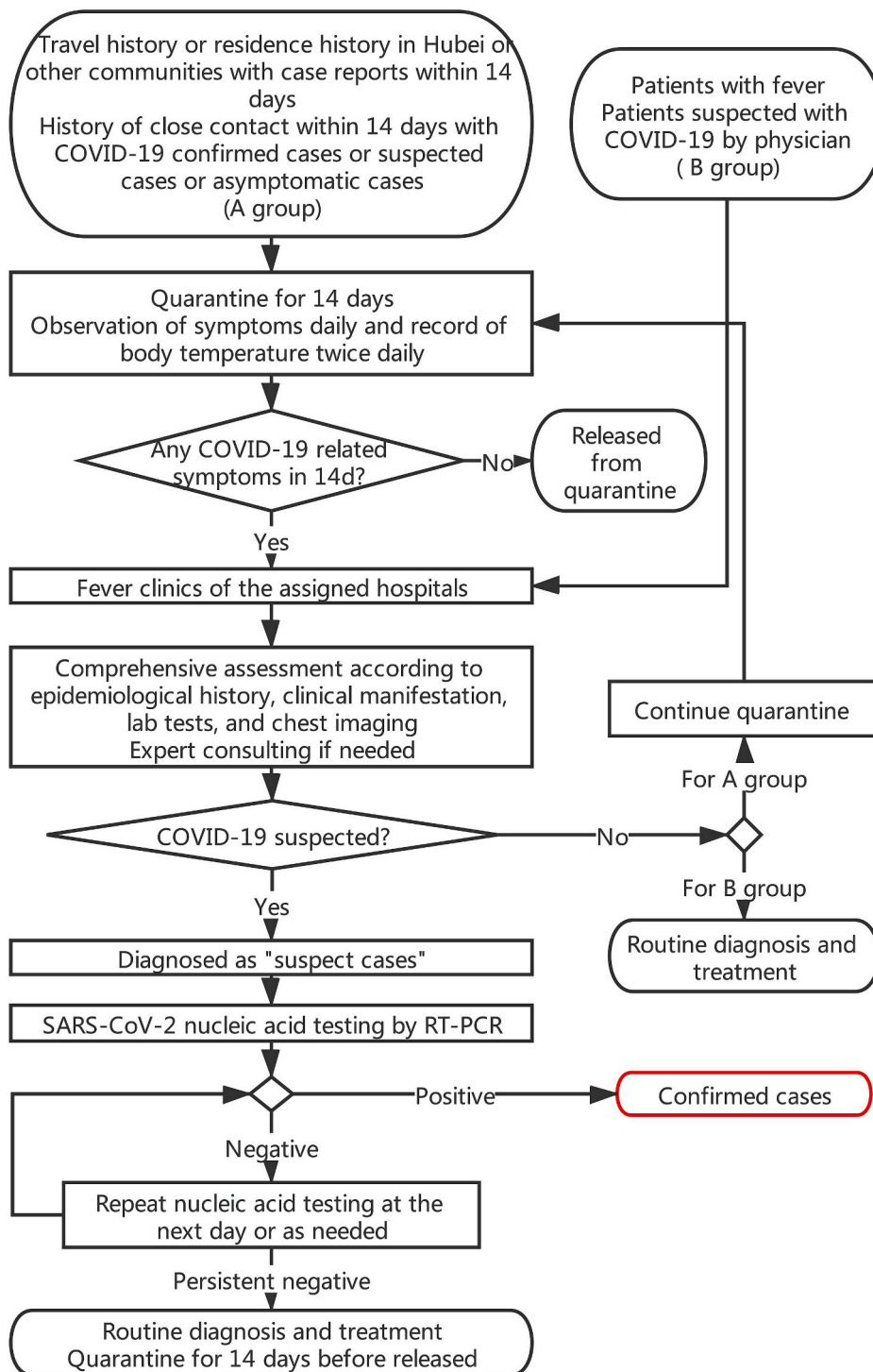


Fig. 1. Screening strategy for native COVID-19 cases in Shanghai (Jan-Feb 2020).

This was an ecological study of 247 Chinese patients who returned to Shanghai, China from 21 countries between March 6 and April 30, 2020, and have been diagnosed with COVID-19. Only patients aged ≥ 15 years were enrolled. Patients were screened and diagnosed according to national guidelines and local protocols³ (Figs. 1 and 2). All patients were followed-up until May 30, 2020. In addition, we included 265 native Chinese patients from a Shanghai cohort and 1099 patients from a nationwide cohort. The Shanghai cohort comprised patients admitted to SPHCC, who were diagnosed with COVID-19 before February 7, 2020, and followed up till February 11, 2020 (Lu et al., 2020). The nationwide cohort included patients across China through December 11, 2019, to January 29, 2020, who were followed up till January 31, 2020 (Guan et al., 2020).

2.2. Laboratory confirmation of SARS-CoV-2 infection

SARS-CoV-2 infection was confirmed via viral nucleic acid testing performed by the district Center for Disease Control and Prevention (CDC) or authenticated testing company and confirmed by the Shanghai CDC, according to the recommendation by the National Institute for Viral Disease Control and Prevention, China.

2.3. COVID-19 clinical severity Classification

Disease severity was classified as (1) mild: minor symptoms with no pneumonia manifestations on lung imaging examination; (2) moderate: fever and respiratory symptoms with pneumonia manifestations on CT images, but with no dyspnea or other complications; (3) severe: shortness of breath (respiratory rate [RR] ≥ 30 beats/min); resting state mean oxygen saturation $\leq 93\%$; partial pressure of arterial oxygen/fraction of inspired oxygen ≤ 300 mmHg; or pulmonary imaging showed that lesions had progressed by $> 50\%$ within 24–48-h period), and (4) critical: any one of the following conditions occurred, including respiratory failure requiring mechanical ventilation, shock, or multi-organ failure requiring intensive care unit (ICU) monitoring and treatment (Feng et al., 2020; Qu et al., 2020).

2.4. Data collection

Epidemiological and demographic data, underlying comorbidities, clinical symptoms and signs throughout the disease course, CT imaging, and laboratory findings at admission were extracted from electronic medical records. Laboratory assessments consisted of complete blood count, liver and renal function tests, electrolytes, arterial and venous lactate, C-reactive protein (CRP), procalcitonin, coagulation test, lactate dehydrogenase, and creatine kinase.

2.5. Statistical analysis

The presence or absence of symptoms and comorbidities, and most laboratory test results classified as normal, higher, and lower, were coded as categorical variables. Body temperature and disease severity were coded as rank variables. The intervals between symptom onset and admission, and length of hospital stay (LOS) were coded as continuous variables.

Categorical and rank variables were expressed as frequencies (%), while continuous variables were expressed as the median (interquartile range, IQR). Between-group comparisons of the categorical variables were conducted using the χ^2 test or Fisher's exact test, while rank and continuous variables were compared using the Mann-Whitney *U* test and Kruskal-Wallis *H* test. The association was analyzed using Mann-Whitney *U* test for categorical variables, Kruskal-Wallis *H* test for continuous variables, and Spearman's correlation test for disease severity. All statistical analyses were performed using SPSS version 25.0 (IBM Inc., Armonk, NY). A difference with $P < 0.05$ was regarded as statistically significant.

3. Results

3.1. Demographic and clinical characteristics

A total of 247 imported patients were enrolled, with an average age of 29 years, and 41.3% of whom were female. The most common country of origin was Russia ($n = 86$, 34.82%), followed by the United Kingdom (UK) ($n = 76$, 30.77%) and the United States of America (USA) ($n = 34$, 13.77%). The remaining 51 (20.65%) patients were from other countries. The patients from Russia were mainly businessmen, while the patients from USA and UK were mainly Chinese overseas students.

The baseline demographic characteristics of imported cases and two cohorts were shown in Table 1. The imported cases were significantly younger than the native cases (median [IQR]: 29 years [21–40 years] vs 47 years [35–58 years] (national cohort), $P < 0.001$). In addition, sex and age proportions were different among various countries of disease origins ($P = 0.022$ and $P < 0.001$, respectively). For comorbidities, imported cases had a significantly lower proportion of hypertension (5.3% vs 19.6% and 15.0%) and coronary heart disease (0% vs 5.3% and 2.5%) than native cases.

3.2. COVID-19 characteristics

Based on the most severe situation over the whole disease course, 84 (34.1%) patients were classified as mild, 156 (63.4%) were moderate, 5 (2.0%) were severe, and 1 (0.4%) was critical in the imported cases, which were less severe than native cases ($P < 0.001$). Furthermore, the severity was also different among cases with different origins overall ($P = 0.004$). The cases from Russia were more severe than the cases from UK ($P < 0.001$).

The proportion of pneumonia was lower in imported cases, compared with native cases (65.6% vs 91.1% (national cohort), $P < 0.001$, Table 2). Compared with native cases, imported cases had a lower prevalence of fever (44.1% vs 90.9% (Shanghai cohort) and 88.7% (national cohort), both $P < 0.001$), chills (5.3% vs 11.5% (national cohort), $P < 0.001$), and fatigue (10.1% vs 25.3% (Shanghai cohort) and 38.1% (national cohort), both $P < 0.001$). While, imported cases had a higher prevalence of nasal congestion (15.8% vs 4.8% (national cohort), $P < 0.001$). Meanwhile, there was no significant between-group difference concerning the proportion of patients with cough, productive sputum, myalgia or arthralgia, dyspnea or chest tightness, and diarrhea. Ageusia or anosmia was identified in 9.7% of the imported cases.

There was a large disparity of clinical symptoms among cases with different country origins. The proportion of patients who had a diagnosis of pneumonia was different ($P = 0.006$), with a higher proportion in cases originating in Russia than those in UK ($P = 0.002$). In addition, the prevalence of chills and dyspnea/chest tightness differed among the cases originating from Russia were higher than those from UK ($P = 0.012$ and 0.003, respectively). While, the highest body temperature and the prevalence of other symptoms had no significant difference by country of origin.

In patients with moderate severity, the most frequent symptom was cough (53.8%), followed by fever (44.2%), itchy throat (31.4%), and sputum production (26.9%). The proportion of patients with fever (44.2% vs 82.2%, $P < 0.001$), dyspnea (8.3 vs 14.9%, $P = 0.040$), and elevated CRP (7.7% vs 55.0%, $P < 0.001$) in moderate imported cases remained significantly lower than in moderate native cases. There was no significant difference in the proportion of patients with the remaining clinical characteristics.

3.3. Laboratory and imaging characteristics

The laboratory and imaging findings were shown in Table 3. Compared with native cases, imported cases showed a lower prevalence of leukopenia (14.6% vs 33.7%, $P < 0.001$), lymphopenia (39.3% vs 83.2%, $P < 0.001$), thrombocytopenia (8.9% vs 36.2%, $P < 0.001$),

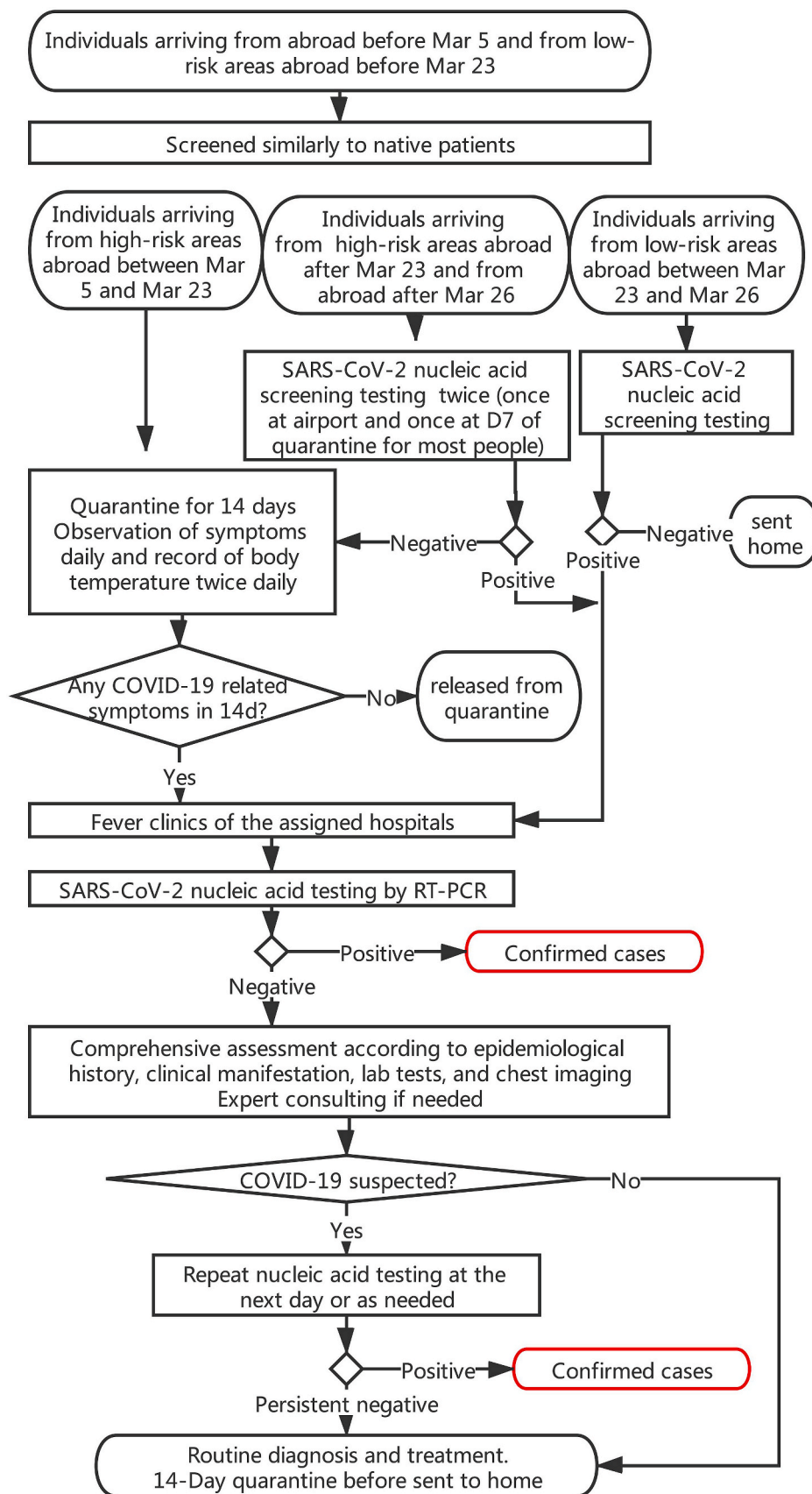


Fig. 2. Screening strategy for imported COVID-19 cases in Shanghai (Mar–April 2020).

Table 1

The demographics and baseline characteristics of COVID-19 imported cases from different countries outside of China, as compared to native cases in China.

	Imported COVID-19 cases					P1	Native Shanghai cohort		National native cohort	
	US	Russia	UK	Other	Total		P2	P3		
Number	34	86	76	51	247		265		1099	
Female sex	18 (52.9%)	25 (29.1%)	33 (43.4%)	26 (51.0%)	102 (41.3%)	0.022			41.9%	
Age (years), median (IQR)	22 (19–34)	35 (31–44)	21 (19–24)	32 (23–49)	29 (21–40)	<.001ⓐ			47 (35–58)	
15–49	29 (85.3%)	75 (87.2%)	73 (96.1%)	39 (76.5%)	216 (87.4%)	0.003			55.1%	
50–64	3 (8.8%)	11 (12.8%)	3 (3.9%)	11 (21.6%)	28 (11.3%)	0.003			28.9%	
≥65	2 (5.9%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	3 (1.2%)	0.003			15.1%	
Smoking history	1 (2.9%)	20 (23.3%)	4 (5.3%)	2 (3.9%)	27 (10.9%)	0.001ⓑ			12.6%	
Current smoker									0.395	
Former smoker	0 (0.0%)	1 (1.2%)	0 (0.0%)	1 (2.0%)	2 (0.8%)	0.001			1.9%	
Smoking history pack*years	0.1 (0.1–0.1)	7.5 (5–15)	2.35 (0.7–)	20 (20–20)	7 (4–15)	0.009			0.395	
Alcohol drinker	3 (8.8%)	10 (11.6%)	2 (2.6%)	0 (0.0%)	15 (6.1%)	0.013				
Coexisting disorders										
Any	13 (38.2%)	29 (33.7%)	10 (13.2%)	15 (29.4%)	67 (27.1%)	0.005ⓐ			23.7%	
Asthma	0 (0.0%)	2 (2.3%)	1 (1.3%)	2 (3.9%)	5 (2.0%)	0.754			0.286	
COPD	0	0	0	0	0	NA	1.5%		1.1%	
Allergic rhinitis	3 (8.8%)	7 (8.1%)	0 (0.0%)	2 (3.9%)	12 (4.9%)	0.025				
Hepatitis B infection	0 (0.0%)	4 (4.7%)	2 (2.6%)	2 (3.9%)	8 (3.2%)	0.764	0.4%	0.017	2.1%	
Hypertension	2 (5.9%)	7 (8.1%)	0 (0.0%)	4 (7.8%)	13 (5.3%)	0.032	19.6%	<.001	15.0%	
Coronary heart disease	0	0	0	0	0	NA	5.3%	<.001	2.5%	
Other cardiovascular disease	1 (2.9%)	1 (1.2%)	0 (0.0%)	1 (2.0%)	3 (1.2%)	0.5				
Cerebrovascular disease	0	0	0	0	0	NA	0.8%		1.4%	
Diabetes	2 (5.9%)	6 (7.0%)	0 (0.0%)	3 (5.9%)	11 (4.5%)	0.062	7.9%	0.143	7.4%	
Hyperlipidemia	0	0	0	0	0	NA	1.5%		0.124	
Chronic renal disease	0	0	0	0	0	NA	1.9%		0.7%	
Immunodeficiency	2 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.8%)	0.018			0.2%	
Autoimmune diseases	0 (0.0%)	0 (0.0%)	2 (2.6%)	0 (0.0%)	2 (0.8%)	0.296	0.8%	1	0.156	
Tumor	0	0	0	0	0	NA	2.3%		0.9%	

P1, P value of differences among different countries. P2, P value of differences between Shanghai native cases and imported cases. P3, P value of differences between national native cases and imported cases. T max: the maximum body temperature.

In pairwise comparison, ⓐ values of cases originating from Russia were significantly higher than those of cases originating from the US and UK; values of cases from other countries were higher than those of cases from the UK. ⓑ Values of cases from Russia were significantly higher than those of cases from the UK and other countries, P = 0.001 and 0.004, respectively. ⓒ Values of cases originating from the US and Russia were significantly higher than those of cases originating from the UK, P = 0.005 and P = 0.003, respectively.

Data are presented as n (%), unless otherwise specified.

elevated CRP (7.3% vs 60.7%, $P < 0.001$), elevated alanine aminotransferase (ALT) (15% vs 21.3%, $P = 0.034$), elevated aspartate aminotransferase (AST) (3.6% vs 22.2%, $P < 0.001$), renal insufficiency (0.0% vs 1.6%, $P = 0.045$), elevated creatine kinase (6.9% vs 13.7%, $P = 0.005$), elevated lactate dehydrogenase (8.5% vs 41.0%, $P < 0.001$), and elevated D-dimer (16.3% vs 46.4%, $P < 0.001$).

Abnormalities on chest CT on admission were detected in 56.7% of imported cases, which was lower than that in native cases (86.2%, $P < 0.001$). The proportion of patients with bilateral lung involvement was also significantly lower in imported cases (34.0% vs 77.4%, $P < 0.001$). The most common abnormal findings on CT were ground-glass opacities (38.1%), followed by patchy effusion or consolidation (25.9%) and interlobular septal thickening (23.1%) in imported cases, similar to native cases.

3.4. Association between baseline and clinical characteristics and disease severity

The results of baseline and clinical characteristics classified with disease severity were shown in Table 4, Supplementary Tables 1–2. There was a significant correlation between disease severity and age (Spearman’s correlation $r = 0.386$, $P < 0.001$). Furthermore, disease severity was significantly associated with hypertension ($P = 0.002$), diabetes ($P < 0.001$), cough ($P < 0.001$), productive sputum ($P = 0.004$), leukopenia ($P = 0.026$), lymphocytopenia ($P < 0.001$), hypoalbuminemia ($P < 0.001$), increased CRP ($P = 0.001$), increased ALT ($P = 0.018$), increased AST ($P = 0.002$), increased lactate dehydrogenase ($P < 0.001$), D-dimer ($P = 0.040$), and more lung lobes involved (in moderate to critical patients, $r = 0.160$, $P = 0.049$).

The comparison of clinical characteristics between asymptomatic patients and symptomatic patients was shown in Supplementary

Table 3. Asymptomatic patients had a lower prevalence of bilateral lung involvement ($P = 0.042$), multiple lobar involvements ($P = 0.018$), and ground-glass opacities ($P = 0.014$). Meanwhile, there was no significant difference in age, sex, comorbidities and laboratory abnormalities between the asymptomatic and symptomatic patients.

4. Discussion

Our findings indicated that COVID-19 infection was less severe in imported cases than that in native cases, reflected by lower overall severity, a higher percentage of asymptomatic patients and lower number of patients with fever, pneumonia, leukopenia, lymphopenia, and elevated CRP, ALT, AST, creatine kinase, lactate dehydrogenase, and D-dimer.

In this study, three Chinese cohorts were involved in the comparison. Shanghai cohort reported by Lu et al. (Lu et al., 2020) was used as a reference for comparison because it involved native Chinese COVID-19 patients who were diagnosed, treated, and followed up by the same hospitals, using the same protocol. Meanwhile, the national cohort reported by Guan et al. (Guan et al., 2020) was a complete and detailed case series report of native Chinese patients, with a relatively large sample size. In addition, another cohort reported by Feng et al. (Feng et al., 2020) was used as a reference for comparison in patients with moderate severity.

Several factors might contribute to less severe manifestations in imported cases. First, the imported cases were younger and had fewer comorbidities, which were reported to have an influence on disease severity (Chen et al., 2020; Liu et al., 2020; Zhou et al., 2020). Second, in the early stage of the epidemic, severe cases were more likely to be tested, diagnosed, and admitted, which might cause a selection bias (Weiss & Murdoch, 2020). The evolution of the screening strategy might

Table 2
The clinical manifestations of COVID-19 imported cases from different countries outside of China, as compared to native cases in China.

	Imported COVID-19 cases						Native Shanghai cohort		National native cohort	
	US	Russia	UK	Other	Total	P1	P2	P3		
Number	34	86	76	51	247		265	1099		
Interval between symptom onset and admission (days)	3 (2–7)	5 (2.25–7)	4 (2–8.25)	5 (2–10)	4 (2–8)	0.643				
Asymptomatic	7 (20.6%)	6 (7.0%)	10 (13.2%)	6 (11.8%)	29 (11.7%)	0.189				
Fever during disease course (%)	15 (44.1%)	37 (43.0%)	37 (48.7%)	20 (39.2%)	109 (44.1%)	0.766	90.9%	<.001	88.7%	<.001
T max <37.5 °C	20 (58.8%)	52 (60.5%)	42 (55.3%)	33 (64.7%)	147 (59.5%)	0.915			9.9%	<.001
37.5–38.0 °C	9 (26.5%)	23 (26.7%)	27 (35.5%)	11 (21.6%)	70 (28.3%)				30.9%	
38.1–39.0 °C	5 (14.7%)	9 (10.5%)	7 (9.2%)	7 (13.7%)	28 (11.3%)				46.9%	
>39.0 °C	0 (0.0%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	2 (0.8%)				12.3%	
Chills	1 (2.9%)	9 (10.5%)	0 (0.0%)	3 (5.9%)	13 (5.3%)	0.012①			11.5%	0.003
Night sweats	0 (0.0%)	0 (0.0%)	1 (1.3%)	1 (2.0%)	2 (0.8%)	0.644				
Dizziness	0 (0.0%)	2 (2.3%)	1 (1.3%)	0 (0.0%)	3 (1.2%)	0.866				
Headache	2 (5.9%)	12 (14.0%)	5 (6.6%)	10 (19.6%)	29 (11.7%)	0.097	9.8%	0.569	13.6%	0.469
Sore throat	4 (11.8%)	9 (10.5%)	5 (6.6%)	2 (3.9%)	20 (8.1%)	0.419	4.5%	0.143	13.9%	0.012
Itchy throat	5 (14.7%)	28 (32.6%)	18 (23.7%)	16 (31.4%)	67 (27.1%)	0.177				
Nasal congestion	1 (2.9%)	14 (16.3%)	13 (17.1%)	11 (21.6%)	39 (15.8%)	0.091			4.8%	<.001
Rhinorrhea	2 (5.9%)	10 (11.6%)	8 (10.5%)	6 (11.8%)	26 (10.5%)	0.858	6.0%	0.078		
Cough	13 (38.2%)	43 (50.0%)	33 (43.4%)	24 (47.1%)	113 (45.7%)	0.663	49.4%	0.48	67.8%	<.001
Sputum production	7 (20.6%)	22 (25.6%)	16 (21.1%)	12 (23.5%)	57 (23.1%)	0.914	23.0%	1	33.7%	0.001
Hemoptysis	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	1			0.9%	0.7
Fatigue	3 (8.8%)	9 (10.5%)	9 (11.8%)	4 (7.8%)	25 (10.1%)	0.919	25.3%	<.001	38.1%	<.001
Myalgia or arthralgia	2 (5.9%)	10 (11.6%)	5 (6.6%)	1 (2.0%)	18 (7.3%)	0.206	8.7%	0.626	14.9%	0.001
Chest pain	0 (0.0%)	3 (3.5%)	0 (0.0%)	0 (0.0%)	3 (1.2%)	0.227	2.3%	0.506		
Dyspnea or chest tightness	0 (0.0%)	14 (16.3%)	2 (2.6%)	6 (11.8%)	22 (8.9%)	0.003①	6.4%	0.322	18.7%	<.001
Ageusia or anosmia	5 (14.7%)	5 (5.8%)	10 (13.2%)	4 (7.8%)	24 (9.7%)	0.272				
Nausea or vomiting	0 (0.0%)	4 (4.7%)	2 (2.6%)	0 (0.0%)	6 (2.4%)	0.415	2.3%	1	5.0%	0.09
Abdominal pain	0 (0.0%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	2 (0.8%)	0.515				
Abdominal distention	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	1				
Diarrhea	3 (8.8%)	15 (17.4%)	4 (5.3%)	4 (7.8%)	26 (10.5%)	0.081	6.4%	0.084	3.8%	<.001
Highest severity during disease course						0.004②		<.001		
Mild	10 (29.4%)	18 (21.2%)	35 (46.1%)	21 (41.2%)	84 (34.1%)		1.9%			
Moderate	23 (67.6%)	64 (75.3%)	41 (53.9%)	28 (54.9%)	156 (63.4%)		89.8%			
Severe	0 (0.0%)	3 (3.5%)	0 (0.0%)	2 (3.9%)	5 (2.0%)		3.8%			
Critical	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)		4.5%			
Diagnosed pneumonia	24 (70.6%)	67 (77.9%)	41 (53.9%)	30 (58.8%)	162 (65.6%)	0.006③			91.1%	<.001
Severe-critical	1 (2.9%)	3 (3.5%)	0 (0.0%)	2 (3.9%)	6 (2.4%)	0.254	8.3%	0.003	15.7%	<.001
Hospital LOS (days)	16 (13–20)	14 (12–19)	16 (12–21)	14 (12–19)	15 (12–20)	0.099				

P1, P value of differences among different countries. P2, P value of differences between Shanghai native cases and imported cases. P3, P value of differences between national native cases and imported cases. T max: the maximum body temperature.

In pairwise comparison, ① Values of cases originating from Russia were significantly higher than those of cases originating from the UK, P = 0.004. ② Values of cases originating from Russia were significantly higher than those of cases originating from the UK, P < 0.001. ③ Values of cases originating from Russia were significantly higher than those of cases originating from the UK, P = 0.002.

Data are presented as n (%), unless otherwise specified.

have helped the timely identification of more asymptomatic and mild patients. However, the native cases were also largely identified in a timely manner under Shanghai’s active surveillance program, shown in the Shanghai cohort (Lu et al., 2020). In addition, the pathogenicity of the virus may be diminished after multigenerational transmission under selection pressure (Lei et al., 2020). For instance, the cases in Guangzhou were reported to have a less severity, compared with those in Wuhan (Lei et al., 2020). However, the evolution of the manifestations and severity of the disease over the course of the epidemic remains

unknown. Further studies were warranted to confirm the findings.

A recent meta-analysis (Liu et al., 2020) showed a significantly higher incidence of cough, dyspnea, nasal congestion, and digestive symptoms in patients from North American, European, and Middle East countries than those from East and South-East Asian countries. While, there were no significant differences in the incidence of fever, lymphocytopenia, and thrombocytopenia by country of origin. Given the high incidence of the asymptomatic patients in West countries (Oran & Topol, 2020), these manifestations of patients in West countries were

Table 3

Laboratory and radiographic findings of COVID-19 cases imported from different countries at admission, as compared with native Chinese cases

	Import COVID-19 cohort					P1	Native Shanghai cohort		Native national cohort
	U.S.A.	Russia	U.K.	Other	Total		P2	P3	
White blood cell count <4*10 ⁹ /L	6 (17.6%)	10 (11.6%)	12 (15.8%)	8 (15.7%)	36 (14.6%)	0.944	33.7%	<.001	
White blood cell count >10*10 ⁹ /L	1 (2.9%)	2 (2.3%)	3 (3.9%)	1 (2.0%)	7 (2.8%)	0.944	5.9%		
Platelet count <150,000/mm ³	4 (11.8%)	10 (11.6%)	3 (3.9%)	5 (9.8%)	22 (8.9%)	0.284	36.2%	<.001	
Platelet count >400,000/mm ³	1 (2.9%)	2 (2.3%)	0 (0.0%)	1 (2.0%)	4 (1.6%)	0.284			
Neutrophil % <50%	11 (32.4%)	12 (14.0%)	13 (17.1%)	6 (11.8%)	42 (17.0%)	0.304			
Neutrophil % >70%	5 (14.7%)	13 (15.1%)	11 (14.5%)	10 (19.6%)	39 (15.8%)	0.304			
Lymphocyte count <1500/mm ³	11 (32.4%)	40 (46.5%)	22 (28.9%)	24 (47.1%)	97 (39.3%)	0.06	83.2%	<.001	
C-reactive protein ≥10 mg/L	1 (2.9%)	11 (12.8%)	3 (3.9%)	3 (5.9%)	18 (7.3%)	0.129	60.7%	<.001	
Alanine aminotransferase >40 U/L	4 (11.8%)	17 (19.8%)	9 (11.8%)	7 (13.7%)	37 (15.0%)	0.526	21.3%	0.034	
Aspartate aminotransferase >40 U/L	1 (2.9%)	4 (4.7%)	1 (1.3%)	3 (5.9%)	9 (3.6%)	0.477	22.2%	<.001	
Total bilirubin >17.1 μmol/L	2 (5.9%)	11 (12.8%)	7 (9.2%)	2 (3.9%)	22 (8.9%)	0.348	10.5%	0.541	
Creatinine ≥133 μmol/L	0	0	0	0	0	NA	1.6%	0.045	
Creatine kinase ≥200 U/L	1 (2.9%)	8 (9.3%)	6 (8.1%)	2 (3.9%)	17 (6.9%)	0.543	13.7%	0.005	
Lactate dehydrogenase ≥250 U/L	2 (5.9%)	9 (10.5%)	4 (5.3%)	6 (11.8%)	21 (8.5%)	0.489	41.0%	<.001	
D-dimer ≥0.5 mg/L	5 (14.7%)	14 (16.5%)	11 (14.5%)	10 (19.6%)	40 (16.3%)	0.883	46.4%	<.001	
Albumin <40 g/L	1 (2.9%)	15 (17.4%)	3 (3.9%)	4 (7.8%)	23 (9.3%)	0.015			
Venous lactate >2.2 mmol/L	9 (26.5%)	54 (62.8%)	25 (34.2%)	21 (42.0%)	109 (44.9%)	0.001ⓐ			
Arterial lactate ≤1.5 mmol/L	22 (71.0%)	29 (34.5%)	48 (69.6%)	40 (80.0%)	139 (59.4%)	0			
Arterial lactate 1.5-2 mmol/L	4 (12.9%)	17 (20.2%)	11 (15.9%)	6 (12.0%)	38 (16.2%)	0			
Arterial lactate 2-4 mmol/L	5 (16.1%)	32 (38.1%)	10 (14.5%)	4 (8.0%)	51 (21.8%)	0			
Arterial lactate >4 mmol/L	0 (0.0%)	6 (7.1%)	0 (0.0%)	0 (0.0%)	6 (2.6%)	0			
SARS-COV-2 antibody									
Positive	12 (35.3%)	43 (50.0%)	43 (56.6%)	29 (56.9%)	127 (51.4%)	0.24			
Weakly positive	3 (8.8%)	7 (8.1%)	2 (2.6%)	3 (5.9%)	15 (6.1%)				
Negative	19 (55.9%)	36 (41.9%)	31 (40.8%)	19 (37.3%)	105 (42.5%)				
Abnormalities on chest CT	17 (50.0%)	59 (68.6%)	34 (44.7%)	30 (58.8%)	140 (56.7%)	0.017ⓑ		86.2%	
Unilateral involvement	8 (23.5%)	16 (18.6%)	18 (23.7%)	14 (27.5%)	56 (22.7%)	0.001ⓐ	19.2%	<.001	
Bilateral involvement	9 (26.5%)	43 (50.0%)	16 (21.1%)	16 (31.4%)	84 (34.0%)		77.4%		
Number of lung lobes involved									
0	17 (53.1%)	27 (32.9%)	42 (56.8%)	21 (42.9%)	107 (45.1%)	0.000ⓐ			
1	6 (18.8%)	14 (17.1%)	17 (23.0%)	14 (28.6%)	51 (21.5%)				
2	6 (18.8%)	12 (14.6%)	7 (9.5%)	6 (12.2%)	31 (13.1%)				
3	1 (3.1%)	8 (9.8%)	5 (6.8%)	3 (6.1%)	17 (7.2%)				
4	1 (3.1%)	7 (8.5%)	1 (1.4%)	2 (4.1%)	11 (4.6%)				
5	1 (3.1%)	14 (17.1%)	2 (2.7%)	3 (6.1%)	20 (8.4%)				
Ground-glass opacity	14 (41.2%)	37 (43.0%)	21 (27.6%)	22 (43.1%)	94 (38.1%)	0.155	56.4%	<.001	
Interlobular septal thickening	5 (14.7%)	25 (29.1%)	14 (18.4%)	13 (25.5%)	57 (23.1%)	0.246			
Patchy effusion or consolidation	5 (14.7%)	31 (36.0%)	16 (21.1%)	12 (23.5%)	64 (25.9%)	0.054			

P1, P value of the difference among different countries. P2, P value of differences between the native Shanghai cases and the imported cases. P3, P value of differences between the national native cases and imported cases. In pairwise comparisons, ⓐ the values of cases originating from Russia were significantly higher than those of cases originating from the UK, P = 0.001. ⓑ The values of cases originating from Russia were significantly higher than those of cases originating from the UK, P = 0.003. ⓒ The values of cases originating from Russia were significantly higher than those of cases originating from the UK, P < 0.001. Data are presented as n (%).

consistent with the imported patients in the present study. This suggested that, in this epidemic, the incidence of fever, lymphocytopenia, and thrombocytopenia decreased, while the incidence of dyspnea and digestive symptoms (i.e., diarrhea) persisted or even increased regardless of ethnicity. In addition, it was reported that 55% of COVID-19 patients presented with anosmia or ageusia in a London population (Patel et al., 2020), which might be related to the damage of olfactory and taste receptors (Jasti et al., 2020). The incidence of ageusia or anosmia in COVID-19 patients in China was reported to be 32%, significantly lower than that in Germany and France (Qiu et al., 2020). Only 9.8% of the imported cases presented with ageusia or anosmia in the present study, suggesting that the low incidence of ageusia or anosmia in Chinese patients in a previous study may have been due to the Chinese ethnicity. Patients with ageusia or anosmia in the study had less severe disease, which was consistent with the previous findings (Haehner et al., 2020; Moein et al., 2020). Furthermore, liver involvement was a common occurrence in COVID-19 infection (Saviano et al., 2020). Recent studies showed that 41.6% and 66.9% of the 1827 patients in the USA presented with elevated ALT and AST on admission (Hundt et al., 2020). However, only 27.3% (227/830) of the Chinese COVID-19 patients showed liver biochemistry abnormality on admission (Chen et al., 2020). A meta-analysis including former data also showed that the cases from West countries had a higher incidence of elevated

ALT and AST than those from East countries (Liu et al., 2020). In the present study, the imported Chinese cases showed a lower prevalence of elevated ALT and AST than did the native Chinese cases, indicating that a low prevalence of liver injury may be related to the Chinese ethnicity.

Previous studies reported that patients with older age (Chen et al., 2020; Liu et al., 2020; Zhou et al., 2020), hypertension (Zhou et al., 2020), diabetes (Zhou et al., 2020), leukopenia (Feng et al., 2020; Guan et al., 2020), lymphocytopenia (Feng et al., 2020; Guan et al., 2020), hypoalbuminemia (Chen et al., 2020; Zhou et al., 2020), high CRP (Chen et al., 2020; Feng et al., 2020), high ALT and AST (Chen et al., 2020), high lactate dehydrogenase (Chen et al., 2020), and high D-dimer (Chen et al., 2020) levels had a more serious disease. Our findings on the association between certain clinical characteristics and disease severity were consistent with those in previous studies on native Chinese COVID-19 patients. However, previous studies on the association between incidence of fever and disease severity in native Chinese patients had inconsistent findings. Two studies found that fever was not a predicting factor for ICU admission and in-hospital death (Chen et al., 2020; Zhou et al., 2020). In contrast, another study reported a significantly higher proportion of patients with fever in severe patients (Feng et al., 2020). The proportion of patients with fever was higher in the more severely affected patients, but with no statistical significance in the present study.

Table 4

The demographics and baseline characteristics of imported COVID-19 cases with different severity, compared to the native cases.

	Imported cases						Native cases	
	Mild	Moderate	Severe	Critical	Total	P1	Moderate	P2
Number	84	156	5	1	246			
Female sex	35 (41.7%)	65 (41.7%)	1 (20.0%)	0 (0.0%)	101 (41.1%)	0.7	162 (46.0%)	0.385
Age (years), median (IQR)	22 (19–31)	32 (22–44)	49 (34–52)	75 (75–75)		<.001		
15–49	81 (96.4%)	131 (84.0%)	3 (60.0%)	0 (0.0%)	215 (87.4%)	<.001		
50–64	3 (3.6%)	23 (14.7%)	2 (40.0%)	0 (0.0%)	28 (11.4%)			
≥65	0 (0.0%)	2 (1.3%)	0 (0.0%)	1 (100.0%)	3 (1.2%)			
Smoking history	11 (13.1%)	15 (9.6%)	1 (20.0%)	0 (0.0%)	27 (11.0%)	0.525	27 (8.1%)	0.314
Current								
Former	0 (0.0%)	2 (1.3%)	0 (0.0%)	0 (0.0%)	2 (0.8%)	0.525		
Alcohol drinker	4 (4.8%)	11 (7.1%)	0 (0.0%)	0 (0.0%)	15 (6.1%)	0.727	20 (6.0%)	0.692
Coexisting disorder								
Any	13 (15.5%)	49 (31.4%)	4 (80.0%)	1 (100.0%)	67 (27.2%)	<.001		
Asthma	1 (1.2%)	4 (2.6%)	0 (0.0%)	0 (0.0%)	5 (2.0%)	0.656		
Allergic rhinitis	6 (7.1%)	6 (3.8%)	0 (0.0%)	0 (0.0%)	12 (4.9%)	0.248		
Hepatitis B infection	2 (2.4%)	6 (3.8%)	0 (0.0%)	0 (0.0%)	8 (3.3%)	0.721		
Hypertension	1 (1.2%)	9 (5.8%)	2 (40.0%)	1 (100.0%)	13 (5.3%)	0.002		
Other cardiovascular disease	0 (0.0%)	3 (1.9%)	0 (0.0%)	0 (0.0%)	3 (1.2%)	0.551		
Diabetes	0 (0.0%)	7 (4.5%)	3 (60.0%)	1 (100.0%)	11 (4.5%)	<.001		
Immunodeficiency	0 (0.0%)	2 (1.3%)	0 (0.0%)	0 (0.0%)	2 (0.8%)	0.551		
Autoimmune diseases	1 (1.2%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	2 (0.8%)	0.985		

P1: P value of the difference among different severities. P2: P value of the difference between native and imported cases. T max: the maximum body temperature. Data are presented as n (%), unless otherwise specified.

In the present study, 11.7% of imported cases were asymptomatic throughout the course of their disease, which was markedly higher than that in native Chinese patients (1%) from the nationwide survey (Wu & McGoogan, 2020). In the Diamond Princess cruise ship, approximately 17.9% of patients were asymptomatic (Mizumoto et al., 2020). In Italy, 6.7% of cases had no symptoms and 6.7% had few symptoms, based on a nationwide research (Livingston & Bucher, 2020). However, it should be noted that asymptomatic patients could still be infectious (Bai et al., 2020). The laboratory and chest CT examination in this study suggested that pathophysiological changes occurred in asymptomatic patients, who also needed to be quarantined and undergo close observation.

Our study had some limitations. First, the sample size was relatively small. Second, native cases were identified from published data, and detailed individual information could not be obtained. Thus, it was difficult to minimize the influence of the confounding factors. Third, the laboratory findings were mainly classified as dichotomy or grade, which might reduce the sensitivity to find differences among COVID-19 patients. Fourth, information on virus generation and evolution were not available. Further studies are needed to evaluate the impact of different SARS-CoV-2 lineages, host (including ethnicity) and environmental factors on the disease manifestations and severity.

In summary, COVID-19 infection was less severe in imported cases than that in native cases.

Funding

This work was supported by Scientific Research Projects of the Shanghai Municipal Health Commission for youths (Project No. 20204Y0016), Shanghai Municipal Key Clinical Specialty (shslczdzk02202), Shanghai Top-Priority Clinical Key Disciplines Construction Project (2017ZZ02014), Shanghai Key Laboratory of Emergency Prevention, Diagnosis and Treatment of Respiratory Infectious Diseases (20dz2261100) and Cultivation Project of Shanghai Major Infectious Disease Research Base (20dz2210500).

Declaration of competing interest

The authors declare that they have no conflicts of interest.

List of abbreviations

ALT	alanine aminotransferase
AST	aspartate aminotransferase
CDC	Center for Disease Control and Prevention
COVID-19	coronavirus disease 2019
CRP	C-reactive protein
CT	computed tomography
ICU	intensive care unit
IQR	interquartile range
LOS	length of stay
SPHCC	Shanghai Public Health Clinical Center
UK:	United Kingdom
USA:	United States of America
WHO	World Health Organization

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jrras.2022.04.007>.

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