Retrospective cohort study comparing the epidemiological and clinical characteristics between imported and local COVID-19 inpatients in Nanyang, China

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ABSTRACT

China has experienced an outbreak of COVID-19 since December 2019. This study investigated the differences between the imported and local cases of COVID-19 in Nanyang, China. In this study, a total of 129 COVID-19 confirmed cases with a clear epidemiological history admitted to hospitals in Nanyang from January 24 to February 26, 2020 were enrolled. Patients who had a travel history to or a residence history in Wuhan or in the surrounding areas in Hubei Province within 14 days before the illness onset were assigned to the imported group (n=70), and the others were assigned to the local group (n=59). The differences in epidemiological characteristics, clinical features, laboratory and imaging results, and prognosis were compared between the 2 groups. The early diagnosed cases were mainly imported cases, and the later diagnosed ones were mainly local cases. The most common first symptom was fever; moderate fever was commonly seen in imported cases whereas low fever was commonly seen in local cases. Lymphocyte counts in the imported group were lower than those in the local group. The imported group showed more advanced and severe abnormalities in the CT scan whereas the local group showed milder pulmonary abnormalities. The proportion of severe and critically severe patients in the imported group was higher than that in the local group. In conclusion, the imported cases have more severe or critically severe patients with a higher mortality rate than the local cases.

Significance of this study

What is already known about this subject?

- At the beginning of December 2019, the first case of unexplained pneumonia occurred in Wuhan, Hubei Province in China.
- The pathogen was identified as a type B coronavirus, which was called SARS-CoV-2.
- Some clinical characteristics and the risk factors of mortality for patients with COVID-19 have been reported.

What are the new findings?

- The moderate fever was commonly seen in imported cases.
- Lymphocyte counts in the imported group were lower than the local group.
- The imported group showed more severe abnormalities in the CT scan.
- The proportion of severe and critically severe patients in the imported group was higher.

How might these results change the focus of research or clinical practice?

- Differences are observed between the imported and local cases. The imported cases have more severe or critically severe patients with a higher mortality rate than the local cases.

INTRODUCTION

At the beginning of December 2019, the first case of unexplained pneumonia occurred in Wuhan, Hubei Province in China.[1] The pathogen was identified as a type B coronavirus,[2] which was called SARS-CoV-2 by the International Virus Classification Commission, and caused a global pandemic infection. At the end of January 2020, the Chinese Center for Disease Control and Prevention gave the first R0 value (reproductive number; ie, the average number of infected individuals by an infected patient) of 2.2 for SARS-CoV-2 by analyzing 435 cases.[3] In February 2020, Liu *et al* found that the mean R0 value of SARS-CoV-2 was 2.79 by analyzing more than 10 studies of SARS-CoV-2 epidemiology, suggesting the strong infectivity of SARS-CoV-2.[4] On February 11, 2020, the WHO officially named the new coronavirus disease 2019 as COVID-19.[5] Patients with laboratory-confirmed COVID-19, with or without clinical symptoms or abnormal radiologic findings, could be diagnosed with COVID-19.[6]

Nanyang, which is located in Henan Province in China, is a city adjacent to Wuhan.

Many migrant workers in Wuhan and surrounding cities had returned to Nanyang because of the Chinese Spring Festival, bringing in imported COVID-19 cases. At the end of January 2020, many Nanyang local cases continued to occur because of the migration. The first Nanyang COVID-19 case was diagnosed on January 24, 2020, and 156 COVID-19 cases were diagnosed before February 26 in Nanyang. Before February 29, most of the patients had met the discharge standards and had been cured, except for 3 deaths and 3 cases of referral to a superior hospital. There were no inpatient COVID-19 cases in Nanyang afterwards. This study collected data from 129 COVID-19 cases in Nanyang and compared the epidemiological characteristics, clinical manifestations, laboratory tests, imaging characteristics, severity, and prognosis between the imported and local COVID-19 cases.

METHODS

Study design and subjects

A retrospective study was conducted on 129 patients with laboratory-confirmed COVID-19 with a clear epidemiological history admitted to hospitals in Nanyang from January 24 to February 26, 2020. According to the epidemiological characteristics, they were divided into the imported COVID-19 cases (n=70) and the local COVID-19 cases (n=59). The imported cases had a clear history of travel to or residence in Wuhan or in the surrounding areas in Hubei Province within 14 days whereas the local cases were infected by exposure to imported cases or other laboratory-confirmed COVID-19 cases without a clear travel history to Wuhan or the surrounding areas in Hubei Province. Three medical staff members were included in the local group.

Epidemiological criteria

The included patients must have a travel history to or a residence history in Wuhan or in the surrounding areas in Hubei Province within 14 days before the onset or have an exposure history to the laboratory-confirmed COVID-19 cases or patients with fever or respiratory symptoms from Wuhan or the surrounding areas in Hubei Province within 14 days before the onset.

Diagnostic criteria

According to the COVID-19 Diagnosis and Treatment Guidelines issued by the National Health Commission of the People's Republic of China (trial version 5), the COVID-19-confirmed cases have to meet the clinical manifestations in the guidelines, and their samples, including sputum, throat swabs, and lower respiratory tract secretions, should be tested for the SARS-CoV-2 nucleic acid by the Center for Disease Control and Prevention of Nanyang using real-time fluorescent reverse transcription PCR. On admission, the patients with COVID-19 were classified by the severity of their condition as follows: (1) mild cases: with mild clinical symptoms without pneumonia abnormalities on imaging; (2) common cases: with fever, respiratory tract symptoms, and pneumonia abnormalities on imaging; (3) severe cases: meet any of the following standards: (A) respiratory distress and respiratory rate ≥30 times/min, (B) fingertip oxygen saturation ≤93% in resting state, and (C) arterial blood oxygen pressure (PaO_2)/oxygen concentration (FiO_2) ≤300 mm Hg (1 mm Hg=0.133 kPa); (4) critically severe cases: meet any of the following standards: (A) with respiratory failure and requiring mechanical ventilation, (B) with shock, and (C) with other organ failures and requiring intensive care.

Data collection

The epidemiological characteristics, symptoms and signs at admission, imaging data using CT, laboratory results between the day before admission and 48 hours after admission, including blood routine results and biochemical results, and the treatment and outcome of the patients were recorded.

Discharge criteria

The patients with COVID-19 were allowed to be discharged from hospital on meeting all 3 standards: (1) body temperature returns to normal for more than 3 days, and respiratory symptoms improve significantly; (2) pulmonary imaging shows an obvious absorption of inflammation; and (3) 2 consecutive negative results of respiratory SARS-CoV-2 nucleic acid tests (sampling interval of at least 1 day).

Statistical analysis

The SPSS V.25.0 software (IBM) was used for statistical analysis. Data of normal distribution were expressed as the mean±SD. Student's t-test was used to compare the two-group data. Data of non-normal distribution were expressed as the median (IQR) and analyzed using the rank-sum test. Count data were expressed by the number of cases (percentage) and analyzed using the χ^2 test. A p value <0.05 was considered statistically significant.

RESULTS

Epidemiological characteristics of the 129 patients with COVID-19

Among the 129 COVID-19 cases, 59 were diagnosed in the first week (January 24–31), including 42 imported cases (71%), and 33 of them were diagnosed in the last 20 days (February 6–26), including 25 local cases (76%). Among the 70 imported cases, the median time from importing to onset was 5 (2–8) days, and the median time from the first symptom to hospitalization was 5 (2–8) days. Among the 59 local cases, the median time from exposure to onset was 6 (3–10) days, and the median time from the first symptom to hospitalization was 3 (1–5) days, which was significantly lower than that of the imported cases ($p<0.05$).

Clinical characteristics of the 129 patients with COVID-19

Among the 70 imported cases, 37 were males (53%) and 33 were females (47%), with a median age of 39 (31–53) years. Among the 59 local cases, 22 were males (37%) and 37 were females (63%), with a median age of 48 (33–58) years. No statistical difference was found in the age of patients with COVID-19 between the 2 groups. The proportion of several illnesses, including hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular and cerebrovascular diseases, malignant tumors, chronic hepatic disease, chronic kidney disease, and pregnancy, of the 2 groups was nearly the same. The most common first symptom was fever, accounting for 90% of the imported cases (63 of 70)

Table 1 Baseline clinical characteristics of the 129 patients with COVID-19

	Total (n=129)	Imported cases (n=70)	Local cases (n=59)	P value
Sex, n (%)				0.11
Male	59 (46)	37 (53)	22 (37)	
Female	70 (54)	33 (47)	37 (63)	
Age (y)	45 (31–56)	39 (31–53)	48 (33–58)	0.06
Comorbidity, n (%)	28 (22)	14 (20)	14 (24)	0.67
Hypertension	12 (9)	7 (10)	5 (9)	1.0
Diabetes	8 (6)	5 (7)	3 (5)	1.0
COPD	4 (3)	2 (3)	2 (3)	1.0
Coronary heart disease	4 (3)	2 (3)	2 (3)	1.0
Cerebrovascular disease	2 (2)	1 (1)	1 (2)	1.0
Malignant tumor	2 (2)	1 (1)	1 (2)	1.0
Chronic hepatic disease	2 (2)	1 (1)	1 (2)	1.0
Chronic renal disease	2 (2)	1 (1)	1 (2)	1.0
Rheumatoid arthritis	1 (1)	0	1 (2)	0.45
Tuberculosis	1 (1)	1 (1)	0	0.45
Gynecological disease	1 (1)	0	1 (2)	0.45
Pregnancy	2 (2)	1 (1)	1 (2)	1.0
First symptoms, n (%)				
Fever	112 (87)	63 (90)	49 (83)	0.3
37.3°C–38°C	41 (32)	18 (26)	23 (39)	**0.04**
38.1°C–39°C	62 (48)	41 (59)	21 (36)	**0.02**
>39°C	9 (7)	4 (6)	5 (9)	0.45
Cough	73 (57)	42 (60)	31 (53)	0.39
Fatigue	26 (20)	14 (20)	11 (19)	0.85
Poor appetite	7 (5)	5 (7)	2 (3)	0.35
Nasal congestion and runny nose	8 (6)	1 (1)	7 (12)	**0.01**
Myalgia	6 (5)	1 (1)	5 (9)	0.06
Dry and sore throat	12 (9)	3 (4)	9 (15)	**0.03**
Headache	6 (5)	2 (3)	4 (7)	0.53
Diarrhea	3 (2)	2 (3)	1 (2)	1.0
Wheezing	43 (33)	30 (43)	13 (22)	**0.01**
RR (times/min)	20 (20–21)	20 (20–21)	20 (19–21)	0.17
Pulse (times/min)	90 (80–99)	90 (80–98)	90 (80–100)	0.87
Arterial pressure (mm Hg)	97.19 (11.32)	96.44 (11.40)	96.89 (11.11)	0.78

P values in bold represent statistical significance.
COPD, chronic obstructive pulmonary disease; RR, respiratory rate.

and 83.1% of the local cases (49 of 59). The imported cases mainly had moderate fever (58.6% with 38.1°C–39°C), unlike the local cases who mainly had low fever (39% with 37.3°C–38°C, $p<0.05$). For the first symptoms, nasal congestion, runny nose, dry throat, sore throat, and other upper respiratory symptoms appeared more frequently in the local cases ($p<0.05$) whereas wheezing symptoms appeared more frequently in the imported cases ($p<0.05$). No significant differences were found in symptoms such as cough, fatigue, poor appetite, diarrhea, myalgia, and headache between the 2 groups, and no significant differences were observed in the vital signs between the 2 groups at admission. The clinical characteristics of the 129 patients with COVID-19 are shown in table 1.

Laboratory results of the 129 patients with COVID-19

The major laboratory examinations were tracked within 24 hours of hospitalization in the 2 groups. The baseline lymphocyte count in the imported cases (1.03, with a range of 0.69–1.24) was significantly lower than that in the local cases (1.07, with a range of 0.88–1.49, $p<0.05$). No significant differences were found in the other blood routine results, liver and kidney functions, or myocardial enzymes between the 2 groups. Among the inflammation-related indicators, the median C-reactive protein of the local cases was 17.31 (8.15–37.06) mg/L, which was significantly higher than that of the imported cases of 8.6 (1.48–19.2) mg/L ($p<0.05$). The procalcitonin value in the local cases was significantly lower than that in the imported cases ($p<0.05$). The erythrocyte sedimentation rate was increased in both groups. The baseline laboratory findings are shown in table 2.

Disease severity and prognosis of the 129 patients with COVID-19

The number of severe and critically severe cases in the imported group (27 of 70 cases, 38.6%) was higher than that in the local group (11 of 59 cases, 18.6%, $p<0.05$). All cases were given general support, antiviral, anti-infection, and traditional Chinese medicine treatments according to the recommended protocols of the National Health

Table 2 Baseline laboratory findings of the 129 patients with COVID-19

	Total (n=129)	Imported cases (n=70)	Local cases (n=59)	P value
White cell count (×10^9/L) (NR 3.5–9.5)	4.8 (3.6–6.0)	4.64 (3.45–5.68)	4.84 (3.60–6.87)	0.26
Red cell count (×10^{12}/L) (NR 3.8–5.5)	4.58 (0.49)	4.64 (0.47)	4.51 (0.51)	0.13
Hemoglobin (g/L) (NR 115–150)	136.47 (18.81)	139.43 (16.2)	132.98 (20.99)	0.07
Platelet count (×10^9/L) (NR 125–350)	188 (150–234)	187 (157–228)	190 (145–234)	0.98
Neutrophil count (×10^9/L) (NR 1.8–6.3)	3.17 (2.16–4.4)	2.79 (2.17–4.04)	3.57 (2.00–4.75)	0.34
Lymphocyte count (×10^9/L) (NR 1.1–3.2)	1.06 (0.74–1.42)	1.03 (0.69–1.24)	1.07 (0.88–1.49)	**0.04**
Monocyte count (×10^9/L) (NR 0.1–0.6)	0.34 (0.24–0.51)	0.36 (0.23–0.53)	0.34 (0.23–0.53)	0.97
Eosinophil count (×10^9/L) (NR 0.02–0.52)	0.1 (0–0.03)	0.005 (0–0.02)	0.01 (0–0.04)	0.54
Total bilirubin (µmol/L) (NR 0–21)	8.05 (5.67–10.85)	8.40 (5.90–11.04)	7.67 (5.35–10.77)	0.70
Direct bilirubin (µmol/L) (NR 0–6.4)	2.8 (2–3.98)	2.85 (2.00–3.92)	2.70 (2.06–4.19)	0.82
ALT (U/L) (NR 9–50)	22 (14.85–38.3)	24.2 (17–41)	18.12 (14–32.07)	0.21
AST (U/L) (NR 15–40)	23 (17–32)	23.3 (18–30.75)	23 (15–32.9)	0.62
Albumin (g/L) (NR 35–52)	41.5 (37.85–43.9)	41.2 (37.2–44.3)	41.8 (38.5–43.5)	0.72
Creatinine (µmol/L) (NR 59–104)	61.52 (50.52–72.85)	65.4 (20–69)	62.5 (27–32)	0.54
Urea nitrogen (mmol/L) (NR 2.8–7.3)	3.82 (2.92–4.7)	3.66 (2.92–4.83)	4.01 (2.99–4.67)	0.63
Lactate dehydrogenase (U/L) (NR 114–240)	205 (175.3–264)	209.5 (179.75–265.75)	191 (164.9–264.51)	0.38
Creatine kinase (U/L) (NR 26–192)	69 (41–106.65)	61.5 (40.1–90.8)	72.75 (41–127.97)	0.42
Creatine kinase isoenzyme (U/L) (NR 0–25)	11 (7–16)	11.56 (7.00–17.25)	10.4 (6.6–13.4)	0.31
Hydroxybutyrate dehydrogenase (U/L) (NR 72–182)	154 (129.2–189.5)	161.7 (135–190.62)	150 (117.8–190.75)	0.25
Prothrombin time (s) (NR 9–14)	11.3 (10.5–12.2)	11.3 (10.37–12.25)	11.3 (10.57–12.4)	0.89
D-dimer (µg/L) (NR 0–0.55)	0.29 (0.17–0.69)	0.47 (0.15–0.75)	0.27 (0.19–0.43)	0.23
CRP (mg/L) (NR 0–10)	11.7 (2.5–32.26)	8.6 (1.48–19.2)	17.31 (8.15–37.06)	**0.04**
PCT (ng/mL) (NR 0–0.5)	0.08 (0.02–0.38)	0.15 (0.04–1.38)	0.04 (0.02–0.09)	**0.005**
ESR (mm/h) (NR 0–15)	32.04 (24.03)	34.87 (26.45)	26.85 (20.31)	0.22

P values in bold represent statistical significance.
NR, normal range; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; PCT, procalcitonin; ESR, erythrocyte sedimentation rate.

Commission of the People's Republic of China. Three deaths were recorded in the imported group (all males) before the cut-off date (February 29). No deaths occurred in the local group. The severity of patients in the 2 groups is shown in table 3. The average length of stay was 17 (13–21) days in the imported group and 17 (13–20) days in the local group.

Table 3 The severity of the 129 patients with COVID-19

Severity	Mild	Common	Severe	Critically severe
Imported cases (n=70)	2	41	20	7
Local cases (n=59)	4	44	10*	1*
Total (n=129)	6	86	28	9

*P<0.05 versus imported cases.

Imaging characteristics of the 129 patients with COVID-19

All mild cases (n=6) had no pulmonary imaging abnormalities when they were admitted to the hospital. The remaining 123 patients had pulmonary imaging abnormalities at the beginning of the illness onset, among which 68 cases were in the imported group and 55 cases in the

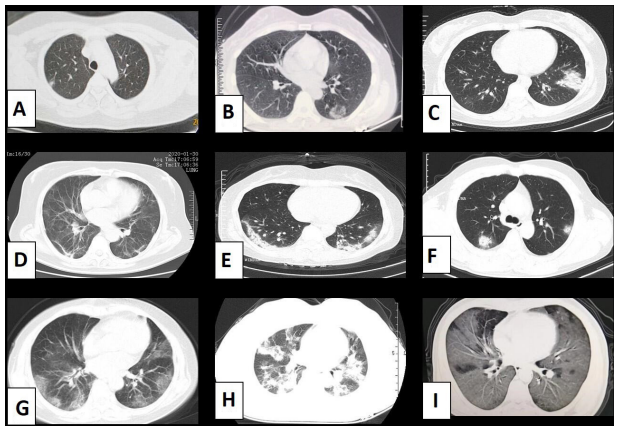

Figure 1 Pulmonary abnormalities of patients with COVID-19 on CT scan. (A) An imported case of a male patient in his 20s with fever for 2 d and chest CT showing ground-glass nodules in the right upper lobe. (B) A local case of a female patient in her 20s with cough for 2 d and chest CT showing pale ground-glass shadow in the left lower lobe. (C) An imported case of a female patient in her 30s with fever for 3 d and chest CT showing a patchy ground-glass shadow in the left lower lobe. (D) A local case of a male patient in his 40s with fever for 4 d and chest CT showing subpleural patchy lesions in both lungs with air bronchus signs. (E) An imported case of a male patient in his 50s with fever for 6 d and chest CT showing confined, flaky ground-glass shadows in both lungs. (F) A local case of a male patient in his 40s with fever and cough for 7 d and chest CT showing multiple patchy lesions in both lungs with bronchiectasis. (G) An imported case of a male patient in his 50s with fever and cough for 10 d and chest CT showing multiple diffuse ground-glass shadows in both lungs. (H) An imported case of a female patient in her 20s with fever for 3 d and chest CT showing multiple patchy shadows in both lungs with air bronchus signs. (I) An imported case of a male patient in his 50s with fever and cough for 7 d and chest CT showing 'white lungs' in both lungs.

local group. The early imaging abnormalities of the patients with COVID-19 mainly showed single or multiple localized ground-glass shadows, small patchy ground-glass shadows, and subpleural strip shadows (figure 1A–E). The advanced imaging abnormalities showed multiple diffuse lesions with density unevenness, which could have air bronchus signs and bronchiectasis, whereas the non-consolidation areas showed patchy ground-glass shadows (figure 1F–H). The severe imaging abnormalities involved both lungs showing 'white lungs' (figure 1I).[7] At the time of admission, 31 cases (44%) showed early imaging abnormalities; 37 cases (53%) showed advanced or severe imaging abnormalities in the imported group, and 35 cases (59%) showed early imaging abnormalities and 20 cases (34%) showed advanced or severe imaging abnormalities in the local group. The proportion of advanced or severe imaging abnormalities was significantly higher in the imported group than in the local group ($p<0.05$).

DISCUSSION

Since Wuhan reported the first patient with COVID-19 in December 2019, the disease has rapidly spread in Hubei Province in China and worldwide. Owing to the Chinese Spring Festival, 5 million workers from Hubei Province migrated into cities across the country, and local people were infected because of close contact with imported cases. This study found that from January 24 to February 26, the patients with earlier confirmed COVID-19 in Nanyang were mainly imported cases, and the patients with later confirmed COVID-19 were mainly local cases, including 3 cases of medical staff. The median incubation period was 5 days, consistent with the study conducted by Guan *et al*.[6]

As reported, virulence of the virus weakens during virus passaging.[8 9] Therefore, attenuated vaccines for various viruses have been produced, such as attenuated rabies virus vaccine and attenuated Japanese encephalitis virus vaccine.[10 11] Huang *et al* first reported that the mortality rate of 41 patients with COVID-19 who were infected with the first generation of SARS-CoV-2 was 15%, and later studies showed that the mortality rate gradually decreased.[1] In Nanyang, the mortality rate of patients with COVID-19 was 1.9% (3 of 156). The latest report by the Chinese Center for Disease Control and Prevention showed that the mortality rate of over 70,000 cases in China was 2.3%,[12] which is lower than the mortality rate of the severe acute respiratory syndrome (SARS; 9.6%) and the Middle East respiratory syndrome (MERS; 37%).[13] The difference in the mortality rate of patients with COVID-19 between Wuhan and Nanyang, China is believed to be related to the number of enrolled cases or the weakened virulence of SARS-CoV-2 after several passages.

In this study, the gender and age compositions of the 2 groups were the same. The most common first symptoms were fever and cough, consistent with the first symptoms reported in previous articles.[14 15] However, the imported cases were dominated by moderate fever (38.1°C–39°C) whereas the local cases were dominated by low fever (37.3°C–38°C). In the local cases, upper respiratory symptoms, such as nasal congestion, runny nose, dry throat, and sore throat, were more common. Such patients could be misdiagnosed with upper respiratory tract infections, making it more difficult to isolate patients with COVID-19 from patients with common influenza. This difference in the first symptoms between the local and imported cases may be due to the different clinical manifestations caused by the different generations of SARS-CoV-2. Therefore, fully understanding the clinical characteristics of patients in different epidemic periods is important.

Wang *et al* compared the laboratory results of 102 COVID-19 mild cases and 36 COVID-19 severe cases and found that the lymphocyte counts of the severe cases were significantly lower than those of the mild cases, suggesting that the degree of lymphocyte decline could be related to the severity of COVID-19.[16] Chang *et al* found that the lymphocyte counts of COVID-19 mild cases were normal, whereas 63%–70.3% of the COVID-19 severe cases had decreased lymphocyte counts.[17] Liu *et al* confirmed that the incidence of lymphopenia in COVID-19 severe cases was higher than that in COVID-19 mild cases (84.6% vs 44.4%) and that the lymphopenia in severe cases was mainly the reduction of T lymphocytes (especially CD8+ T lymphocytes) rather than B lymphocytes or the natural killer cells.[18] The current study found that the lymphocyte counts in the imported cases were significantly lower than those in the local cases. However, whether the decline in lymphocytes is

related to the severity of COVID-19 still requires analyzing a larger sample of cases.

In the current study, the proportion of severe and critically severe cases in the imported group was significantly higher than that in the local group (38.6% vs 18.6%). Three deaths occurred in the imported group whereas no deaths occurred in the local group. These data indicate that the severity and mortality of the local cases were lower than the imported cases. The 3 deaths were all male patients, suggesting that males could have a higher mortality rate than females, consistent with the previous study.[12] Moreover, we found that 6 patients in the 2 groups were mild cases without any clinical symptoms or pulmonary imaging abnormalities. They were diagnosed with COVID-19 by a positive SARS-CoV-2 nucleic acid. As these patients did not have obvious symptoms and did not even see a doctor, they had a high risk of virus transmission. Several studies have reported the existence of asymptomatic virus transmitters.[19–21] Patients with SARS and MERS have obvious clinical symptoms that are not easy to overlook. The fact that COVID-19 has spread faster and wider than SARS in 2002 could be due to the existence of many mild or asymptomatic patients, whom we should be highly vigilant about. Moreover, this study found that the pulmonary lesions of the imported cases showed more advanced and severe lesions at admission whereas the local cases showed mild lesions in the CT images.

In summary, this retrospective cohort study indicates that the patients with COVID-19 in Nanyang were mainly imported cases at the beginning of the spread and were mainly local cases in the later spread. Differences were found in the clinical symptoms, laboratory results, and imaging findings between the imported and local cases. The number of severe or critically severe patients and the mortality rate in imported cases were higher. At present, the complete understanding of COVID-19 is still beyond our knowledge, and whether its virulence weakens after passaging remains unclear and requires further investigation.

Contributors XZ and JZ had the idea for and designed the study and had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. XZ, CS, PL, and YC drafted the paper. JZ, KL, WQ, BJ, and FP did the analysis. All authors critically revised the manuscript for important intellectual content and gave final approval for the version to be published. XZ, CS, PL, YC, JZ, KL, WQ, BJ, and FP collected the data. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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