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Original Article

Clinical characteristics of COVID-19 patients in Xiaogan, China: comparison between recent imported cases and earlier local cases

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Abstract: Object: In this study, we aim to investigate if there exists some change in the pathogenicity of SARS-CoV-2 by comparing the clinical characteristics between recent imported patients and earlier local patients. Methods: 227 local COVID-19 patients diagnosed before February 15, 2020 (local group) and 23 imported COVID-19 patients diagnosed between July 1, 2020, and January 15, 2021 (imported group) were included in this study. Baseline characteristics and characteristics of computed tomography (CT), routine blood test, liver functions, and infectious markers upon admission were collected and compared. Results: The neutrophil-to-lymphocyte ratio (NLR) of the imported group was 3.21 ± 1.25, which was significantly higher than that of the local group (2.55 ± 1.19) with a *P*-value of 0.030. The concentration of C-reactive protein of the imported group was 12.34 ± 5.25, which was significantly higher than that of the local group (7.76 ± 6.54 mg/L) with a *P*-value of 0.0005. No significant difference was observed in the rest characteristics. Conclusion: The recent imported cases had higher NLR and C-reactive protein levels than the earlier local cases, indicating that the pathogenicity of SARS-CoV-2 is getting worse during the pandemic.

Keywords: Coronavirus disease 2019 (COVID-19), imported cases, local cases, clinical characteristics

Introduction

Coronavirus disease 2019 (COVID-19) is caused by infection of the virus SARS-CoV-2, which has a RNA size of about 30 kb. SARS-CoV-2 belongs to β-Coronavirus, and infects host cells through the interaction between its Spike protein to ACE2 of the host cells [1-4]. COVID-19 is easy to induce cluster and hospital infection through droplets and close contact [5], indicating its strong ability to cause spreading from person to person. On January 23, 2020, the World's Health Organization (WHO) announced that the basic reproduction number (R_0) of SARS-CoV-2 ranged from 1.4 to 2.5 [6]. Predictions of other research groups reveal that R_0 of SARS-CoV-2 may be as high as 2.08 to 3.58 [7-10]. Unlike other coronaviruses, such as SARS, whose sources of infection are mainly the patients after the occurrence of symptoms, SARS-CoV-2 can spread by the patients without symptoms, increasing the difficulty to prevent its spreading [11, 12]. COVID-19 patients often have an incubation period ranged from one to 14 days, and most patients appear to have symptoms three to seven days after the infection [13]. COVID-19 is strongly infectious for all people, especially for elders [14]. Elder people also have higher mortality [15].

Since the outbreak of COVID-19 at the end of 2019, it takes a worldwide pandemic until now. WHO had declared COVID-19 as a Public Health Emergencies of International Concern (PHEIC) on January 30, 2020 [16]. As of January 31, 2021, nearly a hundred million people have been diagnosed with COVID-19 and the admitted number is growing rapidly, taking great harm to the economy and people's lives [17]. Contrary to the pandemic of COVID-19 in most countries, China has effectively controlled the spreading of COVID-19 by the lockdown of high-risk regions and regular screening of high-risk populations [18]. Therefore, import from abroad

Table 1. Baseline characteristics of COVID-19 patients

	Local patients (n=227)	Imported patients (n=23)	*P*-value	Significance
Date of diagnosis	Before 15 February 2020	1 July 2020-15 January 2021		
Age, years (Mean ± SD)	50.2 ± 14.7	45.1 ± 12.7	0.351	n.s.
Range of age (years old)	25-81	23-72		
Sex, n (%)			0.828	n.s.
Male	119 (52.42)	13 (56.52)		
Female	108 (47.57)	10 (43.47)		
Clinical types, n (%)			NA	n.s.
Non-severe type	227 (100.00)	23 (100.00)		
Severe type	0 (0.00)	0 (0.00)		
Signs and symptoms, n (%)				
Fever	211 (92.95)	20 (86.96)	0.396	n.s.
Cough	137 (60.35)	15 (65.22)	0.823	n.s.
Chilly	57 (25.11)	7 (30.43)	0.618	n.s.
Myalgia	42 (18.50)	4 (17.39)	1.000	n.s.
Headache	35 (15.42)	7 (30.43)	0.080	n.s.
Chest distress or pain	28 (12.33)	3 (13.04)	1.000	n.s.
Sore throat	11 (4.85)	1 (4.35)	1.000	n.s.
Diarrhea	9 (3.96)	1 (4.35)	1.000	n.s.
Nausea and vomiting	13 (5.73)	1 (4.35)	1.000	n.s.

n.s.: no significance.

is one of the major sources of COVID-19 patients in China. A previous study has shown that there is no significant difference in clinical characteristics between imported and local patients before February 29, 2020 [19]. Recently, several studies have reported the occurrence of mutant strains of SARS-CoV-2, which may affect the infectious ability and pathogenicity of SARS-CoV-2 [20-22]. However, the exact changes of SARS-CoV-2 during the worldwide pandemic remains to be determined. Here, we aim to study if there exists some change in the pathogenicity of SARS-CoV-2 by comparing theclinical characteristics between recent imported patients and earlier local patients.

Materials and methods

Patients

227 local COVID-19 patients that were diagnosed before February 15, 2020 (named as local group) and 23 imported COVID-19 patients that were diagnosed between July 1, 2020, and January 15, 2021 (named as imported group) are enrolled in this study. All the patients were admitted to Hanchuan People's Hospital and had confirmed diagnosis by positive results for SARS-CoV-2 nucleic acid or specific IgM and IgG antibodies of SARS-CoV-2. The clinical typing of COVID-19 patients was performed based on the Diagnosis and Treatment Protocol for COVID-19 established by the National Health Commission [ref]. In brief, patients with any of the following symptoms were considered as severe type: respiratory rate (RR) was more than 30 times per minute, finger arterial oxygen saturation was lower than 93%, or the arterial oxygen partial pressure was lower than 300 mmHg. There is no severe case in imported patients (**Table 1**), so only non-severe cases in local patients were included.

Human samples involved in this study were managed using protocols approved by the Ethical Committee of the Hanchuan People's Hospital (E2020015). Informed consents were obtained from all the patients.

Research methods

Baseline and clinical characteristics of all the COVID-19 patients were confirmed or analyzed upon admission. In detail, characteristics of age, sex, clinical types, signs and symptoms,

Table 2. CT characteristics of COVID-19 patients

	Local patients (n=227)	Imported patients (n=23)	*P*-value	Significance
Unilateral pneumonia, n (%)	31 (13.66)	4 (17.39)	0.541	n.s.
Bilateral pneumonia, n (%)	172 (75.77)	19 (82.61)	0.609	n.s.
Multiple mottling and ground-glass opacity, n (%)	34 (14.98)	5 (21.74)	0.373	n.s.
Normal, n (%)	33 (14.54)	3 (13.04)	1.000	n.s.

n.s.: no significance.

computed tomography (CT), blood routine, liver functions, and infectious markers were collected.

Statistical analysis

Continuous variables were presented as mean ± SD and categorical variables were presented as number (present). Statistical analysis was performed using SPSS18.0 software. Comparisons of continuous variables between different groups were performed using the Mann-Whitney test. Comparisons of categorical variables between different groups were performed using Fisher's exact test. *P*-values less than 0.05 were considered significant.

Results

Baseline characteristics of imported and local COVID-19 patients

227 local COVID-19 patients that were diagnosed before February 15, 2020 (named as local group) and 23 imported COVID-19 patients (named as imported group) that were diagnosed between July 1, 2020, and January 15, 2021, were included in this study. The baseline characteristics of the patients are listed in **Table 1**. The age of the local group ranged from 25 to 81 years, while the age of the imported group ranged from 23 to 72 years. Although the average age of the imported group (45.1 ± 12.7 years) was lower than that of the local group (50.2 ± 14.7 years), there was no statistical difference between them (P= 0.351). And there was no significant difference in the sex constitution between the local group (119 (52.43%) males and 108 (47.57%) females) and the imported group (13 (56.52%) males and 10 (43.47%) females). All the imported patients were of the non-severe type, so only non-severe local patients were included.

There was no statistical difference between the signs and symptoms of both groups. The main symptoms of the COVID-19 patients were fever (92.95% in the local group and 86.96% in the imported group) and cough (60.35% in the local group and 65.22% in the imported group). Other common symptoms included chilly (25.11% in the local group and 30.43% in the imported group), myalgia (18.50% in the local group and 17.39% in the imported group), headache (15.42% in the local group and 30.43% in the imported group), and chest distress or pain (12.33% in the local group and 13.04% in the imported group). It seemed that the imported group had a higher headache ratio. However, there was no statistical difference. Sore throat, diarrhea, and nausea and vomiting were less common with ratios of no more than 5% in both groups.

Clinical characteristics of imported and local COVID-19 patients

The CT characteristics of the patients are listed in **Table 2**. Most patients (75.77% in the local group and 82.61% in the imported group) had the symptom of bilateral pneumonia. 13.66% to 21.74% of patients had symptoms of unilateral pneumonia or multiple mottling and ground-glass opacity. However, a portion of the COVID-19 patients (14.54% in the local group and 13.04% in the imported group) had no CT symptoms. We did not observe any significant difference between the CT characteristics of both groups.

The information about blood routine of the patients is listed in **Table 3**. The concentrations of the leucocytes, neutrophils, monocytes, platelets, and hemoglobin of the COVID-19 patients had no big changes using the normal ranges as references. The average concentration of the COVID-19 patients' lymphocytes was lower than the bottom limitation of the normal range,

Table 3. Blood routine of COVID-19 patients

	Normal range	Local patients (n=227)	Imported patients (n=23)	*P*-value	Significance
Leucocytes, $*10^9$ per L	4-10	5.28 ± 1.66	4.92 ± 1.87	0.397	n.s.
Neutrophils, $*10^9$ per L	2-7.7	2.93 ± 1.43	3.19 ± 1.57	0.228	n.s.
Monocytes, $*10^9$ per L	0.1-0.6	0.37 ± 0.11	0.40 ± 0.13	0.520	n.s.
Lymphocytes, $*10^9$ per L	1.2-3.2	1.13 ± 0.42	0.95 ± 0.46	0.258	n.s.
Platelets, $*10^9$ per L	100-300	184.56 ± 53.27	169.73 ± 59.67	0.374	n.s.
Hemoglobin, g/L	120-160	133.85 ± 13.27	136.76 ± 15.29	0.593	n.s.
Neutrophil-to-lymphocyte ratio, NLR	NA	2.55 ± 1.19	3.21 ± 1.25	0.030	*
Lymphocyte-to-monocyte ratio, LMR	NA	3.01 ± 1.03	2.73 ± 0.81	0.193	n.s.
Platelet-to-lymphocyte ratio, PLR	NA	160.58 ± 46.91	170 ± 55.32	0.354	n.s.

n.s.: no significance; *P<0.05.

Table 4. Liver functions of COVID-19 patients

	Normal range	Local patients (n=227)	Imported patients (n=23)	*P*-value	Significance
Albumin, g/L	40-55	36.81 ± 3.57	37.60 ± 4.12	0.218	n.s.
Alanine aminotransferase, U/L	7-40	19.61 ± 5.49	20.91 ± 7.46	0.342	n.s.
Aspartate aminotransferase, U/L	15-40	26.85 ± 10.52	27.59 ± 11.19	0.223	n.s.
Total protein, g/L	65-85	67.36 ± 6.59	64.29 ± 8.67	0.483	n.s.
Total bilirubin, mmol/L	0-21	11.21 ± 3.88	11.16 ± 3.69	0.598	n.s.

indicating most COVID-19 patients had obviously decrease in lymphocytes. We did not observe any significant difference between the blood routine indexes of both groups except neutrophil-to-lymphocyte ratio (NLR). The NLR of the imported group was 3.21 ± 1.25, which was significantly higher than that of the local group (2.55 ± 1.19) with a *P*-value of 0.030.

The information about liver functions of the patients is listed in **Table 4**. The liver function indexes included albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total protein, and total bilirubin. We did not observe any significant difference between the liver functions of both groups.

The information about infectious markers of the patients is listed in **Table 5**. In detail, the concentrations of procalcitonin of the local and imported groups were 0.24 ± 0.34 ng/mL and 0.27 ± 0.24 ng/mL, respectively, which were both higher than the reference value. Moreover, both groups had higher concentrations of C-reactive protein, of which, the imported group had a concentration of C-reactive protein even higher than the local group with a *P*-value of 0.0005 (7.76 ± 6.54 mg/L in the local group and 12.34 ± 5.25 mg/L in the imported group).

Discussion

COVID-19 is now a worldwide pandemic and is threatening people's lives erery day. In this study, we reported the clinical characteristics of the recent imported COVID-19 patients (diagnosed between July 1, 2020, and January 15, 2021) and the earlier local patients (diagnosed before February 15, 2020), and compared the differences between them, aiming to determine if there exists some change in the pathogenicity of SARS-CoV-2.

A Chinese group has shown that there is no difference between the imported patients and the local patients before February 25, 2020 [19]. Therefore, our study strategy may represent the changes in the pathogenicity of SARS-CoV-2 during the pandemic.

We found that fever and cough are the most initial common signs in both groups, consistent with previous studies [23-25]. Body temperature detection is now the most regular method for primary screening of COVID-19. However, in our study, about 10% of COVID-19 patients had no sign of fever, indicating the necessity of the combination of other screening methods to pre-

Table 5. Infectious markers of COVID-19 patients

	Normal range	Local patients (n=227)	Imported patients (n=23)	*P*-value	Significance
Procalcitonin, ng/mL	0-0.046	0.24 ± 0.34	0.27 ± 0.24	0.846	n.s.
C-reactive protein, mg/L	0-5	7.76 ± 6.54	12.34 ± 5.25	0.0005	***

n.s.: no significance; ***P<0.001.

vent missed diagnosis, especially in high-risk populations.

Several research groups had reported that the COVID-19 patients had low concentrations of lymphocytes [26-28]. We observed the same phenomenon in COVID-19 patients. Until now, the pathogenesis of COVID-19 is not clear and has its unique features distinguished from other virus-induced diseases, which often leads to an increased number of lymphocytes [29]. It has been reported that the lymphocytes of COVID-19 patients often reached the minimum three to seven days after the onset of sick, which is longer than that of Severe Acute Respiratory Syndrome (SARS) [ref], indicating a longer influence of COVID-19 on lymphocytes. Other studies have shown that the viral particles of SARS-CoV-2 may invade lymphocytes and thus lead to necrosis of the lymphocytes [ref], which may explain why the number of lymphocytes decreases in COVID-19 patients.

SARS-CoV-2 is a kind of RNA virus that has a high mutant frequency. Recently, several studies have reported the occurrence of mutant strains of SARS-CoV-2. A mutant strain VUI-202012/01 found in Britain is reported to have a dramatically higher growth rate (71% higher, 95% CI: 67%-75%) than the normal strains [30]. Another variant 501.V2 Variant found in South Africa is reported to have three mutations in the receptor-binding domain (RBD) of SARS-CoV-2, higher viral load and infectivity, and an ability to escape the neutralization of antibodies [31, 32]. These studies indicate that SARS-CoV-2 may probably have changes in its pathogenicity. In our study, even though there is no significant difference between the age of the two groups, the average age of the imported group is lower than the local group, indicating increased infectivity of SARS-CoV-2 to the young people. However, a larger size of the imported group is needed. Hong-Liang Li's group has reported that a higher NLR refers to a poor prognosis [33]. Our data showed that the imported group had a higher NLR than the local group, indicating the pathogenicity of SARS-CoV-2 is getting worse. Additionally, the concentration of C-reactive protein was higher in the imported group than the local group, indicating SARS-CoV-2 may induce worse inflammation now. This may be explained by the ability to escape the neutralization of antibodies and the higher viral load of SARS-CoV-2 variants. It is worth noting that the imported group had a higher rate of headache, however, this needs further studies to prove.

In conclusion, this study found that the recent imported cases had higher NLR and C-reactive protein levels than the earlier local cases, indicating that the pathogenicity of SARS-CoV-2 is getting worse during the pandemic. However, some improvements may apply to this study. First, the size of the imported group could be enlarged to improve the accuracy of the data. Secondly, there is no severe patients were included in this study, limiting the applicability of the findings and calling for more patients in more disease types. Finally, a comparison of the genome sequences may be needed in further study to construct better relationships between the symptoms and the viral strains.

Disclosure of conflict of interest

None.

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