Original Article

Optimizing screening strategies for coronavirus disease 2019: A study from Middle China

Li Liu a, Xiuxin Hong b, Xin Su c, Haiou Chen a, Dongcui Zhang a, Shigang Tang a, Liang Chen a, Baining Zhu a, Xiaosong Li b,⁎, Yi Shi c,⁎

a Department of Infectious Disease, Hunan Provincial People’s Hospital (The First Affiliated Hospital of Hunan Normal University), Changsha, Hunan Province, China
b Laboratory of Clinical Epidemiology, Hunan Provincial People’s Hospital (The First Affiliated Hospital of Hunan Normal University), Changsha, Hunan Province, China
c Department of Respiratory and Critical Care Medicine, Jinling Hospital, Medical School of Nanjing University, Nanjing, China

A R T I C L E   I N F O

Article history:
Received 21 February 2020
Received in revised form 3 May 2020
Accepted 5 May 2020

Keywords:
COVID-19
Screening strategies

A B S T R A C T

Background: Coronavirus disease 2019 (COVID-19) has been highly epidemic in China since January 2020. Rapid detection of the causative agent, severe acute respiratory coronavirus-2 (SARS-CoV-2), is very important due to its high rate of infectivity. This study aimed to clarify the epidemiology and clinical characteristics of COVID-19 outside of Hubei province, China, and to optimize screening strategies for COVID-19 in attempts to contain spread of the virus.

Methods: This retrospective study included all confirmed cases of COVID-19 in Hunan Provincial People’s Hospital (Changsha, China) between January 22 and February 15, 2020. All cases were detected using a real-time reverse transcription polymerase chain reaction assay. The epidemiology and clinical characteristic of these cases were investigated according to outcome in attempts to optimize screening strategies for COVID-19.

Results: There were 24 confirmed cases of COVID-19 in the fever outpatient department of Hunan Provincial People’s Hospital. Three patients were asymptomatic, and 3 exhibited mild and 3 moderate disease. There was a family cluster phenomenon.

Conclusion: Individuals with COVID-19 can be asymptomatic or exhibit mild manifestations of disease. Close monitoring and an optimized screening strategy for COVID-19 could help deter spread of the virus.

副主任: © 2020 Published by Elsevier Ltd on behalf of King Saud Bin Abdulaziz University for Health Sciences. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Reports of infections caused by a novel coronavirus, severe acute respiratory coronavirus-2 (SARS-CoV-2), began to emerge from Wuhan, Hubei province, China, shortly after December 8, 2019 [1–3]. The disease caused by the virus reached epidemic status in January 2020 [4–7]. On January 7, 2020, the novel coronavirus (i.e., SARS-CoV-2) was identified by the Chinese Center for Disease Control and Prevention (CDC) from a throat swab sample of a patient, and the disease caused by this virus was officially termed “COVID-19” by the World Health Organization on February 11, 2020 [8]. In the initial stages of the outbreak, most infected patients were exposed to SARS-CoV-2 at the local Huanan Seafood Market [9], and the epidemiological history has subsequently been replaced by a history of travel or residence in Wuhan within 14 days of onset. This later changes, with most patients emerging in other provinces of China [10,11]. Initially, researchers found that SARS-CoV-2 infection caused severe acute respiratory symptoms, and some patients developed respiratory distress syndrome, acute respiratory failure, and other organ complications including sepsis and sepsis shock approximately 1 week after infection [9,12,13]. However, it was found that many patients experienced only symptoms and many others who exhibited no symptoms [10].

COVID-19 is characterized by rapid transmission and atypical clinical symptoms. It is easy to miss diagnosis and/or to misdiagnose. To contain spread of the epidemic, it is very important

Abbreviations: CDC, Center for Disease Control and Prevention (China); COVID-19, coronavirus disease 2019; CT, computed tomography; PCT, procalcitonin; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; SARS-CoV, severe acute respiratory syndrome coronavirus; MERS-CoV, Middle East respiratory syndrome coronavirus; RT-PCR, real-time reverse transcription polymerase chain reaction; CAP, acquired community pneumonia; lymphocytes; WBC, white blood cells; IgM, immunoglobulin (Ig) M; IgG, immunoglobulin (Ig) G.

⁎ Corresponding authors.

E-mail addresses: lhx0308@sina.com (X. Li), shiys56@126.com (Y. Shi).

https://doi.org/10.1016/j.jiph.2020.05.003
1876-0341/© 2020 Published by Elsevier Ltd on behalf of King Saud Bin Abdulaziz University for Health Sciences. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
to screen for patients with COVID-19, especially in areas outside of Hubei province. This retrospective study included 24 patients, who were diagnosed with confirmed COVID-19 at the fever outpatient department at Hunan Provincial People's Hospital (Changsha, China), to explore disease characteristics and optimize screening strategies for COVID-19.

Methods

Study design and participants

This retrospective study included patients diagnosed with COVID-19 according to guidelines from the Chinese National Health Commission [14] at the fever outpatient department of Hunan Provincial People’s Hospital (Tianxinge Hospital and Mawangdui Hospital, Changsha, China) between January 22 and February 15, 2020. The study was approved by the Ethics Committee of the Hunan Provincial People’s Hospital.

Procedures

Epidemiology data, demographic information, clinical symptoms, laboratory test results, and chest CT images of all patients with confirmed COVID-19 were collected from fever outpatient medical records. Throat swab specimens from the upper respiratory tract were obtained from all patients for real-time RT-PCR assay. Tests for other respiratory viruses including adenovirus, influenza A virus and B virus, and H7N9 virus, were also performed. At the same time, routine laboratory investigations were also performed, including those for procalcitonin (PCT), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), in addition to chest CT.

Statistical analysis

Continuous data with normal distribution are expressed as mean; non-normally distributed continuous data are expressed as median. Categorical variables are expressed as count and percentage (i.e., n [%]). Results of laboratory investigations were also assessed as to whether they were normal or outside the normal range. Statistical analysis was performed using SPSS version 20.0 (IBM Corporation, Armonk, NY, USA).

Results

Real-time RT-PCR confirmed SARS-CoV-2 infection in 24 patients, 16 (66.7%) of whom were women; the mean age of the patients was 43 years (range, 12–84 years). Nearly every patient had a clear epidemiological history. Of 9 (37.5%) patients with a history of travel or residence in Wuhan within 14 days of onset, 3 (12.5%) were in contact with patients from Wuhan. Eleven (45.83%) patients had contact with confirmed cases in Changsha, and only 1 patient did not have any known epidemiological history; 4 family clusters were detected (Table 1).

Among all confirmed cases in the fever outpatient department, 19 (79.17%) had fever, 6 (25%) had dry cough, 6 (25%) had fatigue, 4 (16.67%) had dizziness; other symptoms included loss of appetite, muscle ache, headache, and shortness of breath (Table 2). In the fever outpatient department, leukocycte, lymphocyte, and platelet counts were in the normal range in most patients (Table 2). Three (12.5%) patients were asymptomatic, 3 exhibited mild symptoms, most of them were of medium severity. No patients experienced organ damage from sepsis, septic shock, or respiratory failure. There was a family cluster phenomenon (Table 2). No patients were co-infected with other viruses. PCT levels and ESR were tested, most of which were in the normal range (Table 2); however, one-half

| Table 1 | Demographics and baseline characteristics of patients with COVID-19. |
|---------|---------------------------------------------------------------|
| Patients (n = 24) | Age, years |
| | Mean |
| | 43 (12–84) |
| Range | 18–60 |
| | 14 (58.33%) |
| >60 | 9 (37.5%) |
| Sex | Female |
| | 16 (66.67%) |
| Male | 8 (33.33%) |
| Expositional history (within 14 days of onset) | Exposure to Huanan seafood market |
| | 0 |
| History of travel or residence in Wuhan | 9 (37.5%) |
| Contact with patients from Wuhan | 3 (12.5%) |
| Contact with confirmed patients in Changsha | 11 (45.83%) |
| Have no clear epidemiological history | 1 (4.17%) |
| Family cluster | 4 families |

| Table 2 | Clinical characteristics of patients with COVID-19. |
|---------|---------------------------------------------------------------|
| Patients (n = 24) | Signs and symptoms |
| | Fever |
| | 19 (79.17%) |
| | Dry cough |
| | 6 (25%) |
| | Fatigue |
| | 6 (25%) |
| | Dizziness |
| | 4 (16.67%) |
| | Loss appetite |
| | 2 (8.33%) |
| | Muscle ache |
| | 2 (8.33%) |
| | Headache |
| | 4 (16.67%) |
| | Shortness of breath |
| | 2 (8.33%) |
| Laboratory test | Leucocytes (× 10⁹ per L; normal range: 3.5–10) |
| | Normal range |
| | 19 (79.17%) |
| | Decreased |
| | 5 (20.83%) |
| Lymphocytes (× 10⁹ per L; normal range: 1.1–3.2) |
| | Normal range |
| | 22 (91.67%) |
| | Decreased |
| | 2 (8.33%) |
| Platelets (× 10⁹ per L; normal range: 100–300) |
| | Normal range |
| | 24 (100%) |
| Procalcitonin (ng/mL; normal range: 0–0.5) |
| | Normal range |
| | 22 (91.67%) |
| | Decreased |
| | 2 (8.33%) |
| Erythrocyte sedimentation rate (mm/h; normal range: 0–15) |
| | Increased |
| | 6 (25%) |
| | Normal range |
| | 18 (75%) |
| C-reactive protein (mg/L; normal range: 0–5) |
| | Increased |
| | 12 (50%) |
| | Normal range |
| | 12 (50%) |
| CT findings | No pneumonia |
| | 6 (25%) |
| | Pneumonia |
| | 18 (75%) |
| Symptoms and pneumonia | Neither symptoms nor pneumonia |
| | 3 (12.5%) |
| | Both symptoms and pneumonia |
| | 18 (75%) |
| | Symptoms but no pneumonia |
| | 3 (12.5%) |
| | No symptoms but pneumonia |
| | 0 |
| Type | Asymptomatic infection |
| | 3 (12.5%) |
| Mild |
| | 3 (12.5%) |
| Moderate |
| | 18 (75%) |
| Severe |
| | 0 |

patients exhibited increased CRP levels. According to chest CT, 19 (79.17%) patients exhibited pneumonia while all others were normal. All patients were transferred to designated hospitals for isolation and treatment.

Discussion

Since the outbreak of COVID-19 in Wuhan City, Hubei province, in December 2019 [13,14], the disease has spread to the entire country, including Hong Kong, Macao, and Taiwan, and to at least
23 countries globally [4–7,15,16]. It has already surpassed severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) in the number of individuals infected. COVID-19 is considered to be a serious disease and, perhaps more severe than SARS, although this is only speculation by the scientific community. Overall, COVID-19 in Wuhan appears to be clinically milder than SARS or MERS in terms of severity, mortality rate, and transmissibility [17]. SARS, which was caused by SARS-CoV, first emerged in China in 2002, and then spread to 29 countries/regions in 2003, with 8089 cases. The fatality rate of SARS was 9.6% and that of MERS was 37% [18]. However, the fatality rate of COVID-19 is only 2.1% in China according to new data from Chinese authorities. In areas outside of non-Hubei province, the mortality rate is low (0.16%) [19]. Results of the present study, however, provide some information about COVID-19 outside of Hubei province.

Initially, virtually all patients exhibited significant epidemiological characteristics. Nine (37.5%) patients had travel or residence history in Wuhan; all of these cases were imported. Fourteen (58.33%) patients had contact with individuals with confirmed COVID-19; these were two-generation cases. Only one patient had no clear epidemiological history and, perhaps, was a third-generation case. At the same time, there was a family cluster phenomenon [15,20]. There were four families in which most members were infected accounting for one-half of the total cases.

We found that 12.5% patients exhibited asymptomatic infection. They were suspected based on epidemiological history and confirmed by RT-PCR; as such, they were infectious sources. This could explain why COVID-19 rapidly spread across the entire country in <2 months. Chang et al. reported that the higher number of infections may be attributed to asymptomatic infection and delayed identification of etiology [10].

Chart 1. Optimizing screening strategies for COVID-19.
Third, in our study, the main clinical manifestations of COVID-19 were fever (79.17%), often accompanied by respiratory symptoms such as dry cough. Some patients experienced systemic symptoms such as fatigue, dizziness, and headache. Few patients presented with loss of appetite, muscle ache, and/or shortness of breath.

Fourth, our results were different from those of studies from Wuhan when comparing laboratory investigations and chest CT findings. In our study, the results of most blood tests were normal. Regarding lymphocyte count, 91.67% of patients were normal. Data from previously published studies [12,13] from Wuhan conflict with this finding. For chest CT, 75% patients had pneumonia, the majority of patients had both symptoms and pneumonia, and few patients had neither symptoms nor pneumonia, and few had symptoms but no pneumonia; however, there were no patients with pneumonia and no symptoms.

Although the present study included only a small number of patients, it provides another perspective to assess the epidemiology and clinical characteristics of COVID-19 outside of Wuhan, Hunan province, which in turn may provide valuable clues about screening for COVID-19 in other regions, both domestically and abroad.

All cases were imported from non-Hubei province in China before January 25, 2020, followed by family cluster cases. Currently, non–Hubei provinces are mainly experiencing imported and family cluster cases. Prevention and control measures are critical, and attempts to terminate the community transmission chain should be resolute. An optimized screening strategy for COVID-19 could help contain spread of the virus.

Based on the above observations, we propose that the current screening process for COVID-19 should be combined with epidemiological history, clinical manifestations, laboratory investigations, and chest CT for individuals outside of Hubei province. Asymptomatic carriers contribute to the difficulty of prevention and management. Screening asymptomatic carriers played an important role in controlling the initial spread of the epidemic [21]. Therefore, at first, we suggest close follow up for all individuals with an epidemiological history but no symptoms; second, it was reported that the sensitivity of the RT-PCR method for throat swab samples ranged from 30% to 60% due to the limitations of sample collection and detection method [22]. It has been reported that some patients with positive chest CT findings may have negative RT-PCR results. Chest CT can provide important diagnostic information; therefore, individuals who have negative RT-PCR with an epidemiological history or have fever or respiratory symptoms after chest CT revealing pneumonia should undergo RT-PCR testing for COVID-19. Lymphopenia is a significant characteristic of COVID-19. For patients without pneumonia but abnormal routine blood tests, RT-PCR should also be performed for COVID-19. Finally, in addition to viral RNA detection, measurement of immunoglobulin (Ig) M and IgG antibody levels would be very helpful. Antibody testing can aid in the diagnosis of COVID-19 when combined with RT-PCR [23] (Chart 1).

These processes will help optimize screening for COVID-19 outside of Hubei province. It is very important to effectively screen for and isolate infected patients due to the high transmissibility of SARS-CoV-2.

In conclusion, individuals with COVID-19 can be asymptomatic or present only mild manifestations of the disease. Close monitoring and an optimized screening strategy for COVID-19 could help contain spread of the virus and limit the extent of the pandemic.

Authors’ contributions

DZ, ST, BZ, HC, and LC collected the epidemiological and clinical data and processed statistical data, XQ analyzed all data, LL drafted and edited the manuscript. YS and XS participated in the design and XL revised the manuscript.

Funding

This study was supported by the Scientific Research Fund from Hunan Provincial Health Committee (No. 20200034).

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee of the Hunan Provincial People’s Hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of interests

All authors declare that they have no conflict of interest.

Acknowledgements

We would like to thank Editage (www.editage.cn) for English language editing.

References

[1] WHO. Novel coronavirus–China. January 12, 2020. http://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/ [accessed 19 January 2020].

[2] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727–33, http://dx.doi.org/10.1056/NEJMoa2001017.

[3] Roujian Lu, Xiang Zhao, Juan Li, et al. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. January 29, 2020. https://www.thelancet.com. Published online January 29, 2020. https://doi.org/10.1016/S0140-6736(20)30251-8.

[4] WHO. Novel coronavirus – Thailand (ex-China). January 14, 2020. http://www.who.int/csr/don/14-january-2020-novel-coronavirusthailland/en/ [accessed 19 January 2020].

[5] WHO. Novel coronavirus – Japan (ex-China). January 17, 2020. http://www.who.int/csr/don/17-january-2020-novel-coronavirusjapan-ex-china/en/ [accessed 19 January 2020].

[6] WHO. Novel coronavirus – Republic of Korea (ex-China). January 21, 2020. http://www.who.int/csr/don/21-january-2020-novel-coronavirus-republic-of-korea-ex-china/en/ [accessed 23 January 2020].

[7] CDC. First travel-related case of 2019 novel coronavirus detected in United States. January 21, 2020. https://www.cdc.gov/media/releases/2020/p0121-novel-coronavirus-travel-case.html [accessed 23 January 2020].

[8] WHO. Director-General’s remarks at the media briefing on COVID-19 outbreak on 14 February 2020. January 21, 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-covid-19-outbreak-on-14-february-2020 [accessed 14 February 2020].

[9] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. January 29, 2020. www.thelancet.com. Published online January 29, 2020. https://doi.org/10.1016/S0140-6736(20)30211-7.

[10] Chang, Lin M, Wei L, Xie L, Zhu G, Della Cruz CS, et al. Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. JAMA 2020. http://dx.doi.org/10.1001/jama.2020.1623, 2020 February 7.

[11] WHO. Emergencies preparedness, response. Pneumonia of unknown origin – China. Disease outbreak news. 2020-01-22. https://www.who.int/csr/don/22-january-2020-novel-coronaviruschina/en/ [accessed 12 January 2020].

[12] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. www.thelancet.com. Published online January 24, 2020. https://doi.org/10.1016/S0140-6736(20)30183-5.

[13] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020. http://www.jama.com. Published online February 17, 2020. [http://dx.doi.org/10.1001/jama.2020.1585. Published online February 17, 2020.]

[14] [http://www.nhc.gov.cn/xcs/zxwjwxx2020/d48b95337e19445fd728cafe13e1a.shtml].

[15] Phan LT, Nguyen TV, Luong QC, Nguyen TV, Nguyen HT, Le HQ, et al. Importation and human-to-human transmission of a novel coronavirus in Vietnam. N Engl J Med 2020;382:872–4. http://dx.doi.org/10.1056/NEJMoa2001272.

[16] Holsue ML, DeBolt C, Lindquist S, Loify KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med 2020;382:926–9, http://dx.doi.org/10.1056/NEJMoa2001347.

[17] Hui DS, Azhar I, Madani E, Ntoumi TA, Kock F, Dar RO, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health – the latest 2019
novel coronavirus outbreak in Wuhan, China. Int J Infect Dis 2020;91:264–6, http://dx.doi.org/10.1016/j.ijid.2020.01.009.

[18] de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol 2016;14:523–34, http://dx.doi.org/10.1038/nrmicro.2016.81.

[19] http://www.nhc.gov.cn/xcs/fkdt/202002/35990d56cfcb43f4a70d7f9703b113c0.shtml.

[20] Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020;395(10223):514–23, http://dx.doi.org/10.1016/S0140-6736(20)30154-9.

[21] Lu S, Lin J, Zhang Z, Xiao L, Jiang Z, Chen J, et al. Alert for non-respiratory symptoms of coronavirus disease 2019 (COVID-19) patients in epidemic period: a case report of familial cluster with three asymptomatic COVID-19 patients. J Med Virol 2020, http://dx.doi.org/10.1002/jmv.25776. March 19.

[22] Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of chest ct and rt-pcr testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology 2020:200642.

[23] Liu W, Liu L, Kou G, Zheng Y, Ding Y, Ni W, et al. Evaluation of nucleocapsid and spike protein-based ELISAs for detecting antibodies against SARS-CoV-2. J Clin Microbiol 2020, http://dx.doi.org/10.1128/JCM.00461-20.