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Research Article

COVID-19 screening-A report from a fever clinic in Shenzhen, China

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Abstract

Background: PCR screening for COVID-19 has a significant false-negative rate and requires several hours to complete. A fever clinic was set up at Shekou Hospital, Shenzhen, China to rapidly identify high-risk patients.

Methods: A total of 5,710 patients were screened on the basis of (1) epidemiological history and symptoms, (2) pneumonia on chest CT scan, (3) white blood cell count, and (4) evaluation by a senior physician. Confirmative diagnosis was based on two positive PCR tests.

Results: A total of 247 patients were quarantined pending confirmative diagnosis. Nine had confirmed COVID-19. Of those, all had COVID-19–related symptoms, and eight had positive epidemiological history. Chest CT scans for pneumonia were positive in seven confirmed cases and indeterminate in two confirmed cases. The sensitivity, specificity, positive predictive value, and negative predictive value of the rapid screening were 100%, 93.39%, 3.64%, and 100%, respectively.

Conclusion: Rapid screening helped to quickly identify and isolate patients with COVID-19.

Introduction

In December 2019, a new coronavirus pneumonia occurred in Wuhan, Hubei Province, China [1-3]. The World Health Organization named the disease COVID-19 on February 11, 2020 [4]. At the same time, the International Committee for Virus Classification named the novel coronavirus SARS-CoV-2 [5]. With the spread of COVID-19, many cases appeared in other parts of China and around the world.

Because of the effective prevention and control measures taken in China, COVID-19 is now under control in this country. However, the situation is still serious in many other parts of the world. More than 95 million cases have been reported, and the cumulative death toll is 2,029,938 according to a report on Jan 17, 2021 [6].

Screening to identify patients with COVID-19, among other patients with fever or cough with a different etiology, is one of the key steps in controlling the COVID-19 pandemic. This report describes experiences with COVID-19 screening in the fever clinic of Shekou Hospital, Shenzhen, China in order to inform medical staffs and policy makers elsewhere that are faced with a similar situation.

Shenzhen has more immigrants than any other city in China and is also one of the most economically important cities in China. Until Jan 17, 2021, 485 confirmed cases of COVID-19 were reported in Shenzhen [7]. In order to avoid nosocomial spread of COVID-19, Shekou Hospital set up a fever clinic on January 20, 2020 that remained opened 24 h to deal with patients with undiagnosed fever or respiratory symptoms or a history of exposure to COVID-19. Any patients that presented

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unstable vital signs were immediately transferred to the emergency room.

Materials and methods

Design

In this retrospective study, presenting symptoms, epidemiological data, peripheral white blood-cell count and classification, chest CT scan and RT-PCR results, and other clinical data were collected from the patients' medical charts. The primary goal of the study was to assess the reliability of a rapid screening and quarantine model based on a constellation of four parameters: Clinical symptoms, Epidemiological history, White blood-cell count and Chest CT scan results. The details of the screening process are shown in Figure 1. This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Shekou People's Hospital, Shenzhen, China.

Subjects and data collection

This report describes the screening of patients referred to the fever clinic of Shekou Hospital from January 20, 2020 to February 29, 2020. During that period, patients with COVID-19 mainly came to Shenzhen from Wuhan and nearby areas.

The first case imported from a foreign country was confirmed in Shenzhen city on March 1, 2020 [8]. The screening for COVID-19 after March 1, 2020 will be described in another paper.

The purpose of the fever clinic was to receive, screen, and quarantine patients with fever or respiratory symptoms or positive epidemiological history of COVID-19 exposure. Patients with unstable vital signs were sent to the emergency room instead of the fever clinic. Patients that visited the fever clinic repeatedly, had incomplete clinical data, or those without SARS-CoV-2 test results were excluded from the current report.

The COVID-19 incubation period

The incubation period was defined as the interval between the earliest day of potential contact with the infection source (animal or person with suspected or confirmed infection) and the first day of symptoms [9]. The usual incubation period of COVID-19 is 3–7 days according to the Chinese national prevention and treatment guidelines for COVID-19 [10]. Each patient's exposure to COVID-19 was classified as category 1 (<7 days since first contact with the potential source), category 2 (7–14 days since first contact), or category 3 (>14 days since first contact; patients with an incubation period longer than 14 days were reported very early in the COVID-19 pandemic). Confirmed contact with infected individuals and family clustering were recorded specifically.

Epidemiological history

Patients meeting any one of the following criteria were defined as having a positive epidemiological history [10]: return from Wuhan or other high-risk area within the past 14 days, contact with an individual with confirmed COVID-19 within the past 14 days, or contact with an individual with fever who returned from a high-risk area within the past 14 days. Cluster cases were defined as two or more cases of fever and/or respiratory symptoms in the same family or office within 14 days.

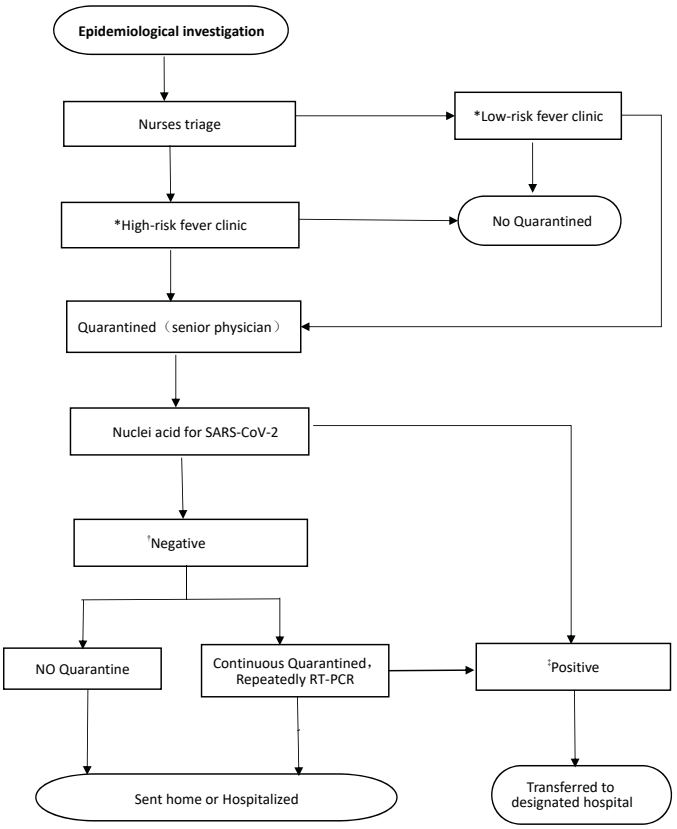

Figure 1: *Symptoms, epidemiological history, white blood cell count, nucleic acid for SARS-Coronavirus-2, chest CT scan, and other tests.
†Nucleic acid should be negative at least two times for highly suspected patients before quarantine is cancelled. Regularly follow-up is still necessary for some patients at home by telephone if he /she is not ruled out thoroughly.
‡The sample must be sent to the municipal CDC for confirmation if the first laboratory result is positive.

Chest CT scan

Chest CT scan was performed on all consenting adult patients using a high-resolution Light Speed VCT CT16 scanner (GE MEDICAL SYSTEMS, China), as long as there was no contraindication. The CT results were classified as positive (indicating pneumonia), indeterminate (possible pneumonia), or negative (no pneumonia) for statistical purposes.

Nucleic acid testing for SARS-CoV-2

According to the national COVID-19 surveillance scheme and guidelines for laboratory detection of COVID-19 [10], throat swabs and/or nasal swabs were collected from the patients and shipped to designated laboratories for SARS-CoV-2 nucleic acid detection by Real-Time (RT)-PCR. The PCR kits were made by Da'an Company (Guangzhou, China). Two SARS-CoV-2 genes were targeted in the PCR assay: ORF 1ab and N. The sample

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was determined to be positive if both genes were detected in a single sample or if one of the genes was detected twice in two separate samples from the same individual. All positive results were confirmed by a municipal CDC laboratory.

Diagnostic criteria

The diagnostic criteria for rapid screening prior to RT-PCR testing were based on the Guidelines for the Diagnosis and Treatment of COVID-19 published by the Chinese government [10]. Fever was defined as a temperature of 37.3°C or higher measured by a mercurial thermometer or ear thermometer in the fever clinic. Suspected cases were defined as those involving individuals with a positive epidemiological history and any two of the following three clinical features: fever and/or respiratory symptoms, white blood-cell count within or below the normal range, and pneumonia evident on chest X-ray or CT scan. Confirmed cases were defined as suspected cases with a positive RT-PCR result for SARS-CoV-2. The Shenzhen government requires all positive RT-PCR results for SARS-CoV-2 to be confirmed by the Shenzhen municipal CDC laboratory.

Quarantine indication

Patients were quarantined if they met any of the following conditions: positive epidemiological history and fever or respiratory symptoms; pneumonia evident on chest CT scan, especially if the white blood-cell count was within or below the normal range; the senior physician decided to quarantine the patient because of special conditions.

Statistical analysis

Descriptive statistics were used to summarize the data. Measurement data are reported as means and standard deviations. Categorical variables are summarized as counts and percentages. Repeated RT-PCR testing for SARS-CoV-2 was regarded as the gold standard for the diagnosis of COVID-19. A given patient was confirmed to have COVID-19 if any specimen from the patient tested positive for SARS-CoV-2 at the Shenzhen municipal CDC laboratory. Sensitivity, specificity, positive predictive value, and negative predictive value were used as criteria to access the effectiveness and cost of the COVID-19 screening. No imputation was made for missing data.

Statistical analysis was performed using the SPSS 20 software.

Results

A total of 5,710 patients visited the fever clinic from January 20, 2020 to February 29, 2020. Only the first visit by each patient was considered in the analysis. After 551 patients were excluded because of missing data and 749 patients were excluded due to lack of RT-PCR, 3,607 patients were included in the analysis. Of those, 2,031 had symptoms (fever, cough) with negative epidemiological history; 194 had symptoms with positive epidemiology history; 1,321 had no symptoms and negative epidemiology history but came to the fever clinic only for COVID-19 testing; 61 had no symptoms but had a positive epidemiology history. A total of 2,267 patients received routine blood examination, which revealed leukopenia and lymphocytopenia in 24 and 299 patients, respectively. A total of 866 patients were tested for influenza A and B. Chest CT examinations were completed on 1,826 patients. The results of the chest CT were positive for pneumonia in 160 patients and indeterminate for pneumonia in 354 patients. A total of 3,607 patients were tested by RT-PCR for SARS-CoV-2 nucleic acid. The RT-PCR results were positive for nine patients. The diagnostic workflow and results are shown in Figure 2.

Quarantined patients

Two hundred forty seven patients were quarantined in isolation wards in the fever clinic pending their RT-PCR results from January 20, 2020 to February 29, 2020. Of those, 96 (38.87%) had a positive epidemiological history and fever or respiratory symptoms, 96 (38.87%) had definite or possible pneumonia signs on chest CT scan with positive epidemiological history, 95 (38.46%) showed definite or indeterminate pneumonia signs on chest CT scan with negative epidemiology history, and 64 (25.91%) were quarantined because of a special medical situation determined by the senior physician. The clinical characteristics and epidemiological history of the patients are shown in Tables 1–4 (supporting data).

Patients with confirmed COVID-19

Nine patients were confirmed to have COVID-19 on the basis of repeated positive RT-PCR results. All of those patients had fever or respiratory symptoms eight had positive epidemiological history: eight had returned from Wuhan or Hubei province recently, and the other had close contact with friends from the Jiangsu province. Seven of the patients with confirmed COVID-19 had definite signs of pneumonia on chest CT scan, and the other two had indeterminate signs of pneumonia. The initial RT-PCR test was positive in eight of the nine confirmed cases. In a single confirmed case, where the initial RT-PCR test was negative, a second RT-PCR test performed one week later was positive. The clinical characteristics and epidemiological histories of the patients with confirmed COVID-19 are shown in Tables 5,6 (supporting data). The sensitivity, specificity, positive predictive value, and negative predictive value of the rapid screening based on the constellation of epidemiological and clinical characteristics were 100%, 93.39%, 3.64%, and 100%, respectively.

Discussion

COVID-19 is a global pandemic with an estimated death rate of about 2.14% [6]. More than 2,029,938 deaths due to COVID-19 were reported by Jan 17, 2021. Currently, there is still no effective treatment. The most important measure to control the COVID-19 pandemic is early detection and isolation, though vaccine is under emergency usage. Screening large numbers of patients for COVID-19 might be the most important component to control COVID-19 when the prevalence is low. Since Professor Zhong first reported human-to-human transmission and suggested that COVID-19 might be highly contagious

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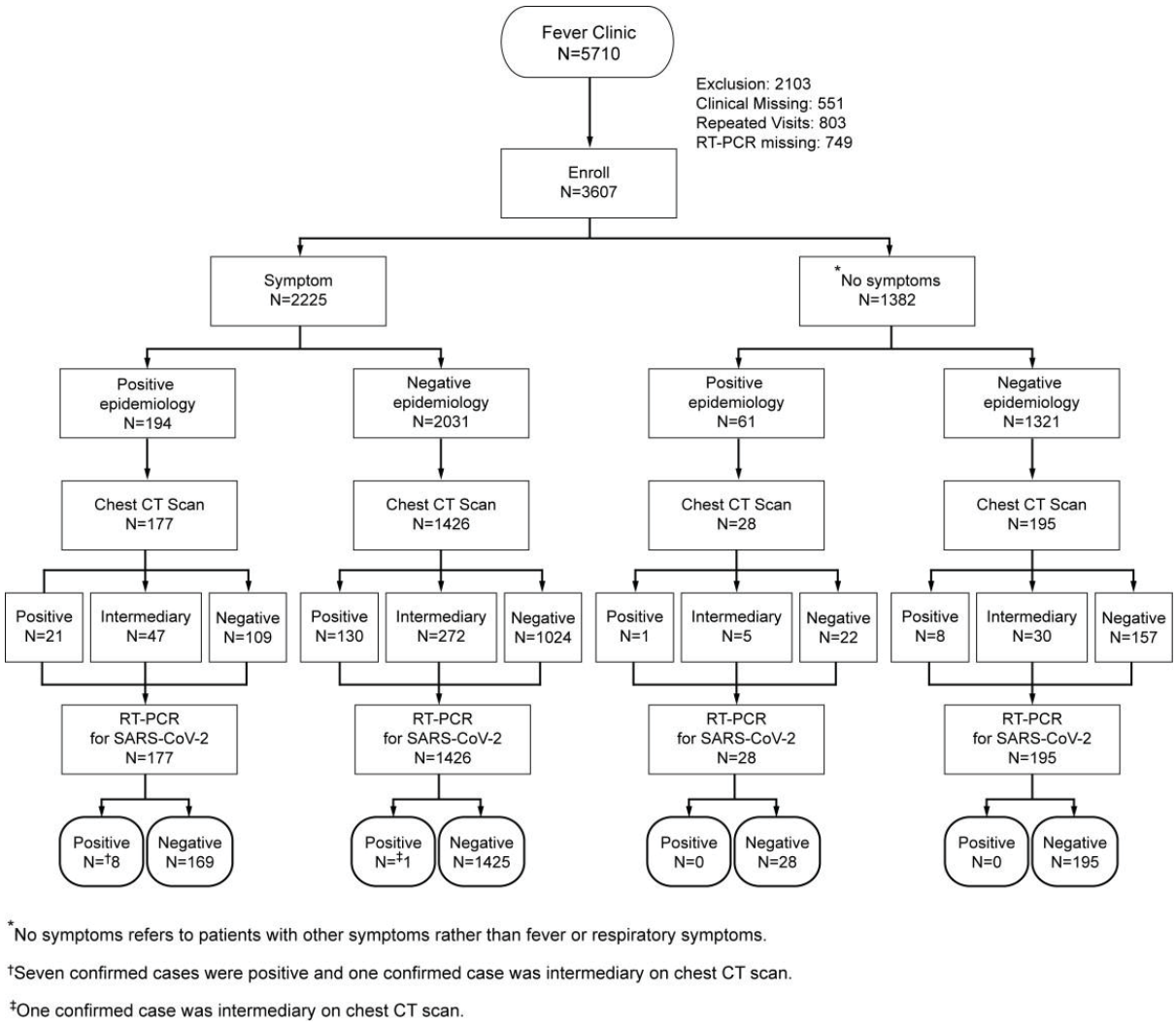

*No symptoms refers to patients with other symptoms rather than fever or respiratory symptoms.

†Seven confirmed cases were positive and one confirmed case was intermediary on chest CT scan.

‡One confirmed case was intermediary on chest CT scan.

Figure 2: COVID-19 diagnostic procedures and results.

on January 20, 2020 [11], the Chinese government has made control of COVID-19 a top priority. Accordingly, a new fever clinic was built in Shekou Hospital to rapidly screen patients with fever, respiratory symptoms, or an epidemiological history of contact with COVID-19 before those patients entered any other healthcare facilities.

Between January 20, 2020 and February 29, 2020, most patients with COVID-19 were expected to have either been in Hubei province (including Wuhan city) or had direct contact with individuals who had been in Hubei province within 14 days prior to developing symptoms. The four parameters thought to be most important in COVID-19 screening were the presence of symptoms, epidemiological history, white blood-cell count, and chest CT scan results. As expected, most of the patients with confirmed COVID-19 have displayed fever or cough, although asymptomatic infection has also been reported. We therefore believe that the presence of those symptoms is the most important signal for COVID-19 screening. The United States Centers for Disease Control estimated that as many as 40% of SARS-CoV-2 infections might be asymptomatic [12]. Because asymptomatic infections can be a major source of further infections, screening based solely on presenting symptoms is not enough to control the disease, although it is important, especially in the early stage of an outbreak. We therefore screened all patients with a positive epidemiological history who visited our hospital, no matter what symptoms they presented. No confirmed cases were found among individuals who were screened solely on the basis of a positive epidemiological history.

In the early stage of the outbreak, there were very few community infections without an epidemiological history of potential COVID-19 exposure. Hence, the survey of epidemiological history was an important step in the screening and quarantine processes used in Shenzhen. Epidemiological data were used to select individuals for chest CT scans while the available isolation rooms were allocated for quarantine. Even now, control of imported cases is one of the most important steps in stopping the spread of COVID-19 in China. Two hundred and fifty five of the 3607 patients that underwent screening in the fever clinic had a positive epidemiological history. Of the nine confirmed cases identified in the fever clinic, eight had either been in the Wuhan or Hubei province within the last 14 days or had been in contact with symptomatic patients who had been in the Wuhan or Hubei province. One confirmed case had no definite epidemiological history; however, that patient

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had recently travelled to Shenzhen, Hong Kong, and Macau with some friends. That patient's wife was also eventually diagnosed with COVID-19. We cannot rule out the possibility that the patient was infected during the travel, although the patient's friends all tested negative for SARS-CoV-2. That case suggests that travel control might be important even if the journey does not expose the traveler to high-risk areas.

Table 1: Basic clinical data of the quarantined patients.

Total quarantined	247
Average age	39.77 ± 19.52 years
Female	110 (44.53%)
Symptomatic	236 (95.55%)
Pulmonary underlying diseases*	14
Non-pulmonary underlying diseases†	44
Patients with blood routine results	241
CRP	239
Leukocytosis	64 (25.91%)
Leukopenia	8 (3.24%)
Neutrocytosis	71 (28.74%)
Neutropenia	7 (2.83%)
Lymphocytosis	16 (6.48 %)
Lymphocytopenia	48 (19.43%)
Average white blood-cell count (× 109 cells/L)	9.02 ± 10.97
Mean neutrophil count (× 109 cells/L)	5.50 ± 2.80
Average lymphocyte count (× 109 cells/L)	1.83 ± 1.00
CRP elevation	94 (38.05%)
Influenza A and B	115 tested; 3 positive for influenza A
Chest CT scan	204
Pneumonia in chest CT scan	101
Possible pneumonia in chest CT scan	93
Novel coronavirus antibodies	9 tested; all negative
RT-PCR for SARS-COV-2	247 tested; 9 positive

*Pulmonary basic diseases include chronic obstructive emphysema, bronchiectasis, lung cancer, pulmonary tuberculosis, and bronchial asthma.
†Non-pulmonary basic diseases include diabetes, hypertension, coronary heart disease, hyperlipidemia, and fatty liver

Table 2: Epidemiological history of returnees from Wuhan or other high-risk areas.

	No contact with fever patients	Contact with fever patients	Contact with patients with confirmed COVID-19
Returnees from Wuhan	**43**	**2**	**1**
Category 1 exposure	25	0	1
Category 2 exposure	14	2	0
Category 3 exposure	4	0	0
Returnees from other high-risk areas	**42**	**3**	**2**
Category 1 exposure	30	1	2
Category 2 exposure	6	1	0
Category 3 exposure	6	1	0

Category 1 Exposure (<7 days); *Category* 2 exposure (7-14 days); *Category* 3 exposure (>14 days, patients with incubation period longer than 14 days have been reported very early)

Table 3: Epidemiological history of contacts with returnees from Wuhan or other high-risk areas.

	Returnees with no fever	Returnees with fever	Returnees infected with novel coronavirus
Contact with returnees from Wuhan	**12**	**2**	**1**
Category 1 exposure	9	2	0
Category 2 exposure	1	0	1
Category 3 exposure	2	0	0
Contact with returnees from other high-risk areas	**9**	**4**	**0**
Category 1 exposure	2	4	0
Category 2 exposure	2	0	0
Category 3 exposure	5	0	0

Category 1 Exposure (<7 days); Category 2 exposure (7-14 days); Category 3 exposure (>14 days, patients with incubation period longer than 14 days have been reported very early)

Table 4: Epidemiological history of contacts with confirmed cases or family gathering cases.

	Contact with patients infected with novel corona virus (except Wuhan, Hubei province)	Family clustering
Total	**9**	**3**
Category 1 exposure	5	3
Category 2 exposure	2	0
Category 3 exposure	2	0

Category 1 Exposure (<7 days); *Category* 2 exposure (7-14 days); *Category* 3 exposure (>14 days, patients with incubation period longer than 14 days have been reported very early)

The results of chest CT scans might be the most important examination for COVID-19 screening before SARS-CoV-2 nucleic acid testing. Chest CT has a high sensitivity for COVID-19 diagnosis and can be considered a primary tool for COVID-19 detection in epidemic areas [13]. No nucleic acid testing was available in many fever clinics in the very early stage of the pandemic. Despite that, nucleic acid testing became available on January 23, 2020 in our fever clinic. Prior to that date, samples for PCR testing were sent to the local CDC lab. Chest CT scan has at least three advantages compared with SARS-CoV-2 nucleic acid testing. First, chest CT can reflect the severity of the disease, and dynamic CT follow-ups can monitor the progress or improvement of the disease and the effectiveness of therapy. Second, CT results are available within half an hour, whereas RT-PCR testing for SARS-CoV-2 requires at least six hours. Doctors must decide how to manage each patient as soon as possible; patients in our clinic with any quarantine indications were sent to an isolation room, while those without quarantine indications were either sent home or hospitalized according to the common rule. Third, there have been many reports of false-negative results of SARS-CoV-2 nucleic acid testing. However, chest CT can reveal pulmonary abnormalities consistent with COVID-19 in patients with negative RT-PCR results [14,15]. The characteristics of COVID-19 on CT scans have been reported [16,17]. The typical findings include ground-glass opacification and multiple bilateral patchy shadowing, although some patients only show ground-glass nodules [18,19].

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It is very difficult to make a differential diagnosis in such cases. We performed routine blood examinations at the same time as the chest CT scans. Patients were isolated for quarantine if the CT scan showed pneumonia and the white blood-cell count was normal or low. Patients with those characteristics and a positive epidemiological history should be highly suspected to have COVID-19. In Shenzhen, CT scans to detect COVID-19 were free in the early stage of the pandemic. In later stages, patients without health insurance paid about $60 for the CT scan. Some patients might refute chest CT scan because of the cost.

Table 5: Basic clinical data of the patients with confirmed COVID-19.

Total confirmed cases	9 (0.16%)
Average age	54.5 ± 15.42 years
Female	7 (77.78%)
Patients with clinical discomfort	9
Asymptomatic patients	0
Pulmonary underlying diseases*	1
†Non-pulmonary underlying diseases	1
Received blood routine examination	9
Received CRP examination	9
Leukocytosis	0
Leukopenia	2(22.22%)
Neutrocytosis	0
Neutropenia	2(22.22%)
Lymphocytosis	0
Lymphocytopenia	3(33.33%)
Average white blood-cell count (×109 cells/L)	4.75 ± 1.21
Mean neutrophil count (×109 cells/L)	2.85 ± 0.93
Average lymphocyte count (×109 cells/L)	1.29 ± 0.41
CRP elevation	5 (55.56%)
Tested for influenza A and B	4; all results negative
Received chest CT scan	9
Pulmonary inflammation on chest CT	7
Possible changes in inflammatory lesions on chest CT	2
Positive RT-PCR test	9
Displayed novel coronavirus antibodies	0

*Pulmonary basic diseases include chronic obstructive emphysema, bonchiectasis, lung cancer, pulmonary tuberculosis, bronchial asthma.
†Non-pulmonary basic diseases include diabetes, hypertension, coronary heart disease, hyperlipidemia, and fatty liver

Table 6: Epidemiological history of the patients with confirmed COVID-19.

	No contact with fever patients	Contact with fever patients	Contact with patients with confirmed COVID-19
Returnees from Wuhan	7	0	0
Category 1 exposure	6	0	0
Category 2 exposure	1	0	0
Category 3 exposure	0	0	0
Returnees from other high-risk areas	1	0	0
Category 1 exposure	1	0	0
Category 2 exposure	0	0	0
Category 3 exposure	0	0	0

Category 1 Exposure (<7 days); *Category* 2 exposure (7-14 days); *Category* 3 exposure (>14 days, patients with incubation period longer than 14 days have been reported very early)

Peripheral white blood-cell count is also an important factor in the screening and differential diagnosis of COVID-19. A high white blood-cell count suggests a bacterial infection instead of a viral infection, which is especially important if the chest CT scan suggests pneumonia. There is still a possibility of mixed infection if the white blood-cell count is high; however, that situation is rare. None of confirmed cases of COVID-19 showed a high white blood-cell count. Lymphocytopenia is another feature of COVID-19, according to previous reports [9,20]. Three of the confirmed cases identified in the fever clinic showed lymphocytopenia.

We performed screening tests based on epidemiological history, clinical characteristics, white blood-cell count, and chest CT scan. All of those data can be obtained within one hour. Decisions about which patients to quarantine had to be made as quickly as possible. However, RT-PCR is time consuming. We used positive RT-PCR results from the municipal CDC lab as the gold standard to confirm diagnoses of COVID-19. Based on that standard, the sensitivity and negative predictive value of the multifactor rapid screening used in the fever clinic were both 100%, which was important for early diagnosis and isolation. The positive predictive value was only 3.60% which is to say that more than 30 patients had to be quarantined in order to find one patient with COVID-19. The low positive predictive value resulted in a large burden on manpower, materials, and finances, but was necessary in order to have enough sensitivity and specificity to effectively contain the spread of the disease. Therefore, the government must attach great importance to the implementation of screening procedures to contain the spread of COVID-19 despite the high costs.

The fever clinic was a new addition to the Shekou People's Hospital in Shenzhen, China that effectively screened patients with fever, cough, or history of COVID-19 exposure in the early of 2020. Patients in the fever clinic received a chest CT scan and peripheral white blood cell count while repeated RT-PCR testing for SARS-CoV-2 was pending. The first-line doctors, together with consultants, selected patient's forquarantine according to the presenting symptoms, epidemiological history, chest CT results, and white blood-cell count. Patients suspected to have COVID-19 on the basis of those four factors, who have a negative result on the first RT-PCR test, should be quarantined while the RT-PCR test is repeated. If two or more RT-PCR tests are negative, then the patient can be discharged. A summary of the diagnostic and quarantine procedures is shown in Figure 3.

Conclusion

The experiences in a fever clinic Shenzhen, China showed that rapid COVID-19 screening was possible and reliable, although the burden was great, requiring substantial manpower, materials, and financial support from the government and the

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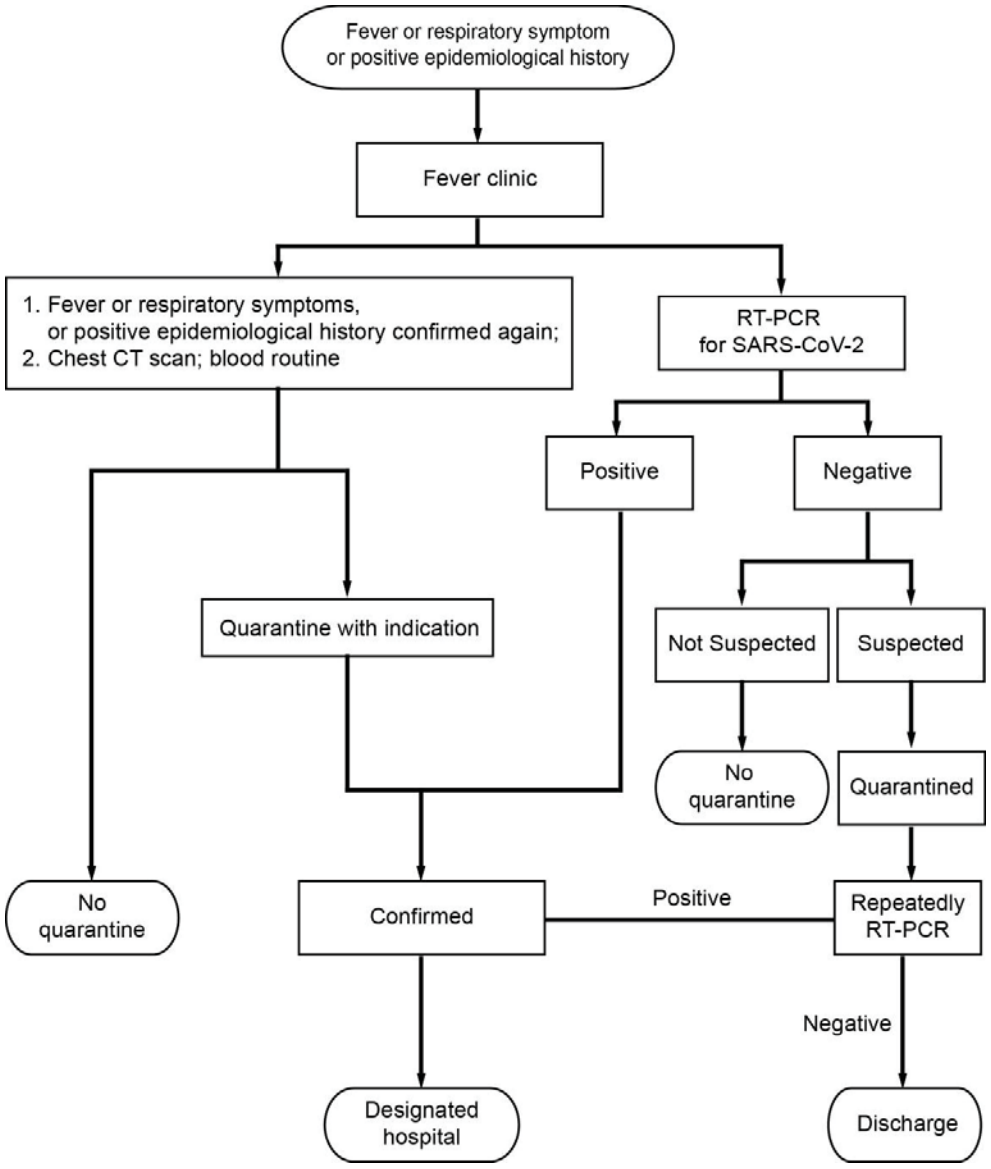

Figure 3: Summary of COVID-19 diagnostic and quarantine procedures.

hospital. The key points in the screening were epidemiological history, symptoms related to COVID-19, chest CT scan results, and white blood-cell count. RT-PCR is the gold standard for the diagnosis of SARS-CoV-2 infection. It is time consuming and has a high rate of false-negative results and it should not be regarded as the only factor to effectively screen for COVID-19.

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Disclaimer

The opinions expressed by authors contributing to this journal do not necessarily reflect the opinions of the Centers for Disease Control and Prevention or the institutions with which the authors are affiliated.

Contribution of the authors

All listed authors have made substantive intellectual contributions to this article.

Highlights

Patients with fever, respiratory symptoms, or an epidemiological history of contact with COVID-19 were screened in a fever clinic.

The quarantine model was based on a constellation of four parameters: clinical symptoms, epidemiological history, white blood-cell count, and chest CT scan results.

Rapid COVID-19 screening was possible and reliable, although the burden was great, requiring substantial manpower,

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