

Rigorous Measures are Vital for Preventing and Controlling Coronavirus Disease 2019 (COVID-19): A Cross-sectional Study

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Abstract

Background

Since December 2019, a novel corona virus disease named COVID-19 outbreak in Wuhan, China and spread worldwide then. Active prevention and control measures have been carried out in China, such as vigorous publicity, active screening and rapid isolation. As the major epidemic area, the passages in and out of Wuhan were temporarily closed since January 23. We aimed to demonstrate the effectiveness of rigorous measures by comparing the characteristics of patients hospitalized before and after implementation of vital measures.

Methods

Clinical data of patients admitted to hospital with COVID-19 during January 17-23 (Phase I) and February 3-9 (Phase II) were collected and compared. The cut-off date for follow-up was March 13, 2020.

Results

Of 176 patients with COVID-19, 97 were admitted in Phase I (43 [44.3%] male; mean age: 47.7), and 79 were in Phase II (33 [41.8%] male; mean age: 50.1). The proportions of severe cases were 21.6% and 10.1% respectively. Fewer patients had comorbidities (13 [16.5%] vs. 7 [7.2%]) and more asymptomatic patients were in Phase II (27.8% vs. 13.9%). Patients in Phase II had less fever (53.2% vs. 70.1%), cough (34.2% vs. 52.6%) and myalgia (11.4% vs. 28.9%), while more diarrhea (11.4% vs. 2.1%). Lymphopenia and elevated CRP, as well as eosinopenia and elevated SAA were common in two groups, but all of that were significantly better in Phase II. More patients in Phase II performed normal CT image on admission (10 [12.7%] vs. 7 [7.2%]). And lower CT scores (3 [2-4] vs. 2 [1-3]) were observed in Phase II. Up to cut-off date, average response time on CT image were 11.2 and 8.1 days in Phase I and II respectively. Shorter average hospitalized days were in Phase II (18.9 vs. 23.3 days). Four patients (4.1%) in Phase I and two (2.5%) in Phase II died.

Conclusions

Various actions (including vigorous publicity, active screening and rapid isolation) prompted more early patients with COVID-19 found, diagnosed and remedied, leading to good prognosis. Call for pretty attention to the epidemics of COVID-19 and timely measures around the world.

Background

Since December 2019, a kind of pneumonia with unknown etiology appeared and has spread rapidly in Wuhan, Hubei Province, China. On January 7, 2020, a novel coronavirus was identified by the Chinese Center for Disease Control and Prevention (CDC)[1] and named 2019-nCoV by World Health Organization (WHO) on January 12 (officially named as SARS-CoV-2 finally[2]). Later, WHO declared the diseases caused by 2019-nCoV named Coronavirus Disease 2019 (COVID-19)[3]. In early phase, with little

awareness of the infectivity and severity of the COVID–19, growing number of people were infected, even including some medical personnel[4]. On January 20, COVID–19 was included in the category B infectious diseases of *Law of the People’s Republic of China on prevention and control of infectious diseases*, and demanded to prevent and control as category A infectious diseases in China[5]. Afterwards, measures like setting up designated hospitals, building interim hospitals, investigating suspicious patients, appealing to everybody fight the epidemic were implemented in China to cut off the transmission of the virus, hold back the spread of the disease, and safeguard the safety and health of people.

At present, the epidemiology, clinical and radiological characteristics have been found out preliminarily[4, 6–8]. However, little literature reported the differences among patients diagnosed at different epidemic phases, which may reflect the efficacy of prevention and control work. Here, we collected and compared the clinical and radiological characteristics, treatment and outcomes of patients diagnosed with COVID–19 in two phases which were before or after implementation of vital measures, to reveal the development trend of COVID–19 in Wuhan.

Methods

Study design and participants

This study was approved by the ethics committee of Renmin Hospital of Wuhan University (No.2020020).

Patients with COVID–19 admitted to hospital from January 17–23 were defined as Phase I, and those admitted from February 3–9 were defined as Phase II. The diagnostic criteria were based on *Guidelines for Diagnosis and treatment of novel coronavirus infected pneumonia, version 6*[9]. All patients were from Renmin Hospital of Wuhan University in Wuhan, China, and were classified into non-severe or severe according to the guidelines above.

Procedures

All patients were laboratory confirmed present SARS-CoV–2 in upper or lower respiratory tract specimens by real-time RT-PCR according to *Guidelines for laboratory detection of novel coronavirus infected pneumonia, version 3*[10]. Data of patients with COVID–19 were collected from electronic medical records, including admission time, sex, age, comorbidity, symptoms, laboratory indexes, computed tomography (CT) manifestation, treatment and outcome. The major CT characteristics were described using internationally standard nomenclature of thoracic imaging[11]. CT score was used to quantitatively estimate the degree of pulmonary involvement. Higher score refers to more serious in pulmonary involvement[12]. The time of response on CT image defined as the interval between the first manifestation of viral pneumonia on CT image and the time of improvement. The cut-off date for follow-up was March 13, 2020.

Statistical analysis

Continuous variables were described as means and standard deviations (SD) if they were normally distributed, otherwise, described as median and interquartile range (IQR). Independent group *t* test or Kruskal-Wallis test was used to compare them. Categorical variables were described as counts and percentages (%), and χ^2 test or Fisher's exact test were applied to compare them. P value <0.05 (two-sided) was considered statistically significant. All statistical analyses were performed using SPSS version 20.0.

Result

General situation

The new laboratory confirmed cases in China, in Hubei and in Wuhan from January 17 to March 13 were showed in Figure 1. In the first three days (January 17–19) in the figure, new confirmed cases daily in China was consistent with that in Wuhan. After that, new confirmed cases in China were obviously more than Wuhan and Hubei. After action of traffic control was taken in Wuhan, and the passages in and out of it were temporarily closed since January 23, the number of new confirmed cases peaked on February 4. Given that the incubation periods of most patients were within 14 days, we included 97 patients admitted in hospital during January 17–23 (before Wuhan was closed, Phase I), and 79 patients admitted during February 3–9 (fourteen days after the previous period, Phase II). Phase I consisted of 43 male and 54 female (mean age: 47.7, range 22–90), and Phase II included 33 male and 46 female (mean age: 50.1 range 20–80)(Table 1).

Clinical Findings

Basic characteristics were showed in Table 1. More patients (27.8% [27/97]) in Phase I suffered from different comorbidities than whom in Phase II (13.9% [11/79]). Common comorbidities in two groups were hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular diseases and cancer. 7 (7.2%) and 13 (16.5%) asymptomatic patients were in Phase I and II respectively. More patients had fever (70.1% vs. 53.2%, $P = 0.028$), cough (52.6% vs. 34.2%, $P = 0.015$) and myalgia (28.9% vs. 11.4%, $P = 0.001$) in Phase I, while diarrhea was more common in Phase II (11.4% vs. 2.1%, $P = 0.013$). According to the conditions of patients on admission, 21 (21.6%) cases in Phase I were severe type, while 8 (10.1%) severe cases in Phase II ($P = 0.040$). Significantly more mild or common type patients admitted in hospital in the latter phase.

As for laboratory findings on admission (Table 2), Except for lymphopenia (41.2% vs. 19.0%) and elevated C-reaction protein (CRP) (30.9% vs. 17.7%), eosinopenia (48.5% vs. 30.4%) and elevated serum amyloid A (SAA) (66.0% vs. 39.2%) were also common in both groups. Compared with Phase I, significantly higher lymphocyte and eosinophils counts and lower levels of CRP and SAA were observed in

Phase II. There were 9 (9.3%) and 26 (32.9%) patients were normal in blood routine in Phase I and II respectively (not given in the table). Cardiac and coagulation function of all cases in both groups were normal on admission. 3 patients with elevated liver enzymes and 2 with increased creatinine were discovered on admission in Phase I, while hepatic and renal function of patients in Phase II were all normal (not given in the table).

Table1. Basic Characteristics of Patients with COVID-19 in Two Phases

	Phase I (n=97)	Phase II (n=79)	P value
Sex			
Male	43 (44.3%)	33 (41.8%)	0.733
Female	54 (55.7%)	46 (58.2%)	
Age, mean±SD (range)	47.7±16.7 (22-90)	50.1±13.1 (20-80)	0.222
Comorbidities	27 (27.8%)	11 (13.9%)	0.026
Hypertension	10 (10.3%)	8 (10.1%)	0.968
Diabetes	7 (7.2%)	3 (3.8%)	0.515
Chronic Obstructive Pulmonary Disease	9 (9.3%)	1 (1.3%)	0.024
Cardiovascular Diseases	7 (7.2%)	1 (1.3%)	0.075
Cancer	6 (6.2%)	1 (1.3%)	0.131
Cerebrovascular Diseases	1 (1.0%)	1 (1.3%)	1.000
Symptoms	90 (92.8%)	66 (83.5%)	0.055
Fever	68 (70.1%)	42 (53.2%)	0.028
Cough	51 (52.6%)	27 (34.2%)	0.015
Dyspnea	19 (19.6%)	20 (25.3%)	0.363
Fatigue	11 (11.3%)	16 (20.3%)	0.103
Pharyngalgia	17 (17.5%)	11 (13.9%)	0.516
Headache	8 (8.2%)	11 (13.9%)	0.227
Myalgia	28 (28.9%)	9 (11.4%)	0.005
Diarrhea	2 (2.1%)	9 (11.4%)	0.013
Nausea	6 (6.2%)	4 (5.1%)	1.000
Chest Pain	1 (1.0%)	1 (1.3%)	1.000
Rhinorrh	0	1 (1.3%)	0.449
Bellyache	1 (1.0%)	0	1.000
Rate of Severe			
Severe	21 (21.6%)	8 (10.1%)	0.040
Non-severe	76 (78.4%)	71 (89.9%)	
Treatments			
Antiviral	97 (100%)	79 (100%)	-
Antibacterial	69 (71.1%)	52 (65.8%)	0.450
Corticosteroid	44 (45.4%)	25 (31.6%)	0.064
Immunoglobulin	37 (38.1%)	26 (32.9%)	0.471
Prognosis			
Discharged	88 (90.7%)	63 (79.7%)	0.038
Discharged Hospitalized Days (days), mean ± SD	23.3±8.8	18.9±8.3	0.002
Mortality	4 (4.1%)	2 (2.5%)	0.692

Table 2. Laboratory Findings of Patients with COVID-19 in Two Phases

	Phase I (n=97)	Phase II (n=79)	P value
Leukocyte ($\times 10^9/L$)	5.03 \pm 2.16	5.14 \pm 1.87	0.711
<3.5	17 (17.5%)	13 (16.5%)	0.875
>9.5	5 (5.2%)	3 (3.8%)	
Neutrophils ($\times 10^9/L$)	3.20 \pm 1.85	2.87 \pm 1.49	0.203
<1.8	16 (16.5%)	17 (21.5%)	0.374
>6.3	8 (8.2%)	3 (3.8%)	
Lymphocyte ($\times 10^9/L$)	1.32 \pm 0.61	1.73 \pm 0.72	<0.001
<1.1	40 (41.2%)	15 (19.0%)	0.003
>3.2	1 (1.0%)	2 (2.5%)	
Eosnophils ($\times 10^9/L$)	0.02 (0-0.05)	0.04 (0.01-0.10)	0.004
<0.02	47 (48.5%)	24 (30.4%)	0.011
>0.52	2 (2.1%)	0	
Basophils ($\times 10^9/L$)	0.01 (0-0.02)	0.01 (0.01-0.02)	0.318
Platelet ($\times 10^9/L$)	183.00 (151.00-245.50)	205.00 (163.00-245.00)	0.209
<125	7 (7.2%)	4 (5.1%)	0.125
>350	7 (7.2%)	1 (1.3%)	
C-reaction protein (mg/L)	5.00 (0.25-12.15)	0.25 (0.25-6.50)	0.001
>10	30 (30.9%)	14 (17.7%)	0.044
Serum amyloid A (mg/L)	40.67 (2.50-98.53)	6.11 (2.50-52.52)	0.002
≥ 10	64 (66.0%)	31 (39.2%)	<0.001

7 (7.2%) and 12 (15.2%) patients were normal on CT image at admission in two groups respectively. Analysis of patients with abnormal CT images showed typical chest CT characteristics in both groups including bilateral and multifocal ground-glass opacity and patchy shadowing with peripheral zone or lower lobe involvement (Table 3). As the representative of progression of pneumonia[13–15], the manifestation of consolidation (43.3% vs. 26.1%, $P = 0.025$) and linear densities (61.1% vs. 36.2%, $P = 0.002$) were less common in Phase II. Median CT scores in Phase I was 3 (IQR 2–4), which was lower in Phase II (2 [IQR 1–3]), accounting for milder pneumonia on CT image in Phase II.

Table 3. Chest CT Characteristics on Admission of Patients with COVID-19 in Two Phases

	n (%)		P value
	Phase I (n=90)	Phase II (n=69)	
Abnormalities on CT			
Ground-glass opacity	84 (93.3%)	58 (84.1%)	0.061
Patchy shadowing	60 (66.7%)	49 (71.0%)	0.558
Interstitial abnormalities	38 (42.2%)	29 (42.0%)	0.980
Crazy paving	29 (32.2%)	22 (31.9%)	0.964
Consolidation	39 (43.3%)	18 (26.1%)	0.025
Linear densities	55 (61.1%)	25 (36.2%)	0.002
Zonal predominance			
Upper	23 (25.6%)	16 (23.2%)	0.731
Middle	38 (42.2%)	24 (34.8%)	0.340
Lower	71 (78.9%)	56 (81.2%)	0.723
Peripheral	85 (94.4%)	64 (92.8%)	0.748
Middle 1/3	37 (41.1%)	20 (29.0%)	0.114
Central	18 (20.0%)	9 (13.0%)	0.247
Distribution of Lesions			
Unilateral	43 (47.8%)	26 (37.7%)	0.203
Bilateral	47 (52.2%)	43 (62.3%)	
Focal	33 (36.7%)	18 (26.1%)	0.157
Multifocal	57 (63.3%)	51 (73.9%)	
CT score, median (IQR)	3 (2-4)	2 (1-3)	0.017
Outcome			
Response on CT	86 (95.6%)	77 (97.5%)	0.686
Time of Response on CT (days), mean± SD (range)	11.2±5.7 (0-33)	8.1±2.2 (4-15)	<0.001

All patients in both groups received antiviral treatment (Table 1). 69 (71.1%) and 52 (65.8%) patients received antibacterial treatment in two groups respectively. Systematic corticosteroids were given to 44 (45.4%) patients in Phase I and 25 (31.6%) in Phase II. Immunoglobulin were given to some patients in two groups to enhance the efficacy of anti-infective therapy. Up to March 13, all patients in our study had notable improvement on CT image except six patients died. The mean time of response on CT image was 11.2 days in Phase I and 8.1 days in Phase II ($P < 0.001$) (Table 3). 88 (90.7%) patients in Phase I and 63 (79.7%) in Phase II had been discharged. Mean hospitalized days for discharged patients were significantly shorter in Phase II (18.9 vs. 23.3, $P = 0.002$). Four patients (4.1%) in Phase I and two (2.5%) in Phase II died.

Discussion

The COVID-19 was first reported at the end of 2019 in Wuhan. Soon after, human-to-human transmission of COVID-19 was confirmed[16]. As the number of new confirmed cases continued to rise, the passages in and out of the major epidemic area, Wuhan, were closed since January 23. Alarm was sounded in the public and around the country. More and more rigorous and effective measures were rolled out to prevent and control the epidemic of COVID-19. Up to March 22, the cumulative number and existing number of confirmed patients with COVID-19 in China is 81093 and 5120 respectively[17]. The number of new patients daily has decreased visibly, mortality was 4.03% (3270/81093) (only 0.88% in areas outside of Hubei), and 11 provinces and autonomous prefectures have been no new confirmed cases for more than 14 consecutive days. Though the situation in China is getting better, the COVID-19 has spread outside of China, especially in European region[18]. Up to March 21, more than 180 countries/territories/areas around the world had reported cases of COVID-19. The cumulative number outside of China was 210644 and six countries (Italy, Iran, Spain, Germany, France and the United States) reported more than ten thousand cases. Increasing trend outside of China continuing. Our study aimed to demonstrate that alert and urgent measures in the early stage were vital and effective to prevent and control the epidemic of COVID-19 by comparing the characteristics of two groups of patients hospitalized in different phases.

In this study, we collected data of COVID-19 patients in our hospital before and after the implementation of a variety of rigorous and effective measures. In the group of patients admitted later (Phase II), fewer suffered from comorbidities, indicating that healthy people without comorbidities were also susceptible to SARS-CoV-2. More asymptomatic patients were detected by CT scanning or throat swab in Phase II. The proportion of patients with fever in Phase II was lower, which provides further evidence that fever is not a specific symptom of COVID-19[7]. Whereas, proportion of diarrhea was higher in Phase II. These findings manifested the existence of recessive infection. Considering fever as the early screening symptom will miss suspicious infections, and attention should also be paid to some atypical symptoms. Here, we reported reduced eosinophils counts in patients with COVID-19 for the first time, which was reported in patients infected with MERS-CoV[19, 20]. In Phase II, improvement in lymphocyte as well as eosinophils and SAA found implied eosinophils and SAA may be biomarkers of severity like lymphocyte. Patients in Phase II are significantly better in laboratory indexes and CT image, as well as shorter in time of response on CT and hospitalized days compared with Phase I. These results attributed to the vigorous publicity of the government to make the public aware of the infectivity and seriousness of COVID-19 and seek for medical treatment at an early stage of the disease, and the actions of comprehensive screening for patients with asymptomatic infections and atypical symptoms. In general, more patients were discovered and treated in isolation in early stage, resulting in good prognosis.

In the early phase, due to different sample size, the proportion of severe cases and mortality in literature were reported as 15.7%–31.7% and 2.01%–15%[7, 21]. Later, a research of 72314 cases from Novel Coronavirus Pneumonia Emergency Response Epidemiology Team showed proportions of severe cases of 13.8% and overall case-fatality rate of 2.3%[22]. Decrease in proportion of severe cases and mortality observed in our study were consistent with these literature, cluing more early patients with COVID-19 were diagnosed and treated after the efforts of the society. Nowadays, new confirmed patients, the proportion of severe cases in new patients and mortality have decreased significantly in China. The

causes of the changes were various but all indispensable. First, government attached great importance to the epidemic situation of COVID-19. Almost all areas in China initiated first-level response to major public health emergencies and many communities implemented strict closed management programs. Second, hospitals responded quickly. Measures like increasing the investment of medical strength (including medical staff, protective equipment and nucleic acid detection kits) and speeding up screening, diagnosis and isolation were keys to reduce outbreaks in hospitals and communities. Third, unique measures were enforced in Wuhan, such as building two temporary hospitals within 10 days for patients needing isolation and close attention, and transforming several venues into *Fangcang* Hospital for segregating mild patients infected with SARS-CoV-2. In addition, a series of beneficial policies to people have been launched by government, including remission in medical expenses for patients with COVID-19, to guarantee the people's livelihood and health during the epidemic period. Also, thanks to the support and encouragement from the world, which brought great confidence and courage to China.

Undoubtedly, there are still a lot of problems need to be solved. For example, some convalescent patients with COVID-19 were detected positive in nucleic acid assay when return visit[23, 24], that indicated a false negative is presenting in kits and the criterion of discharged may be less strict. Some voice thought that COVID-19 may turn into a chronic disease like chronic viral hepatitis B. The preliminary results of autopsy from organs of died patients with COVID-19 showed that not only lung, but also damaged heart, vessels, liver, kidney, even immune organs[25]. Some researchers thought SARS-CoV-2 was the combination of SARS and HIV. The mechanism underlying pathological changes of this disease needs further study. Along with the passage of SARS-CoV-2, whether the viral virulence will weaken or enhance by variation has not been defined[26, 27]. Besides, given COVID-19 has been found in some tropical country, SARS-CoV-2 may exist for a long time. How to fight a "protracted war" of COVID-19 is still under consideration. There are some limitations in our study. Firstly, the patients were restricted to a hospital, which may be lack of typicality. Secondly, due to the incomplete records, some data like the incubation period and the interval of onset to first treatment was not obtained and analyzed, which can reflect the characteristics of the virus and public awareness to the disease.

Nowadays of Wuhan, the transports have not fully resumed. The action of screening every citizen has been going on to ensure not a patient with COVID-19 left out. Nobody in China has let down their guard yet. China has set a good example in preventing and controlling the prevalence of COVID-19. The experience and status quo of China tell the world the epidemics of COVID-19 is controllable and reversible. Other countries should make self-evaluation, and formulate schemes according to own conditions. Everyone in the country needs to participate.

Conclusions

COVID-19 has broken out all over the world. It is vital to attach importance to the prevalence of COVID-19 and implement urgent measures to prevent and control it. As the measures proceeding, more early patients with COVID-19 will be found, diagnosed and remedied, resulting in a good prognosis, so that the prevalence of COVID-19 could be controlled worldwide.

List Of Abbreviations

CDC: Center for Disease Control and Prevention

CT: Computed tomography

COVID–19: Coronavirus Disease 2019

CRP: C-reaction protein

IQR: Interquartile range

SAA: Serum amyloid A

SD: Standard deviations

WHO: World Health Organization

Declarations

Ethics approval and consent to participate: The study protocol was approved by the ethics committee of Renmin Hospital of Wuhan University (No.2020020). Because of the retrospective nature of the study, informed consent of the patients was waived.

Consent for publication: Not applicable.

Availability of data and materials: Patients in our study have not been reported in any other submission. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions: LSY designed the study, collected the data, conducted statistical analysis, interpreted data and drafted the manuscript; YW collected and recorded the data, interpreted results and drafted the manuscript; HHH recorded the data, conducted statistical analysis and drafted the manuscript; YXC conducted statistical analysis, drafted and revised the manuscript; HYF collected, reviewed and analyzed the CT image, and contributed in the writing of the manuscript; YHW collected and reviewed the CT image, made tables and figures and contributed in the writing of the manuscript; JZ collected and recorded the data and contributed in the writing of the manuscript; QBS contributions to the conception and design the study, interpreted data and reviewing the manuscript; HYG contributions to the conception and design the study, collected the data, drafted and revised the manuscript. All authors read and approved the final manuscript.

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Figures

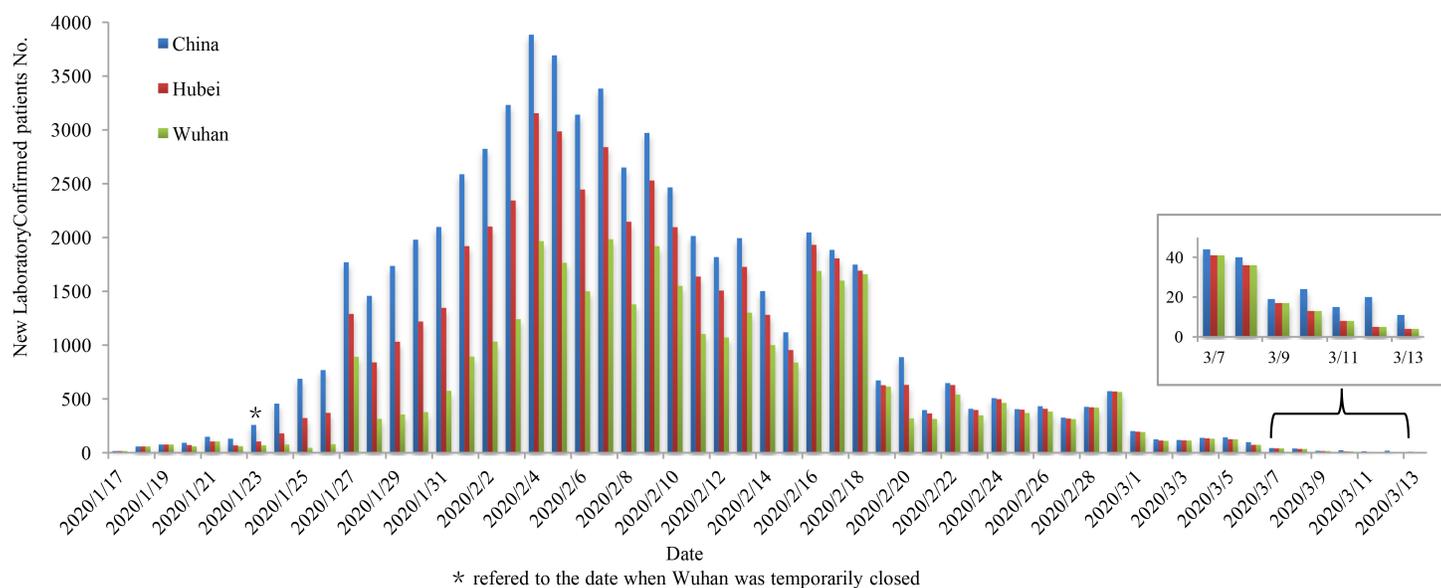


Figure 1

New Patients Laboratory Confirmed as COVID-19 Daily in China. The histogram showed new laboratory confirmed cases daily in China (blue bar), in Hubei (red bar) and in Wuhan (green bar) from January 17 to March 13. During January 17-19, new confirmed cases were only reported in Wuhan. Since January 20, COVID-19 were reported outside of Wuhan and spread around China rapidly. Passages in and out of Wuhan were temporarily closed since January 23. The number of new confirmed cases peaked on February 4, then went down.