4Special: COVID–19

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Transmission

Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia

Bin Cao, Yeming Wang, Danning Wen, Wen Liu, Jingli Wang, Guohui Fan, Lianguo Ruan, Bin Song, Yanping Cai, Ming Wei, Xingwang Li, Jiaan Xia, Nanshan Chen, Jie Xiang, Ting Yu, Tao Bai, Xuelei Xie, Li Zhang, Caihong Li, Ye Yuan, Hua Chen, Huadong Li, Hanping Huang, Shengjing Tu, Fengyun Gong, Ying Liu, Yuan Wei, Chongya Dong, Fei Zhou, Xiaoying Gu, Jiuyang Xu, Zhibo Liu, Yi Zhang, Hui Li, Lianhan Shang, Ke Wang, Kunxia Li, Xia Zhou, Xuan Dong, Zhaohui Qu, Sixia Lu, Xujuan Hu, Shunan Ruan, Shanshan Luo, Jing Wu, Lu Peng, Fang Cheng, Lihong Pan, Jun Zou, Chunmin Jia, Juan Wang, Xia Liu, Shuzhen Wang, Xudong Wu, Qin Ge, Jing He, Haiyan Zhan, Fang Qiu, Li Guo, Chaolin Huang, Thomas Jaki, Frederick G. Hayden, Peter W. Horby, Dingyu Zhang, Chen Wang

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https://www.nejm.org/doi/full/10.1056/NEJMoa2001316

Background
The initial cases of novel coronavirus (2019-nCoV)–infected pneumonia (NCIP) occurred in Wuhan, Hubei Province, China, in December 2019 and January 2020. We analyzed data on the first 425 confirmed cases in Wuhan to determine the epidemiologic characteristics of NCIP.

Methods
We collected information on demographic characteristics, exposure history, and illness timelines of laboratory-confirmed cases of NCIP that had been reported by January 22, 2020. We described characteristics of the cases and estimated the key epidemiologic time-delay distributions. In the early period of exponential growth, we estimated the epidemic doubling time and the basic reproductive number.

Results
Among the first 425 patients with confirmed NCIP, the median age was 59 years and 56% were male. The majority of cases (55%) with onset before January 1, 2020, were linked to the Huanan Seafood Wholesale Market, as compared with 8.6% of the subsequent cases. The mean incubation period was 5.2 days (95% confidence interval [CI], 4.1 to 7.0), with the 95th percentile of the distribution at 12.5 days. In its early stages, the epidemic doubled in size every 7.4 days. With a mean serial interval of 7.5 days (95% CI, 5.3 to 19), the basic reproductive number was estimated to be 2.2 (95% CI, 1.4 to 3.9).

Conclusions
On the basis of this information, there is evidence that human-to-human transmission has occurred among close contacts since the middle of December 2019. Considerable efforts to reduce transmission will be required to control outbreaks if similar dynamics apply elsewhere. Measures to prevent or reduce transmission should be implemented in populations at risk. (Funded by the Ministry of Science and Technology of China and others.)

BACK

A Locally Transmitted Case of SARS-CoV-2 Infection in Taiwan

Ying-Chu Liu, Ching-Hui Liao, Chin-Fu Chang, Chu-Chung Chou, Yan-Ren Lin

N Engl J Med 2020; 382:1070-1072

https://www.nejm.org/doi/full/10.1056/NEJMc2001573

Since December 2019, an outbreak of infection with the novel coronavirus (SARS-CoV-2) has developed in Wuhan, China, and has spread to several countries, typically by travelers returning from China.1,2 Of the 3 million Taiwanese persons who work in China, 2000 work in Wuhan, so the risk of imported SARS-CoV-2 infection to Taiwan from China is high. As of January 29, there were 7 confirmed imported cases of infection with SARS-CoV-2 to Taiwan. We identified a case of locally transmitted infection in Taiwan from a wife to her husband.

On January 25, 2020, a 52-year-old woman with a history of type 2 diabetes presented with fever to an emergency department in central Taiwan. She was admitted to the hospital because of suspicion of pneumonia associated with SARS-CoV-2 infection. She had lived in Wuhan from October 21, 2019, to January 20, 2020. She returned to Taiwan from Wuhan on January 20 on an airplane. On the same day, a throat swab was obtained from another passenger on that flight; that passenger was confirmed to have the first known imported case of SARS-CoV-2 infection in Taiwan when the swab was found to be positive for the virus on January 21.

Fever and myalgia developed in the woman on January 25, a total of 5 days after she returned to Taiwan from Wuhan. She reported that she did not have cough, dyspnea, chest pain, or diarrhea. Chest radiography showed diffuse infiltrates in the bilateral lower lungs (Figure 1A). Assays to detect influenza viruses and a respiratory panel to detect adenovirus, human rhinovirus, parainfluenza virus, respiratory syncytial virus, Bordetella pertussis, Chlamydia pneumoniae, and Mycoplasma pneumoniae were all negative. A throat swab was positive for SARS-CoV-2 on real-time reverse-transcription–polymerase-chain-reaction (RT-PCR) assays on January 273,4; this was the fifth confirmed imported case of Covid-19 (the illness caused by SARS-CoV-2 infection) in Taiwan.

On day 1 of hospitalization, the patient received supportive therapies, and oseltamivir and levofloxacin were added as empirical therapy on day 3 of hospitalization after SARS-CoV-2 was detected on RT-PCR. Cough, rhinorrhea, and sore throat developed on day 5, and chest radiography revealed progressive diffuse interstitial opacities and consolidation in the bilateral parahilar areas and lower lung fields (Figure 1B). She continued to receive supportive therapy with oseltamivir and levofloxacin, but she did not receive oxygen therapy. As of February 11, she remained hospitalized, but her vital signs were stable and she was not receiving oxygen therapy.

The patient’s 50-year-old husband is a music producer who works primarily at home in Taiwan. He reported that he had not traveled to any region where SARS-CoV-2 transmission was known to be occurring and that he had no known contacts with any person returning from such a region; this was confirmed by an investigation by the government health care unit in Taiwan. On January 21, he met his wife when she returned to Taiwan. They shared a bedroom and meals at home.

On January 25, the husband sought medical treatment at the same time as his wife. He presented only with rhinorrhea; he did not have fever, cough, dyspnea, chest pain, or diarrhea. He was admitted to the hospital because of concern regarding Covid-19, given his close contact with his wife. A complete blood count and chest radiography did not show any abnormalities. Assays for influenza viruses and a respiratory panel were negative, but SARS-CoV-2 was detected on RT-PCR on January 28.

The husband's symptoms developed on the same day as those of his wife, January 25. This suggests transmission shortly after his wife returned to Taiwan. During the hospital stay, he had rhinorrhea, and myalgia developed on January 27, but he did not have fever (see Fig. S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org)., available with the full text of this letter at NEJM.org). He received supportive therapy without any antiviral agents or antibiotics. As of February 11, he remained hospitalized, but his vital signs were stable and he was not receiving oxygen therapy.

BACK

Preparedness and vulnerability of African countries against importations of COVID-19: a modelling study

Marius Gilbert, Giulia Pullano, Francesco Pinotti, Eugenio Valdano, Chiara Poletto, Pierre-Yves Boëlle, Eric D'Ortenzio, Yazdan Yazdanpanah, Serge Paul Eholie, Mathias Altmann, Bernardo Gutierrez, Moritz U.G. Kraemer, Vittoria Colizza

The Lancet – Volume 395 – issue 10227 – P871-877

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30411-6/fulltext

Background
The novel coronavirus disease 2019 (COVID-19) epidemic has spread from China to 25 countries. Local cycles of transmission have already occurred in 12 countries after case importation. In Africa, Egypt has so far confirmed one case. The management and control of COVID-19 importations heavily rely on a country's health capacity. Here we evaluate the preparedness and vulnerability of African countries against their risk of importation of COVID-19.

Methods
We used data on the volume of air travel departing from airports in the infected provinces in China and directed to Africa to estimate the risk of importation per country. We determined the country's capacity to detect and respond to cases with two indicators: preparedness, using the WHO International Health Regulations Monitoring and Evaluation Framework; and vulnerability, using the Infectious Disease Vulnerability Index. Countries were clustered according to the Chinese regions contributing most to their risk.

Findings
Countries with the highest importation risk (ie, Egypt, Algeria, and South Africa) have moderate to high capacity to respond to outbreaks. Countries at moderate risk (ie, Nigeria, Ethiopia, Sudan, Angola, Tanzania, Ghana, and Kenya) have variable capacity and high vulnerability. We identified three clusters of countries that share the same exposure to the risk originating from the provinces of Guangdong, Fujian, and the city of Beijing, respectively.

Interpretation
Many countries in Africa are stepping up their preparedness to detect and cope with COVID-19 importations. Resources, intensified surveillance, and capacity building should be urgently prioritised in countries with moderate risk that might be ill-prepared to detect imported cases and to limit onward transmission.

Funding
EU Framework Programme for Research and Innovation Horizon 2020, Agence Nationale de la Recherche.

BACK

Diagnosis and epidemiology

Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China

Dawei Wang, Bo Hu, Chang Hu, Fangfang Zhu, Xing Liu, Jing Zhang, Binbin Wang, Hui Xiang, Zhenshun Cheng, Yong Xiong, Yan Zhao, Yirong Li, Xinghuan Wang, Zhiyong Peng

JAMA. 2020;323(11):1061-1069

https://jamanetwork.com/journals/jama/fullarticle/2761044

Importance
In December 2019, novel coronavirus (2019-nCoV)–infected pneumonia (NCIP) occurred in Wuhan, China. The number of cases has increased rapidly but information on the clinical characteristics of affected patients is limited.

Objective
To describe the epidemiological and clinical characteristics of NCIP.

Design, Setting, and Participants
Retrospective, single-center case series of the 138 consecutive hospitalized patients with confirmed NCIP at Zhongnan Hospital of Wuhan University in Wuhan, China, from January 1 to January 28, 2020; final date of follow-up was February 3, 2020.

Exposures
Documented NCIP.

Main Outcomes and Measures
Epidemiological, demographic, clinical, laboratory, radiological, and treatment data were collected and analyzed. Outcomes of critically ill patients and noncritically ill patients were compared. Presumed hospital-related transmission was suspected if a cluster of health professionals or hospitalized patients in the same wards became infected and a possible source of infection could be tracked.

Results
Of 138 hospitalized patients with NCIP, the median age was 56 years (interquartile range, 42-68; range, 22-92 years) and 75 (54.3%) were men. Hospital-associated transmission was suspected as the presumed mechanism of infection for affected health professionals (40 [29%]) and hospitalized patients (17 [12.3%]). Common symptoms included fever (136 [98.6%]), fatigue (96 [69.6%]), and dry cough (82 [59.4%]). Lymphopenia (lymphocyte count, 0.8 × 109/L [interquartile range {IQR}, 0.6-1.1]) occurred in 97 patients (70.3%), prolonged prothrombin time (13.0 seconds [IQR, 12.3-13.7]) in 80 patients (58%), and elevated lactate dehydrogenase (261 U/L [IQR, 182-403]) in 55 patients (39.9%). Chest computed tomographic scans showed bilateral patchy shadows or ground glass opacity in the lungs of all patients. Most patients received antiviral therapy (oseltamivir, 124 [89.9%]), and many received antibacterial therapy (moxifloxacin, 89 [64.4%]; ceftriaxone, 34 [24.6%]; azithromycin, 25 [18.1%]) and glucocorticoid therapy (62 [44.9%]). Thirty-six patients (26.1%) were transferred to the intensive care unit (ICU) because of complications, including acute respiratory distress syndrome (22 [61.1%]), arrhythmia (16 [44.4%]), and shock (11 [30.6%]). The median time from first symptom to dyspnea was 5.0 days, to hospital admission was 7.0 days, and to ARDS was 8.0 days. Patients treated in the ICU (n = 36), compared with patients not

treated in the ICU (n = 102), were older (median age, 66 years vs 51 years), were more likely to have underlying comorbidities (26 [72.2%] vs 38 [37.3%]), and were more likely to have dyspnea (23 [63.9%] vs 20 [19.6%]), and anorexia (24 [66.7%] vs 31 [30.4%]). Of the 36 cases in the ICU, 4 (11.1%) received high-flow oxygen therapy, 15 (41.7%) received noninvasive ventilation, and 17 (47.2%) received invasive ventilation (4 were switched to extracorporeal membrane oxygenation). As of February 3, 47 patients (34.1%) were discharged and 6 died (overall mortality, 4.3%), but the remaining patients are still hospitalized. Among those discharged alive (n = 47), the median hospital stay was 10 days (IQR, 7.0-14.0).

Conclusions and Relevance
In this single-center case series of 138 hospitalized patients with confirmed NCIP in Wuhan, China, presumed hospital-related transmission of 2019-nCoV was suspected in 41% of patients, 26% of patients received ICU care, and mortality was 4.3%.

BACK

Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China

Yuanyuan Dong, Xi Mo, Yabin Hu, Xin Qi, Fang Jiang, Zhongyi Jiang and Shilu Tong

March 2020, e20200702. Prepublication release.

https://pediatrics.aappublications.org/content/early/2020/03/16/peds.2020-0702

Objectives
To identify the epidemiological characteristics and transmission patterns of pediatric patients with COVID-19 in China.

Methods
Nationwide case series of 2143 pediatric patients with COVID-19 reported to the Chinese Center for Disease Control and Prevention from January 16 to February 8, 2020 were included. The epidemic curves were constructed by key dates of disease onset and case diagnosis. Onset-to-diagnosis curves were constructed by fitting a log-normal distribution to data on both onset and diagnosis dates.

Results
There were 731 (34.1%) laboratory-confirmed cases and 1412 (65.9%) suspected cases. The median age of all patients was 7 years (interquartile range: 2-13), and 1213 cases (56.6%) were boys. Over 90% of all patients were asymptomatic, mild, or moderate cases. The median time from illness onset to diagnoses was 2 days (range: 0 to 42 days). There was a rapid increase of disease at the early stage of the epidemic and then there was a gradual and steady decrease. Disease rapidly spread from Hubei Province to surrounding provinces over time. More children were infected in Hubei province than any other province.

Conclusions
Children at all ages appeared susceptible to COVID-19, and there was no significant gender difference. Although clinical manifestations of children's COVID-19 cases were generally less severe than those of adults' patients, young children, particularly infants, were vulnerable to infection. The distribution of children's COVID-19 cases varied with time and space, and most of the cases concentrated in Hubei province and surrounding areas. Furthermore, this study provides strong evidence for human-to-human transmission.

BACK

Covid-19: a puzzle with many missing pieces

Pauline Vetter, Isabella Eckerle, Laurent Kaiser

BMJ 2020;368:m627

https://www.bmj.com/content/368/bmj.m627.full

No abstract available.

BACK

Treatment and outcomes

A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19

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J Crit Care. 2020 Mar 10. pii: S0883-9441(20)30390-7

https://www.sciencedirect.com/science/article/pii/S0883944120303907

Purpose
COVID-19 (coronavirus disease 2019) is a public health emergency of international concern. As of this time, there is no known effective pharmaceutical treatment, although it is much needed for patient contracting the severe form of the disease. The aim of this systematic review was to summarize the evidence regarding chloroquine for the treatment of COVID-19.

Methods
PubMed, EMBASE, and three trial Registries were searched for studies on the use of chloroquine in patients with COVID-19.

Results
We included six articles (one narrative letter, one in-vitro study, one editorial, expert consensus paper, two national guideline documents) and 23 ongoing clinical trials in China. Chloroquine seems to be effective in limiting the replication of SARS-CoV-2 (virus causing COVID-19) in vitro.

Conclusions
There is rationale, pre-clinical evidence of effectiveness and evidence of safety from long-time clinical use for other indications to justify clinical research on chloroquine in patients with COVID-19. However, clinical use should either adhere to the Monitored Emergency Use of Unregistered Interventions (MEURI) framework or be ethically approved as a trial as stated by the World Health Organization. Safety data and data from high-quality clinical trials are urgently needed.

BACK

A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19

Bin Cao, Yeming Wang, Danning Wen, Wen Liu, Jingli Wang, Guohui Fan, Lianguo Ruan, Bin Song, Yanping Cai, Ming Wei, Xingwang Li, Jiaan Xia, Nanshan Chen, Jie Xiang, Ting Yu, Tao Bai, Xuelei Xie, Li Zhang, Caihong Li, Ye Yuan, Hua Chen, Huadong Li, Hanping Huang, Shengjing Tu, Fengyun Gong, Ying Liu, Yuan Wei, Chongya Dong, Fei Zhou, Xiaoying Gu, Jiuyang Xu, Zhibo Liu, Yi Zhang, Hui Li, Lianhan Shang, Ke Wang, Kunxia Li, Xia Zhou, Xuan Dong, Zhaohui Qu, Sixia Lu, Xujuan Hu, Shunan Ruan, Shanshan Luo, Jing Wu, Lu Peng, Fang Cheng, Lihong Pan, Jun Zou, Chunmin Jia, Juan Wang, Xia Liu, Shuzhen Wang, Xudong Wu, Qin Ge, Jing He, Haiyan Zhan, Fang Qiu, Li Guo, Chaolin Huang, Thomas Jaki, Frederick G. Hayden, Peter W. Horby, Dingyu Zhang, Chen Wang

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https://www.nejm.org/doi/10.1056/NEJMoa2001282

Background
No therapeutics have yet been proven effective for the treatment of severe illness caused by SARS-CoV-2.

Methods
We conducted a randomized, controlled, open-label trial involving hospitalized adult patients with confirmed SARS-CoV-2 infection, which causes the respiratory illness Covid-19, and an oxygen saturation (Sao2) of 94% or less while they were breathing ambient air or a ratio of the partial pressure of oxygen (Pao2) to the fraction of inspired oxygen (Fio2) of less than 300 mm Hg. Patients were randomly assigned in a 1:1 ratio to receive either lopinavir–ritonavir (400 mg and 100 mg, respectively) twice a day for 14 days, in addition to standard care, or standard care alone. The primary end point was the time to clinical improvement, defined as the time from randomization to either an improvement of two points on a seven-category ordinal scale or discharge from the hospital, whichever came first.

Results
A total of 199 patients with laboratory-confirmed SARS-CoV-2 infection underwent randomization; 99 were assigned to the lopinavir–ritonavir group, and 100 to the standard-care group. Treatment with lopinavir–ritonavir was not associated with a difference from standard care in the time to clinical improvement (hazard ratio for clinical improvement, 1.24; 95% confidence interval [CI], 0.90 to 1.72). Mortality at 28 days was similar in the lopinavir–ritonavir group and the standard-care group (19.2% vs. 25.0%; difference, −5.8 percentage points; 95% CI, −17.3 to 5.7). The percentages of patients with detectable viral RNA at various time points were similar. In a modified intention-to-treat analysis, lopinavir–ritonavir led to a median time to clinical improvement that was shorter by 1 day than that observed with standard care (hazard ratio, 1.39; 95% CI, 1.00 to 1.91). Gastrointestinal adverse events were more common in the lopinavir–ritonavir group, but serious adverse events were more common in the standard-care group. Lopinavir–ritonavir treatment was stopped early in 13 patients (13.8%) because of adverse events.

Conclusions
In hospitalized adult patients with severe Covid-19, no benefit was observed with lopinavir–ritonavir treatment beyond standard care. Future trials in patients with severe illness may help to confirm or exclude the possibility of a treatment benefit.

BACK

Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective observational study

Xiaobo Yang, Yuan Yu, Jiqian Xu, Huaqing Shu, Jia'an Xia, Hong Liu, Yongran Wu, Lu Zhang, Zhui Yu, Minghao Fang, Ting Yu, Yaxin Wang, Shangwen Pan, Xiaojing Zou, Shiying Yuan, You Shang

Lancet Respir Med. 2020 Feb 24. pii: S2213-2600(20)30079-5.

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30079-5/fulltext

Background
An ongoing outbreak of pneumonia associated with the severe acute respiratory coronavirus 2 (SARS-CoV-2) started in December, 2019, in Wuhan, China. Information about critically ill patients with SARS-CoV-2 infection is scarce. We aimed to describe the clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia.

Methods
In this single-centered, retrospective, observational study, we enrolled 52 critically ill adult patients with SARS-CoV-2 pneumonia who were admitted to the intensive care unit (ICU) of Wuhan Jin Yin-tan hospital (Wuhan, China) between late December, 2019, and Jan 26, 2020. Demographic data, symptoms, laboratory values, comorbidities, treatments, and clinical outcomes were all collected. Data were compared between survivors and non-survivors. The primary outcome was 28-day mortality, as of Feb 9, 2020. Secondary outcomes included incidence of SARS-CoV-2-related acute respiratory distress syndrome (ARDS) and the proportion of patients requiring mechanical ventilation.

Findings
Of 710 patients with SARS-CoV-2 pneumonia, 52 critically ill adult patients were included. The mean age of the 52 patients was 59·7 (SD 13·3) years, 35 (67%) were men, 21 (40%) had chronic illness, 51 (98%) had fever. 32 (61·5%) patients had died at 28 days, and the median duration from admission to the intensive care unit (ICU) to death was 7 (IQR 3–11) days for non-survivors. Compared with survivors, non-survivors were older (64·6 years [11·2] *vs* 51·9 years [12·9]), more likely to develop ARDS (26 [81%] patients *vs* 9 [45%] patients), and more likely to receive mechanical ventilation (30 [94%] patients *vs* 7 [35%] patients), either invasively or non-invasively. Most patients had organ function damage, including 35 (67%) with ARDS, 15 (29%) with acute kidney injury, 12 (23%) with cardiac injury, 15 (29%) with liver dysfunction, and one (2%) with pneumothorax. 37 (71%) patients required mechanical ventilation. Hospital-acquired infection occurred in seven (13·5%) patients.

Interpretation
The mortality of critically ill patients with SARS-CoV-2 pneumonia is considerable. The survival time of the non-survivors is likely to be within 1–2 weeks after ICU admission. Older patients (>65 years) with comorbidities and ARDS are at increased risk of death. The severity of SARS-CoV-2 pneumonia poses great strain on critical care resources in hospitals, especially if they are not adequately staffed or resourced.

BACK

Pathological findings of COVID-19 associated with acute respiratory distress syndrome

Zhe Xu, Lei Shi, Yijin Wang, Jiyuan Zhang, Lei Huang, Chao Zhang, Shuhong Liu, Peng Zhao, Hongxia Liu, Li Zhu, Yanhong Tai, Changqing Bai, Tingting Gao, Jinwen Song, Peng Xia, Jinghui Dong, Jingmin Zhao, Fu-Sheng Wang

Lancet Respir Med. 2020 Feb 18. pii: S2213-2600(20)30076-X.

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30076-X/fulltext

Abstract
Since late December, 2019, an outbreak of a novel coronavirus disease (COVID-19; previously known as 2019-nCoV)1,2 was reported in Wuhan, China,2 which has subsequently affected 26 countries worldwide. In general, COVID-19 is an acute resolved disease but it can also be deadly, with a 2% case

fatality rate. Severe disease onset might result in death due to massive alveolar damage and progressive respiratory failure.2,3 As of Feb 15, about 66 580 cases have been confirmed and over 1524 deaths. However, no pathology has been reported due to barely accessible autopsy or biopsy.2,3 Here, we investigated the pathological characteristics of a patient who died from severe infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by postmortem biopsies. This study is in accordance with regulations issued by the National Health Commission of China and the Helsinki Declaration. Our findings will facilitate understanding of the pathogenesis of COVID-19 and improve clinical strategies against the disease.

BACK

Effective Treatment of Severe COVID-19 Patients with Tocilizumab

Xiaoling Xu, Mingfeng Han, Tiantian Li, Wei Sun, Dongsheng Wang, Binqing Fu, Yonggang Zhou, Xiaohu Zheng, Yun Yang, Xiuyong Li, Xiaohua Zhang, Aijun Pan, Haiming Wei

Open Source chinaXiv:202003.00026v1

http://www.chinaxiv.org/user/download.htm?id=30387&filetype=pdf

Background
In December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in Wuhan, China, which spread rapidly and has become a world-wide public health challenge. We aimed to assess the efficacy of tocilizumab in severe patients with Corona Virus Disease19 (COVID-19) and seek a new therapeutic strategy.

Methods
The patients diagnosed as severe or critical COVID-19 in The First Affiliated Hospital of University of Science and Technology of China (Anhui Provincial Hospital) and Anhui Fuyang Second People's Hospital were given tocilizumab in addition to routine therapy between February 5 and February 14, 2020. The changes of clinical manifestations, CT scan image, and laboratory examinations were retrospectively analyzed.

Findings
Within a few days, the fever returned to normal and all other symptoms improved remarkably. Fifteen of the 20 patients (75.0%) had lowered their oxygen intake and one patient need no oxygen therapy. CT scans manifested that the lung lesion opacity absorbed in 19 patients (90.5%). The percentage of lymphocytes in peripheral blood, which decreased in 85.0% patients (17/20) before treatment (mean, 15.52 ± 8.89%), returned to normal in 52.6% patients (10/19) on the fifth day after treatment. Abnormally elevated C-reactive protein decreased significantly in 84.2% patients (16/19). chinaXiv:202003.00026v1 2 No obvious adverse reactions were observed. Nineteen patients (90.5%) have been discharged on average 13.5 days after the treatment with tocilizumab and the rest are recovering well.

Interpretation
Tocilizumab is an effective treatment in severe patients of COVID-19, which provided a new therapeutic strategy for this fatal infectious disease.

Funding
This work was supported by Department of Science and Technology of Anhui Province and Health Commission of Anhui Province (grant number: 202004a07020001) and the China National Center for Biotechnology Development 175 (grant number: 2020YFC0843800).

BACK

COVID-19: consider cytokine storm syndromes and immunosuppression

Puja Mehta, Daniel F. McAuley, Michael Brown, Emilie Sanchez, Rachel S. Tattersall, Jessica J. Manson, on behalf of theHLH Across Speciality Collaboration, UK

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https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30628-0/fulltext

As of March 12, 2020, coronavirus disease 2019 (COVID-19) has been confirmed in 125 048 people worldwide, carrying a mortality of approximately 3·7%,[1] compared with a mortality rate of less than 1% from influenza. There is an urgent need for effective treatment. Current focus has been on the development of novel therapeutics, including antivirals and vaccines. Accumulating evidence suggests that a subgroup of patients with severe COVID-19 might have a cytokine storm syndrome. We recommend identification and treatment of hyperinflammation using existing, approved therapies with proven safety profiles to address the immediate need to reduce the rising mortality.

Current management of COVID-19 is supportive, and respiratory failure from acute respiratory distress syndrome (ARDS) is the leading cause of mortality.[2] Secondary haemophagocytic lymphohistiocytosis (sHLH) is an under-recognised, hyperinflammatory syndrome characterised by a fulminant and fatal hypercytokinaemia with multiorgan failure. In adults, sHLH is most commonly triggered by viral infections[3] and occurs in 3·7–4·3% of sepsis cases.[4] Cardinal features of sHLH include unremitting fever, cytopenias, and hyperferritinaemia; pulmonary involvement (including ARDS) occurs in approximately 50% of patients.[5] A cytokine profile resembling sHLH is associated with COVID-19 disease severity, characterised by increased interleukin (IL)-2, IL-7, granulocyte-colony stimulating factor, interferon-γ inducible protein 10, monocyte chemoattractant protein 1, macrophage inflammatory protein 1-α, and tumour necrosis factor-α.[6] Predictors of fatality from a recent retrospective, multicentre study of 150 confirmed COVID-19 cases in Wuhan, China, included elevated ferritin (mean 1297·6 ng/ml in non-survivors *vs* 614·0 ng/ml in survivors; p<0·001) and IL-6 (p<0·0001),[2] suggesting that mortality might be due to virally driven hyperinflammation.

As during previous pandemics (severe acute respiratory syndrome and Middle East respiratory syndrome), corticosteroids are not routinely recommended and might exacerbate COVID-19-associated lung injury.[7] However, in hyperinflammation, immunosuppression is likely to be beneficial. Re-analysis of data from a phase 3 randomised controlled trial of IL-1 blockade (anakinra) in sepsis, showed significant survival benefit in patients with hyperinflammation, without increased adverse events.[8] A multicentre, randomised controlled trial of tocilizumab (IL-6 receptor blockade, licensed for cytokine release syndrome), has been approved in patients with COVID-19 pneumonia and elevated IL-6 in China (ChiCTR2000029765).[9] Janus kinase (JAK) inhibition could affect both inflammation and cellular viral entry in COVID-19.[10]

All patients with severe COVID-19 should be screened for hyperinflammation using laboratory trends (eg, increasing ferritin, decreasing platelet counts, or erythrocyte sedimentation rate) and the HScore[11] (table) to identify the subgroup of patients for whom immunosuppression could improve mortality. Therapeutic options include steroids, intravenous immunoglobulin, selective cytokine blockade (eg, anakinra or tocilizumab) and JAK inhibition.

BACK

Miscellaneous

Audio Interview: Making Decisions about Covid-19 Testing and Treatment for Your Patients

Eric J. Rubin, Lindsey R. Baden, Stephen Morrissey

N Engl J Med 2020; 382:e25

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The rapid spread of SARS-CoV-2, a novel coronavirus that emerged in late 2019, and the resulting Covid-19 disease has been labeled a Public Health Emergency of International Concern by the World Health Organization. What physicians need to know about transmission, diagnosis, and treatment is the subject of ongoing updates from infectious disease experts at the Journal.

In this audio interview conducted on March 10, 2020, the editors discuss the care of two hypothetical patients who present with equivocal symptoms.

BACK

The psychological impact of quarantine and how to reduce it: rapid review of the evidence

Samantha K. Brooks, Rebecca K. Webster, Louise E. Smith, Lisa Woodland, Simon Wessely, Neil Greenberg, Gideon James Rubin

The Lancet – Volume 395 – issue 10227 – P912-920

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30460-8/fulltext

Summary
The December, 2019 coronavirus disease outbreak has seen many countries ask people who have potentially come into contact with the infection to isolate themselves at home or in a dedicated quarantine facility. Decisions on how to apply quarantine should be based on the best available evidence. We did a Review of the psychological impact of quarantine using three electronic databases. Of 3166 papers found, 24 are included in this Review. Most reviewed studies reported negative psychological effects including post-traumatic stress symptoms, confusion, and anger. Stressors included longer quarantine duration, infection fears, frustration, boredom, inadequate supplies, inadequate information, financial loss, and stigma. Some researchers have suggested long-lasting effects. In situations where quarantine is deemed necessary, officials should quarantine individuals for no longer than required, provide clear rationale for quarantine and information about protocols, and ensure sufficient supplies are provided.

Appeals to altruism by reminding the public about the benefits of quarantine to wider society can be favourable.

BACK

Covid-19: out-of-hours providers are drafted in to manage non-urgent patients in community

Elisabeth Mahase

BMJ 2020;368:m959

https://www.bmj.com/content/368/bmj.m959.abstract

Regional NHS leaders in England have been ordered to immediately organise a primary care management service to care for covid-19 patients who “do not require immediate admission” to hospital.

In a letter sent on 8 March, seen by The BMJ, NHS England and NHS Improvement’s strategic incident director for coronavirus, Keith Willett, has ordered regional primary care and public health directors to set up a 24 hour, seven day a week service to manage patients in the community. This service should be delivered by an out-of-hours provider, and every part of England must be covered by Tuesday 10 March, the letter said.

BACK

Covid-19: What’s the current advice for UK doctors?

Abi Rimmer

BMJ 2020;368:m978

https://www.bmj.com/content/368/bmj.m978.abstract

I haven’t been fit tested for the correct masks (FFP3)? Can I be asked to go into a room with a patient with suspected or confirmed covid-19?

UK employers have a legal obligation under the Health and Safety at Work Act 1974 to protect staff from harm. And the Control of Substances Hazardous to Health Regulations place a duty to carry out individual risk assessments to identify hazards, quantify risks, and put suitable controls in place, says Steven Nimmo, editor of the Occupational Medicine Journal. “If the risk assessment establishes that personal protective equipment (PPE) is required then your employer must provide it, properly fit it, and provide suitable instruction and training in its use,” he says.

Public Health England’s guidance says that clinicians preparing to assess a patient with suspected covid-19 must wear PPE, which as a minimum should be a correctly fitted FFP3 respirator, gown, gloves, and eye protection.[1] Doctors seeing patients with confirmed covid-19 must wear full PPE, including a FFP3

respirator, disposable eye protection, and preferably a visor, a long sleeved disposable gown, and gloves, PHE says. For symptomatic, unconfirmed patients, doctors should wear a fluid resistant surgical mask, gloves, apron and eye protection if there is a risk of splashing into the eyes, PHE recommends.[2]

BACK

Covid-19: 90% of cases will hit NHS over nine week period, chief medical officer warns

Elisabeth Mahase

BMJ 2020;368:m918

https://www.bmj.com/content/368/bmj.m918.abstract

Nearly all covid-19 cases will hit the NHS in a “heavily concentrated” burst, with 50% of cases predicted to happen over a three week period and 90% over nine weeks, says the chief medical officer for England, Chris Whitty.

Speaking to the Health and Social Care Committee on 5 March, Whitty said that the NHS would be put under huge pressure and would have to push some routine care to before or after the expected peak of cases.

BACK

Covid-19: roundup of latest news

Gareth Iacobucci

BMJ 2020;368:m969

https://www.bmj.com/content/368/bmj.m969.abstract

A&E departments lack proper isolation facilities, senior medic warns

The vast majority of NHS emergency departments in England don’t have adequate isolation facilities for containing the spread of infectious diseases such as covid-19, one of the country’s most senior emergency doctors told The BMJ. Chris Moulton, consultant in emergency medicine at the Royal Bolton Hospital and former vice president of the Royal College of Emergency Medicine, said he had visited and observed around 80 emergency departments in his current role as joint emergency medicine lead for the NHS’s Getting it Right First Time (GIRFT) programme.

BACK

Covid-19: are we getting the communications right?

Andy Cowper

BMJ 2020;368:m919

https://www.bmj.com/content/368/bmj.m919.abstract

Other countries' experiences are instructive, says Andy Cowper

Handling the covid-19 epidemic requires a balanced approach that promptly tells people what they and the health system can do without causing panic. China, where the SARS-CoV-2 virus originally infected humans, tried to use an authoritarian approach to underplay the seriousness of the outbreak in its early stages.1 It is paradoxical therefore that China's aggressive approach to locking down cities is now credited with having slowed the epidemic's spread there.2

Iran is second to China in the covid-19 death toll to date. The country is also believed to have been less than candid about the situation there, a stance dramatically emphasised when its deputy health minister visibly succumbed to the illness during a televised press conference about the disease.3
In the UK, while the gravity of the situation has become clearer, the official communications response has been mixed.

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