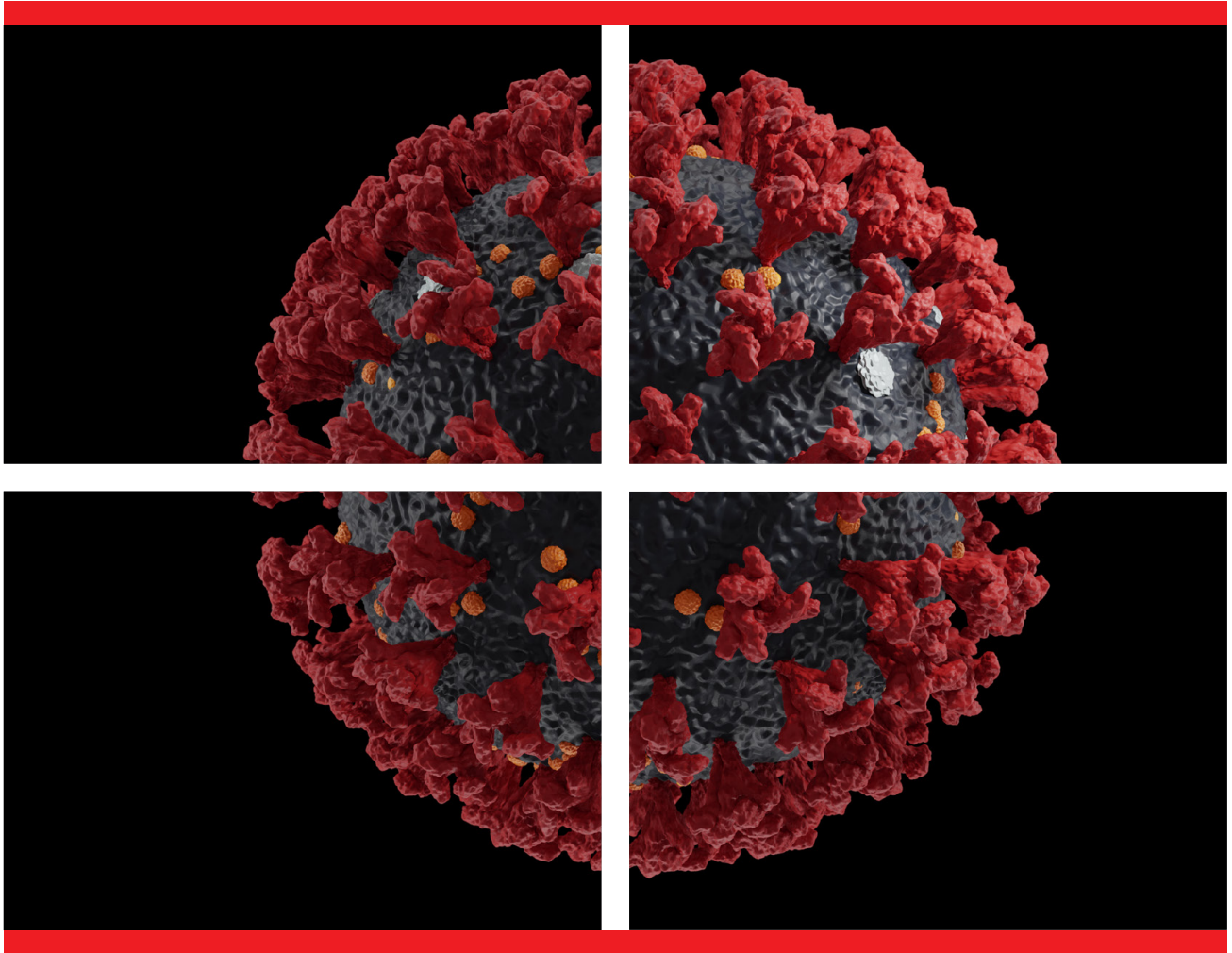


Publication List

COVID-19



Disclaimer

*This document contains a selection of relevant scientific publications related to COVID-19, some of which are not yet peer-reviewed (marked with *).*

The content has been compiled to the best of our knowledge and belief and makes no claim to completeness or correctness.

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COVID-19: Disease state and related laboratory abnormalities

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study

Nanshan Chen, Min Zhou, Xuan Dong, Jieming Qu, Fengyun Gong, Yang Han, Yang Qiu, Jingli Wang, Ying Liu, Yuan Wei, Jia'an Xia, Ting Yu, Xinxin Zhang, Li Zhang

– *Lancet* 2020; 395: 507–13 –

Summary

Background

In December, 2019, a pneumonia associated with the 2019 novel coronavirus (2019-nCoV) emerged in Wuhan, China. We aimed to further clarify the epidemiological and clinical characteristics of 2019-nCoV pneumonia.

Methods

In this retrospective, single-centre study, we included all confirmed cases of 2019-nCoV in Wuhan Jinyintan Hospital from Jan 1 to Jan 20, 2020. Cases were confirmed by real-time RT-PCR and were analysed for epidemiological, demographic, clinical, and radiological features and laboratory data. Outcomes were followed up until Jan 25, 2020.

Results

Of the 99 patients with 2019-nCoV pneumonia, 49 (49%) had a history of exposure to the Huanan seafood market. The average age of the patients was 55·5 years (SD 13·1), including 67 men and 32 women. 2019-nCoV was detected in all patients by real-time RT-PCR. 50 (51%) patients had chronic diseases. Patients had clinical manifestations of fever (82 [83%] patients), cough (81 [82%] patients), shortness of breath (31 [31%] patients), muscle ache (11 [11%] patients), confusion (nine [9%] patients), headache (eight [8%] patients), sore throat (five [5%] patients), rhinorrhoea (four [4%] patients), chest pain (two [2%] patients), diarrhoea (two [2%] patients), and nausea and vomiting (one [1%] patient). According to imaging examination, 74 (75%) patients showed bilateral pneumonia, 14 (14%) patients showed multiple mottling and ground-glass opacity, and one (1%) patient had pneumothorax. 17 (17%) patients developed acute respiratory distress syndrome and, among them, 11 (11%) patients worsened in a short period of time and died of multiple organ failure.

Conclusions

The 2019-nCoV infection was of clustering onset, is more likely to affect older males with comorbidities, and can result in severe and even fatal respiratory diseases such as acute respiratory distress syndrome. In general, characteristics of patients who died were in line with the MuLBSTA score, an early warning model for predicting mortality in viral pneumonia. Further investigation is needed to explore the applicability of the MuLBSTA score in predicting the risk of mortality in 2019-nCoV infection.

Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China

Qiurong Ruan, Kun Yang, Wenxia Wang, Lingyu Jiang, Jianxin Song

– *Intensive Care Med* 2020; <https://doi.org/10.1007/s00134-020-05991-x> –

Abstract

Introduction

The rapid emergence of COVID-19 in Wuhan city, Hubei Province, China, has resulted in thousands of deaths [1]. Many infected patients, however, presented mild flu-like symptoms and quickly recover [2]. To effectively prioritize resources for patients with the highest risk, we identified clinical predictors of mild and severe patient outcomes. Using the database of Jin Yin-tan Hospital and Tongji Hospital, we conducted a retrospective multicenter study of 68 death cases (68/150, 45%) and 82 discharged cases (82/150, 55%) with laboratory-confirmed infection of SARS-CoV-2. Patients met the discharge criteria if they had no fever for at least 3 days, significantly improved respiratory function, and had negative SARS-CoV-2 laboratory test results twice in succession. Case data included demographics, clinical characteristics, laboratory results, treatment options and outcomes. For statistical analysis, we represented continuous measurements as means (SDs) or as medians (IQRs) which compared with Student's t test or the Mann–Whitney–Wilcoxon test. Categorical variables were expressed as numbers (%) and compared by the χ^2 test or Fisher's exact test.

Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths

Chih-Cheng Lai, Yen Hung Liu, Cheng-Yi Wang, Ya-Hui Wang, Shun-Chung Hsueh, Muh-Yen Yen, Wen-Chien Ko, Po-Ren Hsueh

– *Journal of Microbiology, Immunology and Infection*, <https://doi.org/10.1016/j.jmii.2020.02.012> –

Abstract

Since the emergence of coronavirus disease 2019 (COVID-19) (formerly known as the 2019 novel coronavirus [2019-nCoV]) in Wuhan, China in December 2019, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), more than 75,000 cases have been reported in 32 countries/regions, resulting in more than 2000 deaths worldwide. Despite the fact that most COVID-19 cases and mortalities were reported in China, the WHO has declared this outbreak as the sixth public health emergency of international concern. The COVID-19 can present as an asymptomatic carrier state, acute respiratory disease, and pneumonia. Adults represent the population with the highest infection rate; however, neonates, children, and elderly patients can also be infected by SARS-CoV-2. In addition, nosocomial infection of hospitalized patients and healthcare workers, and viral transmission from asymptomatic carriers are possible. The most common finding on chest imaging among patients with pneumonia was ground-glass opacity with bilateral involvement. Severe cases are more likely to be older patients with underlying comorbidities compared to mild cases. Indeed, age and disease severity may be correlated with the outcomes of COVID-19. To date, effective treatment is lacking; however, clinical trials investigating the efficacy of several agents, including remdesivir and chloroquine, are underway in China. Currently, effective infection control intervention is the only way to prevent the spread of SARS-CoV-2.

Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study

Fei Zhou, Ting Yu, Ronghui Du, Guohui Fan, Ying Liu, Zhibo Liu, Jie Xiang, Yeming Wang, Bin Song, Xiaoying Gu, Lulu Guan, Yuan Wei, Hui Li, Xudong Wu, Jiuyang Xu, Shengjin Tu, Yi Zhang, Hua Chen, Bin Cao

– *The Lancet* 2020; [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3) –

Abstract

Background

Since December, 2019, Wuhan, China, has experienced an outbreak of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Epidemiological and clinical characteristics of patients with COVID-19 have been reported but risk factors for mortality and a detailed clinical course of illness, including viral shedding, have not been well described.

Methods

In this retrospective, multicentre cohort study, we included all adult inpatients (≥ 18 years old) with laboratory-confirmed COVID-19 from Jinyintan Hospital and Wuhan Pulmonary Hospital (Wuhan, China) who had been discharged or had died by Jan 31, 2020. Demographic, clinical, treatment, and laboratory data, including serial samples for viral RNA detection, were extracted from electronic medical records and compared between survivors and non-survivors. We used univariable and multivariable logistic regression methods to explore the risk factors associated with in-hospital death.

Results

191 patients (135 from Jinyintan Hospital and 56 from Wuhan Pulmonary Hospital) were included in this study, of whom 137 were discharged and 54 died in hospital. 91 (48%) patients had a comorbidity, with hypertension being the most common (58 [30%] patients), followed by diabetes (36 [19%] patients) and coronary heart disease (15 [8%] patients). Multivariable regression showed increasing odds of in-hospital death associated with older age (odds ratio 1.10, 95% CI 1.03–1.17, per year increase; $p=0.0043$), higher Sequential Organ Failure Assessment (SOFA) score (5.65, 2.61–12.23; $p<0.0001$), and d-dimer greater than 1 $\mu\text{g/L}$ (18.42, 2.64–128.55; $p=0.0033$) on admission. Median duration of viral shedding was 20.0 days (IQR 17.0–24.0) in survivors, but SARS-CoV-2 was detectable until death in non-survivors. The longest observed duration of viral shedding in survivors was 37 days.

Conclusions

The potential risk factors of older age, high SOFA score, and d-dimer greater than 1 $\mu\text{g/L}$ could help clinicians to identify patients with poor prognosis at an early stage. Prolonged viral shedding provides the rationale for a strategy of isolation of infected patients and optimal antiviral interventions in the future.

Clinical Characteristics of Coronavirus Disease 2019 in China

W. Guan, Z. Ni, Yu Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui, B. Du, L. Li, G. Zeng, K.-Y. Yuen, R. Chen, C. Tang, T. Wang, P. Chen, J. Xiang, S. Li, Jin-lin Wang, Z. Liang, Y. Peng, L. Wei, Y. Liu, Ya-hua Hu, P. Peng, Jian-ming Wang, J. Liu, Z. Chen, G. Li, Z. Zheng, S. Qiu, J. Luo, C. Ye, S. Zhu, N. Zhong

– *N Engl J Med* 2020; DOI: 10.1056/NEJMoa2002032 –

Abstract

Background

Since December 2019, when coronavirus disease 2019 (Covid-19) emerged in Wuhan city and rapidly spread throughout China, data have been needed on the clinical characteristics of the affected patients.

Methods

We extracted data regarding 1099 patients with laboratory-confirmed Covid-19 from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China through January 29, 2020. The primary composite end point was admission to an intensive care unit (ICU), the use of mechanical ventilation, or death.

Results

The median age of the patients was 47 years; 41.9% of the patients were female. The primary composite end point occurred in 67 patients (6.1%), including 5.0% who were admitted to the ICU, 2.3% who underwent invasive mechanical ventilation, and 1.4% who died. Only 1.9% of the patients had a history of direct contact with wildlife. Among nonresidents of Wuhan, 72.3% had contact with residents of Wuhan, including 31.3% who had visited the city. The most common symptoms were fever (43.8% on admission and 88.7% during hospitalization) and cough (67.8%). Diarrhea was uncommon (3.8%). The median incubation period was 4 days (interquartile range, 2 to 7). On admission, ground-glass opacity was the most common radiologic finding on chest computed tomography (CT) (56.4%). No radiographic or CT abnormality was found in 157 of 877 patients (17.9%) with nonsevere disease and in 5 of 173 patients (2.9%) with severe disease. Lymphocytopenia was present in 83.2% of the patients on admission.

Conclusions

During the first 2 months of the current outbreak, Covid-19 spread rapidly throughout China and caused varying degrees of illness. Patients often presented without fever, and many did not have abnormal radiologic findings.

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

Dawei Wang, Bo Hu, Chang Hu et al.

—JAMA. 2020;323(11):1061-1069—

Abstract

Background

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.

Methods

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.

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, $0.8 \times 10^9/L$ [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

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%.

Laboratory abnormalities in patients with COVID-2019 infection

Giuseppe Lippi, Mario Plebani

– *Clin Chem Lab Med* 2020; <https://doi.org/10.1515/cclm-2020-0198> –

Abstract

Introduction

Coronavirus disease 2019 (COVID-19), a form of respiratory and systemic zoonosis caused by a virus belonging to the Coronaviridae family, originated from the town of Wuhan in China, is still spreading around the world, thus assuming the dramatic features of a pandemic emergency [1]. According to the recent statistics of the World Health Organization (WHO), the disease has already involved all continents, with over 80,000 diagnosed cases in 34 different countries, and nearly 2700 deaths until February 26, 2020 [2]. Despite the severity of COVID-19 seems lower than that of the two previous coronavirus diseases, i.e. SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome), the long incubation period and the relatively low pathogenicity compared to that of the two previous homologous viruses are contributing to sustain and amplify the outbreak inside and outside China. Therefore, the aim of this article is to provide a brief overview on the most frequent laboratory abnormalities encountered in patients with COVID-2019 infection.

COVID-19: consider cytokine storm syndromes and immunosuppression

Puja Mehta, Daniel F McAuley, Michael Brown, Emilie Sanchez, Rachel S Tattersall, Jessica J Manson

– *Lancet*. 2020 Mar 28;395(10229):1033-1034 –

Introduction

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%, 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. 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 and occurs in 3.7–4.3% of sepsis cases. Cardinal features of sHLH include unremitting fever, cytopenias, and hyperferritinaemia; pulmonary involvement (including ARDS) occurs in approximately 50% of patients. 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 . Predictors of fatality from a recent retrospective, multicenter study of 150 confirmed COVID-19 cases in Wuhan, China, included elevated ferritin (mean 1297.6 ng/ml in nonsurvivors vs 614.0 ng/ml in survivors; $p < 0.001$) and IL-6 ($p < 0.0001$), suggesting that mortality might be due to virally driven hyperinflammation.

Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis.

Alfonso J. Rodriguez-Morales, Jaime A. Cardona-Ospina, Estefanía Gutiérrez-Ocampo, Rhuví Villamizar-Peña, Yeimer Holguin-Rivera, Juan Pablo Escalera-Antezana, Lucia Elena Alvarado-Arnez, Katterine Bonilla-Aldana, Carlos Franco-Paredes, Andrés F. Henao-Martinez, Alberto Paniz-Mondolfi, Guillermo J. Lagos-Grisales, Eduardo Ramírez-Vallejo, Jose A. Suárez, Lysien I. Zambrano, Wilmer E. Villamil-Gómez, Graciela J. Balbin-Ramon, Ali A. Rabaan, Harapan Harapan, Kuldeep Dhama, Hiroshi Nishiura, Hiromitsu Kataoka, Tauseef Ahmad, Ranjit Sah

– *Travel Med Infect Dis.* 2020 Mar 13:101623 –

Abstract

Background

An epidemic of Coronavirus Disease 2019 (COVID-19) began in December 2019 in China leading to a Public Health Emergency of International Concern (PHEIC). Clinical, laboratory, and imaging features have been partially characterized in some observational studies. No systematic reviews on COVID-19 have been published to date.

Methods

We performed a systematic literature review with meta-analysis, using three databases to assess clinical, laboratory, imaging features, and outcomes of COVID-19 confirmed cases. Observational studies and also case reports, were included, and analyzed separately. We performed a random-effects model meta-analysis to calculate pooled prevalences and 95% confidence intervals (95%CI).

Results

660 articles were retrieved for the time frame (1/1/2020-2/23/2020). After screening, 27 articles were selected for full-text assessment, 19 being finally included for qualitative and quantitative analyses. Additionally, 39 case report articles were included and analyzed separately. For 656 patients, fever (88.7%, 95%CI 84.5-92.9%), cough (57.6%, 95%CI 40.8-74.4%) and dyspnea (45.6%, 95%CI 10.9-80.4%) were the most prevalent manifestations. Among the patients, 20.3% (95%CI 10.0-30.6%) required intensive care unit (ICU), 32.8% presented with acute respiratory distress syndrome (ARDS) (95%CI 13.7-51.8), 6.2% (95%CI 3.1-9.3) with shock. Some 13.9% (95%CI 6.2-21.5%) of hospitalized patients had fatal outcomes (case fatality rate, CFR).

Conclusions

COVID-19 brings a huge burden to healthcare facilities, especially in patients with comorbidities. ICU was required for approximately 20% of polymorbid, COVID-19 infected patients and hospitalization was associated with a CFR of >13%. As this virus spreads globally, countries need to urgently prepare human resources, infrastructure and facilities to treat severe COVID-19.

Diagnostic Utility of Clinical Laboratory Data Determinations for Patients With the Severe COVID-19

Yong Gao, Tuantuan Li, Mingfeng Han, Xiuyong Li, Dong Wu, Yuanhong Xu, Yulin Zhu, Yan Liu, Xiaowu Wang, Linding Wang

– *J Med Virol.* 2020 Mar 17. doi:10.1002/jmv.25770 –

Abstract

The role of clinical laboratory data in the differential diagnosis of the severe forms of COVID-19 has not been definitely established. The aim of this study was to look for the warning index in severe COVID-19 patients. We investigated 43 adult patients with COVID-19. The patients were classified into mild group (28 patients) and severe group (15 patients). A comparison of the hematological parameters between the mild and severe groups showed significant differences in interleukin-6 (IL-6), d-dimer (d-D), glucose, thrombin time, fibrinogen, and C-reactive protein ($P < .05$). The optimal threshold and area under the receiver operator characteristic curve (ROC) of IL-6 were 24.3 and 0.795 $\mu\text{g/L}$, respectively, while those of d-D were 0.28 and 0.750 $\mu\text{g/L}$, respectively. The area under the ROC curve of IL-6 combined with d-D was 0.840. The specificity of predicting the severity of COVID-19 during IL-6 and d-D tandem testing was up to 93.3%, while the sensitivity of IL-6 and d-D by parallel test in the severe COVID-19 was 96.4%. IL-6 and d-D were closely related to the occurrence of severe COVID-19 in the adult patients, and their combined detection had the highest specificity and sensitivity for early prediction of the severity of COVID-19 patients, which has important clinical value.

Functional exhaustion of antiviral lymphocytes in COVID-19 patients

Meijuan Zheng, Yong Gao, Gang Wang, Guobin Song, Siyu Liu, Dandan Sun, Yuanhong Xu, Zhigang Tian

– *Cell Mol Immunol.* 2020 Mar 19. doi: 10.1038/s41423-020-0402-2 –

Introduction

In December 2019, a novel coronavirus was first reported in Wuhan, China. It was named by the World Health Organization as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is responsible for coronavirus disease 2019 (COVID-19). Up to 28 February 2020, 79,394 cases have been confirmed according to China's National Health Commission. Outside China, the virus has spread rapidly to over 36 countries and territories.

Cytotoxic lymphocytes such as cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells are necessary for the control of viral infection, and the functional exhaustion of cytotoxic lymphocytes is correlated with disease progression. However, whether the cytotoxic lymphocytes in patients infected with SARS-CoV-2 become functionally exhausted has not been reported.

We showed that the total number of NK and CD8⁺ T cells was decreased markedly in patients with SARS-CoV-2 infection. The function of NK and CD8⁺ T cells was exhausted with the increased expression of NKG2A in COVID-19 patients. Importantly, in patients convalescing after therapy, the number of NK and CD8⁺ T cells was restored with reduced expression of NKG2A. These results suggest that the functional exhaustion of cytotoxic lymphocytes is associated with SARS-CoV-2 infection. Hence, SARS-CoV-2 infection may break down antiviral immunity at an early stage.

Characteristics of peripheral lymphocyte subset alteration in COVID-19 pneumonia

Fan Wang, Jiayan Nie, Haizhou Wang, Qiu Zhao, Yong Xiong, Liping Deng, Shihui Song, Zhiyong Ma, Pingzheng Mo, Yongxi Zhang

– *J Infect Dis.* 2020 Mar 30. pii: jiaa150. doi: 10.1093/infdis/jiaa150 –

Abstract

Background

Since December 2019, novel coronavirus (SARS-CoV-2)-infected pneumonia (COVID-19) occurred in Wuhan, and rapidly spread throughout China. We aimed to clarify the characteristics and clinical significance of peripheral lymphocyte subset alteration in COVID-19.

Methods

The levels of peripheral lymphocyte subsets were measured by flow cytometry in 60 hospitalized COVID-19 patients before and after treatment, and their association with clinical characteristics and treatment efficacy was analyzed.

Results

Total lymphocytes, CD4+ T cells, CD8+ T cells, B cells and natural killer (NK) cells decreased in COVID-19 patients, and severe cases had a lower level than mild cases. The subsets showed a significant association with the inflammatory status in COVID-19, especially CD8+ T cells and CD4+/CD8+ ratio. After treatment, 37 patients (67%) reached clinical response, with an increase of CD8+ T cells and B cells. No significant change of any subset was detected in non-response cases. In multivariate analysis, post-treatment decrease of CD8+ T cells and B cells and increase of CD4+/CD8+ ratio were indicated as independent predictors for poor efficacy.

Conclusions

Peripheral lymphocyte subset alteration was associated with the clinical characteristics and treatment efficacy of COVID-19. CD8+ T cells tended to be an independent predictor for COVID-19 severity and treatment efficacy.

Dysregulation of immune response in patients with COVID-19 in Wuhan, China

Chuan Qin, PhD, Luoqi Zhou, Ziwei Hu, Shuoqi Zhang, PhD, Sheng Yang, Yu Tao, Cuihong Xie, Ke Ma, Ke Shang, Wei Wang, Dai-Shi Tian

– *Clinical Infectious Diseases*, <https://doi.org/10.1093/cid/ciaa248> –

Abstract

Background

In December 2019, coronavirus disease 2019 (COVID-19) emerged in Wuhan and rapidly spread throughout China.

Methods

Demographic and clinical data of all confirmed cases with COVID-19 on admission at Tongji Hospital from January 10 to February 12, 2020, were collected and analyzed. The data of laboratory examinations, including peripheral lymphocyte subsets, were analyzed and compared between severe and non-severe patients.

Results

Of the 452 patients with COVID-19 recruited, 286 were diagnosed as severe infection. The median age was 58 years and 235 were male. The most common symptoms were fever, shortness of breath, expectoration, fatigue, dry cough and myalgia. Severe cases tend to have lower lymphocytes counts, higher leukocytes counts and neutrophil-lymphocyte-ratio (NLR), as well as lower percentages of monocytes, eosinophils, and basophils. Most of severe cases demonstrated elevated levels of infection-related biomarkers and inflammatory cytokines. The number of T cells significantly decreased, and more hampered in severe cases. Both helper T cells and suppressor T cells in patients with COVID-19 were below normal levels, and lower level of helper T cells in severe group. The percentage of naïve helper T cells increased and memory helper T cells decreased in severe cases. Patients with COVID-19 also have lower level of regulatory T cells, and more obviously damaged in severe cases.

Conclusions

The novel coronavirus might mainly act on lymphocytes, especially T lymphocytes. Surveillance of NLR and lymphocyte subsets is helpful in the early screening of critical illness, diagnosis and treatment of COVID-19.

COVID-19: Diagnosis and treatment strategies

Therapeutic and triage strategies for 2019 novel coronavirus disease in fever clinic

Jinnong Zhang, Luqian Zhou, Yuqiong Yang, Wei Peng, Wenjing Wang, Xuelin Chen

– *Lancet* Vol 8,2020; [https://doi.org/10.1016/S22132600\(20\)300710](https://doi.org/10.1016/S22132600(20)300710) –

Introduction

In December, 2019, numerous unexplained pneumonia cases occurred in Wuhan, China. This outbreak was confirmed to be caused by severe acute respiratory syndrome corona virus 2 (SARSCoV2), belonging to the same family of viruses responsible for severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).¹ The SARS epidemic in 2003 was controlled through numerous measures in China. One effective strategy was the establishment of fever clinics for triaging patients. Based on our firsthand experience in dealing with the present outbreak in Wuhan, we have established the following clinical strategies in adult fever clinics.

Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia

– *National Health Commission & State Administration of Traditional Chinese Medicine on March 3, 2020* –

Abstract

Introduction

Since December 2019, multiple cases of novel coronavirus pneumonia (NCP) have been identified in Wuhan, Hubei. With the spread of the epidemic, such cases have also been found in other parts of China and other countries. As an acute respiratory infectious disease, NCP has been included in Class B infectious diseases prescribed in the Law of the People's Republic of China on Prevention and Treatment of Infectious Diseases, and managed as an infectious disease of Class A. By taking a series of preventive control and medical treatment measures, the rise of the epidemic situation in China has been contained to a certain extent, and the epidemic situation has eased in most provinces, but the incidence abroad is on the rise. With increased understanding of the clinical manifestations and pathology of the disease, and the accumulation of experience in diagnosis and treatment, in order to further strengthen the early diagnosis and early treatment of the disease, improve the cure rate, reduce the mortality rate, avoid nosocomial infection as much as possible and pay attention to the spread caused by the imported cases from overseas.

The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks

Giuseppe Lippi, Mario Plebani

– *Clin Chem Lab Med* 2020; <https://doi.org/10.1515/cclm-2020-0240> –

Abstract

Coronavirus disease 2019, abbreviated to COVID-19 and sustained by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is the latest biological hazard to assume the relevance of insidious worldwide threat. One obvious question that is now engaging the minds of many scientists and healthcare professionals is whether and eventually how laboratory medicine could efficiently contribute to counteract this and other (future) viral outbreaks. Despite there being evidence that laboratory tests are vital throughout many clinical pathways, there are at least three major areas where in vitro diagnostics can also provide essential contributions to diagnostic reasoning and managed care of patients with suspected or confirmed SARS-CoV-2 infection. These include etiological diagnosis, patient monitoring, as well as epidemiologic surveillance. Nonetheless, some structural and practical aspects may generate substantial hurdles in providing timely and efficient response to this infectious emergency, which basically include inadequate (insufficient) environment and shortage of technical and human resources for facing enhanced volume of tests on many infected patients, some of whom are with severe disease. Some proactive and reactive strategies may hence be identified to confront this serious healthcare challenge, which entail major investments on conventional laboratory resources, reinforcement of regional networks of clinical laboratories, installation of mobile laboratories, as well as being proactive in establishing laboratory emergency plans.

Rasche Triage symptomatischer Patienten in der Notaufnahme

Martina Lenzen-Schulte

– *Deutsches Ärzteblatt*, Jg. 117, Heft 14, 3. April 2020 –

Introduction

Derzeit strömen Patienten in die Notaufnahmen, die wegen fieberhafter Infekte und respiratorischer Symptome beunruhigt sind. Wie lässt sich rasch und effektiv klären, ob sie dringend COVID-19 verdächtig sind oder nicht? Wichtig ist dies, da viele Testergebnisse auf sich warten lassen.

COVID-19 and hemostasis

Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia

Ning Tang, Dengju Li, Xiong Wang, Ziyong Sun

– *J Thromb Haemost.* 2020;00:1–4 –

Abstract

Background

In the recent outbreak of novel coronavirus infection in Wuhan, China, significantly abnormal coagulation parameters in severe novel coronavirus pneumonia (NCP) cases were a concern.

Methods

Conventional coagulation results and outcomes of 183 consecutive patients with confirmed NCP in Tongji hospital were retrospectively analyzed.

Results

The overall mortality was 11.5%, the non-survivors revealed significantly higher D-dimer and fibrin degradation product (FDP) levels, longer prothrombin time and activated partial thromboplastin time compared to survivors on admission ($P < .05$); 71.4% of non-survivors and 0.6% survivors met the criteria of disseminated intravascular coagulation during their hospital stay.

Conclusions

The present study shows that abnormal coagulation results, especially markedly elevated D-dimer and FDP are common in deaths with NCP.

ISTH interim guidance on recognition and management of coagulopathy in COVID-19

Jecko Thachil, Ning Tang, Satoshi Gando, Anna Falanga, Marco Cattaneo, Marcel Levi, Cary Clark, Toshiaki Iba

– doi: 10.1111/JTH.14810 –

Abstract

Introduction

The novel corona virus infection (now classified as COVID-19), first identified in December 2019 in Wuhan, China, has contributed to significant mortality in several countries with the number of infected cases increasing exponentially worldwide. The majority of the most severely ill patients initially present with single organ failure (i.e. respiratory insufficiency) but some of them progress to more systemic disease and multiple organ dysfunction. One of the most significant poor prognostic features in those patients is the development of coagulopathy. In patients who develop sepsis from various infectious agents, development of coagulopathy is one of the key and persistent features which is associated with poor outcomes. In this context, the role of International Society of Thrombosis and Haemostasis (ISTH) would be crucial in guiding health care professionals how to manage the coagulopathy of COVID-19. A simple and easily follow-able algorithm for the management of COVID-19 coagulopathy would currently be useful in both the well-resourced and less-resourced settings as a guide in managing this complication. This pragmatic statement should clearly be considered as an interim guidance since the clinical experience of managing this pandemic is increasing. The authors are certain that this statement will be modified with developing knowledge and therapeutics in managing COVID-19. The aim of this guidance document is to provide a risk stratification at admission for a COVID-19 patient and management of coagulopathy which may develop in some of these patients, based on easily available laboratory parameters.

D-dimer is Associated with Severity of Coronavirus Disease 2019: A Pooled Analysis

Giuseppe Lippi, Emmanuel J. Favaloro

– *Thrombosis and Haemostasis* April 2020; [https://doi.org/ 10.1055/s-0040-1709650](https://doi.org/10.1055/s-0040-1709650) –

Abstract

Introduction

A new infective outbreak, sustained by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and defined coronavirus disease 2019 (COVID-19), is now spreading all around the world.[1] The clinical course of this respiratory disease is complicated in up to 15% of infected patients by onset of interstitial pneumonia, evolving toward acute respiratory distress syndrome needing mechanical ventilation or admission to the intensive care unit (ICU), and is also often accompanied by multiorgan failure.[2] Since there is now incontrovertible evidence that laboratory hemostasis provides an essential contribution to decision-making and care of the vast majority of human pathologies,[3] we aimed to explore here whether increased D-dimer values—which are a frequent occurrence in patients with COVID-19[4]—may be associated with disease severity.

A New Predictor of Disease Severity in Patients with COVID-19 in Wuhan, China*

Ying Zhou, Zhen Yang, Yanan Guo, Shuang Geng, Shan Gao, Shenglan Ye, Yi Hu, Yafei Wang

– medRxiv; <https://doi.org/10.1101/2020.03.24.20042119> –

Abstract

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) broke out in Wuhan, Hubei, China. This study sought to elucidate a novel predictor of disease severity in patients with coronavirus disease-19 (COVID-19) caused by SARS-CoV-2.

Methods

Patients enrolled in this study were all hospitalized with COVID-19 in the Central Hospital of Wuhan, China. Clinical features, chronic comorbidities, demographic data, and laboratory and radiological data were reviewed. The outcomes of patients with severe pneumonia and those with non-severe pneumonia were compared using the Statistical Package for the Social Sciences (IBM Corp., Armonk, NY, USA) to explore clinical characteristics and risk factors. The receiver operating characteristic curve was used to screen optimal predictors from the risk factors and the predictive power was verified by internal validation.

Results

A total of 377 patients diagnosed with COVID-19 were enrolled in this study, including 117 with severe pneumonia and 260 with non-severe pneumonia. The independent risk factors for severe pneumonia were age [odds ratio (OR): 1.059, 95% confidence interval (CI): 1.036–1.082; $p < 0.001$], N/L (OR: 1.322, 95% CI: 1.180–1.481; $p < 0.001$), CRP (OR: 1.231, 95% CI: 1.129–1.341; $p = 0.002$), and D-dimer (OR: 1.059, 95% CI: 1.013–1.107; $p = 0.011$). We identified a product of N/L*CRP*D-dimer as having an important predictive value for the severity of COVID-19. The cutoff value was 5.32. The negative predictive value of less than 5.32 for the N/L*CRP*D-dimer was 93.75%, while the positive predictive value was 46.03% in the test sets. The sensitivity and specificity were 89.47% and 67.42%. In the training sets, the negative and positive predictive values were 93.80% and 41.32%, respectively, with a specificity of 70.76% and a sensitivity of 89.87%.

Conclusions

A product of N/L*CRP*D-dimer may be an important predictor of disease severity in patients with COVID-19.

Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

Ning Tang, Huan Bai, Xing Chen, Jiale Gong, Dengju Li, Ziyong Sun

– doi: 10.1111/JTH.14817 –

Abstract

Background

A relatively high mortality of severe coronavirus disease 2019 (COVID-19) is worrying, the application of heparin in COVID-19 has been recommended by some expert consensus due to the risk of disseminated intravascular coagulation and venous thromboembolism. However, its efficacy remains to be validated.

Methods

Coagulation results, medications and outcomes of consecutive patients being classified as severe COVID-19 in Tongji hospital were retrospectively analysed. The 28-day mortality between heparin users and nonusers were compared, also in different risk of coagulopathy which was stratified by the sepsis-induced coagulopathy (SIC) score or D-dimer result.

Results

There were 449 patients with severe COVID-19 enrolled into the study, 99 of them received heparin (mainly with low molecular weight heparin, LMWH) for 7 days or longer. The D-dimer, prothrombin time and age were positively, and platelet count was negatively, correlated with 28-day mortality in multivariate analysis. No difference on 28-day mortality was found between heparin users and nonusers (30.3% vs 29.7%, $P=0.910$). But the 28-day mortality of heparin users were lower than nonusers in patients with SIC score ≥ 4 (40.0% vs 64.2%, $P=0.029$), or D-dimer > 6 fold of upper limit of normal (32.8% vs 52.4%, $P=0.017$).

Conclusions

Anticoagulant therapy mainly with LMWH appears to be associated with better prognosis in severe COVID-19 patients meeting SIC criteria or with markedly elevated D-dimer.

Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis

Giuseppe Lippi, Mario Plebani, Brandon Michael Henry

– *Clinica Chimica Acta* 506 (2020); 145–148 –

Abstract

Background

Coronavirus disease 2019 (COVID-19) is a novel infectious disease with lack of established laboratory markers available to evaluate illness severity. In this study, we investigate whether platelet count could differentiate between COVID-19 patients with or without severe disease. Additionally, we evaluate if thrombocytopenia is associated with severe COVID-19.

Methods

An electronic search in Medline, Scopus and Web of Science was performed to identify studies reporting data on platelet count in COVID-19 patients. A meta-analysis was performed, with calculation of weighted mean difference (WMD) of platelet number in COVID-19 patients with or without severe disease and odds ratio (OR) of thrombocytopenia for severe form of COVID-19.

Results

Nine studies with 1779 COVID-19 patients, 399 (22.4%) with severe disease, were included in the metaanalysis. The pooled analysis revealed that platelet count was significantly lower in patients with more severe COVID-19 (WMD $-31 \times 10^9/L$; 95% CI, from -35 to $-29 \times 10^9/L$). A subgroup analysis comparing patients by survival, found an even lower platelet count was observed with mortality (WMD, $-48 \times 10^9/L$; 95% CI, -57 to $-39 \times 10^9/L$). In the four studies ($n = 1427$) which reported data on rate of thrombocytopenia, a low platelet count was associated with over fivefold enhanced risk of severe COVID-19 (OR, 5.1; 95% CI, 1.8–14.6).

Conclusions

Low platelet count is associated with increased risk of severe disease and mortality in patients with COVID-19, and thus should serve as clinical indicator of worsening illness during hospitalization.

Prominent changes in blood coagulation of patients with SARS-CoV-2 infection

Huan Han, Lan Yang, Rui Liu, Fang Liu, Kai-lang Wu, Jie Li, Xing-hui Liu, Cheng-liang Zhu

– *Clin Chem Lab Med* 2020; <https://doi.org/10.1515/cclm-2020-0188> –

Abstract

Background

As the number of patients increases, there is a growing understanding of the form of pneumonia sustained by the 2019 novel coronavirus (SARS-CoV-2), which has caused an outbreak in China. Up to now, clinical features and treatment of patients infected with SARS-CoV-2 have been reported in detail. However, the relationship between SARS-CoV-2 and coagulation has been scarcely addressed. Our aim is to investigate the blood coagulation function of patients with SARS-CoV-2 infection.

Methods

In our study, 94 patients with confirmed SARSCoV-2 infection were admitted in Renmin Hospital of Wuhan University. We prospectively collect blood coagulation data in these patients and in 40 healthy controls during the same period.

Results

Antithrombin values in patients were lower than that in the control group ($p < 0.001$). The values of D-dimer, fibrin/fibrinogen degradation products (FDP), and fibrinogen (FIB) in all SARS-CoV-2 cases were substantially higher than those in healthy controls. Moreover, D-dimer and FDP values in patients with severe SARS-CoV-2 infection were higher than those in patients with milder forms. Compared with healthy controls, prothrombin time activity (PT-act) was lower in SARS-CoV-2 patients. Thrombin time in critical SARS-CoV-2 patients was also shorter than that in controls.

Conclusions

The coagulation function in patients with SARS-CoV-2 is significantly deranged compared with healthy people, but monitoring D-dimer and FDP values may be helpful for the early identification of severe cases.

Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China

Chaomin Wu, Xiaoyan Chen, Yanping Cai et al.

— *JAMA Intern Med.* Published online March 13, 2020. doi:10.1001/jamainternmed.2020.0994 —

Abstract

Background

Coronavirus disease 2019 (COVID-19) is an emerging infectious disease that was first reported in Wuhan, China, and has subsequently spread worldwide. Risk factors for the clinical outcomes of COVID-19 pneumonia have not yet been well delineated.

Methods

Retrospective cohort study of 201 patients with confirmed COVID-19 pneumonia admitted to Wuhan Jinyintan Hospital in China between December 25, 2019, and January 26, 2020. The final date of follow-up was February 13, 2020.

Results

Of 201 patients, the median age was 51 years (interquartile range, 43-60 years), and 128 (63.7%) patients were men. Eighty-four patients (41.8%) developed ARDS, and of those 84 patients, 44 (52.4%) died. In those who developed ARDS, compared with those who did not, more patients presented with dyspnea (50 of 84 [59.5%] patients and 30 of 117 [25.6%] patients, respectively [difference, 33.9%; 95% CI, 19.7%-48.1%]) and had comorbidities such as hypertension (23 of 84 [27.4%] patients and 16 of 117 [13.7%] patients, respectively [difference, 13.7%; 95% CI, 1.3%-26.1%]) and diabetes (16 of 84 [19.0%] patients and 6 of 117 [5.1%] patients, respectively [difference, 13.9%; 95% CI, 3.6%-24.2%]). In bivariate Cox regression analysis, risk factors associated with the development of ARDS and progression from ARDS to death included older age (hazard ratio [HR], 3.26; 95% CI 2.08-5.11; and HR, 6.17; 95% CI, 3.26-11.67, respectively), neutrophilia (HR, 1.14; 95% CI, 1.09-1.19; and HR, 1.08; 95% CI, 1.01-1.17, respectively), and organ and coagulation dysfunction (eg, higher lactate dehydrogenase [HR, 1.61; 95% CI, 1.44-1.79; and HR, 1.30; 95% CI, 1.11-1.52, respectively] and D-dimer [HR, 1.03; 95% CI, 1.01-1.04; and HR, 1.02; 95% CI, 1.01-1.04, respectively]). High fever (≥ 39 °C) was associated with higher likelihood of ARDS development (HR, 1.77; 95% CI, 1.11-2.84) and lower likelihood of death (HR, 0.41; 95% CI, 0.21-0.82). Among patients with ARDS, treatment with methylprednisolone decreased the risk of death (HR, 0.38; 95% CI, 0.20-0.72).

Conclusions

Older age was associated with greater risk of development of ARDS and death likely owing to less rigorous immune response. Although high fever was associated with the development of ARDS, it was also associated with better outcomes among patients with ARDS. Moreover, treatment with methylprednisolone may be beneficial for patients who develop ARDS.

Clinical features and treatment of COVID-19 patients in northeast Chongqing

Suxin Wan, Yi Xiang, Wei Fang, Yu Zheng, Boqun Li, Yanjun Hu, Chunhui Lang, Daoqiu Huang, Qiuyan Sun, Yan Xiong, Xia Huang, Jinglong Lv, Yaling Luo, Li Shen, Haoran Yang, Gu Huang, Ruishan Yang

– *J Med Virol.* 2020;1–10 –

Abstract

The outbreak of the novel coronavirus in China (SARS-CoV-2) that began in December 2019 presents a significant and urgent threat to global health. This study was conducted to provide the international community with a deeper understanding of this new infectious disease. Epidemiological, clinical features, laboratory findings, radiological characteristics, treatment, and clinical outcomes of 135 patients in northeast Chongqing were collected and analyzed in this study. A total of 135 hospitalized patients with COVID-19 were enrolled. The median age was 47 years (interquartile range, 36-55), and there was no significant gender difference (53.3% men). The majority of patients had contact with people from the Wuhan area. Forty-three (31.9%) patients had underlying disease, primarily hypertension (13 [9.6%]), diabetes (12 [8.9%]), cardiovascular disease (7 [5.2%]), and malignancy (4 [3.0%]). Common symptoms included fever (120 [88.9%]), cough (102 [76.5%]), and fatigue (44 [32.5%]). Chest computed tomography scans showed bilateral patchy shadows or ground glass opacity in the lungs of all the patients. All patients received antiviral therapy (135 [100%]) (Kaletra and interferon were both used), antibacterial therapy (59 [43.7%]), and corticosteroids (36 [26.7%]). In addition, many patients received traditional Chinese medicine (TCM) (124 [91.8%]). It is suggested that patients should receive Kaletra early and should be treated by a combination of Western and Chinese medicines. Compared to the mild cases, the severe ones had lower lymphocyte counts and higher plasma levels of Pt, APTT, d-dimer, lactate dehydrogenase, PCT, ALB, C-reactive protein, and aspartate aminotransferase. This study demonstrates the clinic features and therapies of 135 COVID-19 patients. Kaletra and TCM played an important role in the treatment of the viral pneumonia. Further studies are required to explore the role of Kaletra and TCM in the treatment of COVID-19.

Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19

Yong Gao, Tuantuan Li, Mingfeng Han, Xiuyong Li, Dong Wu, Yuanhong Xu, Yulin Zhu, Yan Liu, Xiaowu Wang, Linding Wang

— *J Med Virol.* 2020;1–6. —

Abstract

Background

The role of clinical laboratory data in the differential diagnosis of the severe forms of COVID-19 has not been definitely established. The aim of this study was to look for the warning index in severe COVID-19 patients. We investigated 43 adult patients with COVID-19. The patients were classified into mild group (28 patients) and severe group (15 patients). A comparison of the hematological parameters between the mild and severe groups showed significant differences in interleukin-6 (IL-6), d-dimer (d-D), glucose, thrombin time, fibrinogen, and C-reactive protein ($P < .05$). The optimal threshold and area under the receiver operator characteristic curve (ROC) of IL-6 were 24.3 and 0.795 $\mu\text{g/L}$, respectively, while those of d-D were 0.28 and 0.750 $\mu\text{g/L}$, respectively. The area under the ROC curve of IL-6 combined with d-D was 0.840. The specificity of predicting the severity of COVID-19 during IL-6 and d-D tandem testing was up to 93.3%, while the sensitivity of IL-6 and d-D by parallel test in the severe COVID-19 was 96.4%. IL-6 and d-D were closely related to the occurrence of severe COVID-19 in the adult patients, and their combined detection had the highest specificity and sensitivity for early prediction of the severity of COVID-19 patients, which has important clinical value.

COVID-19 and laboratory diagnostics

Viral Kinetics and Antibody Responses in Patients with COVID-19*

Wenting Tan, Yanqiu Lu, Juan Zhang, Jing Wang, Yunjie Dan, Zhaoxia Tan, Xiaoqing He, Chunfang Qian, Qiangzhong Sun, Qingli Hu, Honglan Liu, Sikuan Ye, Xiaomei Xiang, Yi Zhou, Wei Zhang, Yanzhi Guo, Xiu-Hua Wang, Weiwei He, Xing Wan, Fengming Sun, Quanfang Wei, Cong Chen, Guangqiang Pan, Jie Xia, Qing Mao, Yaokai Chen, Guohong Deng

– medRxiv; <https://doi.org/10.1101/2020.03.24.20042382> –

Abstract

Background

A pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been spreading over the world. However, the viral dynamics, host serologic responses, and their associations with clinical manifestations, have not been well described in prospective cohort.

Methods

We conducted a prospective cohort and enrolled 67 COVID-19 patients admitting between Jan 26 and Feb 5, 2020. Clinical specimens including nasopharyngeal swab, sputum, blood, urine and stool were tested periodically according to standardized case report form with final follow-up on February 27. The routes and duration of viral shedding, antibody response, and their associations with disease severity and clinical manifestations were systematically evaluated. Coronaviral particles in clinical specimens were observed by transmission electron microscopy (TEM).

Results

The median duration of SARS-CoV-2 RNA shedding were 12 (3-38), 19 (5-37), and 18 (7-26) days in nasopharyngeal swabs, sputum and stools, respectively. Only 13 urines (5.6%) and 12 plasmas (5.7%) were viral positive. Prolonged viral shedding was observed in severe patients than that of non-severe patients. Cough but not fever, aligned with viral shedding in clinical respiratory specimens, meanwhile the positive stool-RNA appeared to align with the proportion who concurrently had cough and sputum production, but not diarrhea. Typical coronaviral particles could be found directly in sputum by TEM. The anti-nucleocapsid-protein IgM started on day 7 and positive rate peaked on day 28, while that of IgG was on day 10 and day 49 after illness onset. IgM and IgG appear earlier, and their titers are significantly higher in severe patients than non-severe patients ($p < 0.05$). The weak responders for IgG had a significantly higher viral clearance rate than that of strong responders ($p = 0.011$).

Conclusions

Nasopharyngeal, sputum and stools rather than blood and urine, were the major shedding routes for SARS-CoV-2, and meanwhile sputum had a prolonged viral shedding. Symptom cough seems to be aligned with viral shedding in clinical respiratory and fecal specimens. Stronger antibody response was associated with delayed viral clearance and disease severity.

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

Juanjuan Zhao, Quan Yuan, Haiyan Wang, Wei Liu, Xuejiao Liao, Yingying Su, Xin Wang, Jing Yuan, Tingdong Li, Jinxiu Li, Shen Qian, Congming Hong, Fuxiang Wang, Yingxia Liu, Zhaoqin Wang, Qing He, Zhiyong Li, Bin He, Tianying Zhang, Shengxiang Ge, Lei Liu, Jun Zhang, Ningshao Xia, Zheng Zhang

– medRxiv; <https://doi.org/10.1101/2020.03.02.20030189> –

Abstract

Background

The novel coronavirus SARS-CoV-2 is a newly emerging virus. The antibody response in infected patient remains largely unknown, and the clinical values of antibody testing have not been fully demonstrated.

Methods

A total of 173 patients with confirmed SARS-CoV-2 infection were enrolled. Their serial plasma samples (n = 535) collected during the hospitalization period were tested for total antibodies (Ab), IgM and IgG against SARS-CoV-2 using immunoassays. The dynamics of antibodies with the progress and severity of disease was analyzed.

Results

Among 173 patients, the seroconversion rate for Ab, IgM and IgG was 93.1% (161/173), 82.7% (143/173) and 64.7% (112/173), respectively. Twelve patients who had not seroconverted were those only blood samples at the early stage of illness were collected. The seroconversion sequentially appeared for Ab, IgM and then IgG, with a median time of 11, 12 and 14 days, respectively. The presence of antibodies was < 40% among patients in the first 7 days of illness, and then rapidly increased to 100.0%, 94.3% and 79.8% for Ab, IgM and IgG respectively since day 15 after onset. In contrast, the positive rate of RNA decreased from 66.7% (58/87) in samples collected before day 7 to 45.5% (25/55) during days 15 to 39. Combining RNA and antibody detections significantly improved the sensitivity of pathogenic diagnosis for COVID-19 patients ($p < 0.001$), even in early phase of 1-week since onset ($p = 0.007$). Moreover, a higher titer of Ab was independently associated with a worse clinical classification ($p = 0.006$).

Conclusions

The antibody detection offers vital clinical information during the course of SARS-CoV2 infection. The findings provide strong empirical support for the routine application of serological testing in the diagnosis and management of COVID-19 patients.

A serological assay to detect SARS-CoV-2 seroconversion in humans*

Fatima Amanat, Thi H.O. Nguyen, Veronika Chromikova, Shirin Strohmeier, Daniel Stadlbauer, Andres Javier, Kaijun Jiang, Guha Asthagiri Arunkumar, Jose Polanco, Maria Bermudez-Gonzalez, Daniel Caplivski, Allen Cheng, Katherine Kedzierska, Olli Vapalahti, Jussi M. Hepojoki, Viviana Simon, Florian Krammer

– medRxiv; <https://doi.org/10.1101/2020.03.17.20037713>–

Abstract

Introduction

SARS-Cov-2 (severe acute respiratory disease coronavirus 2), which causes Coronavirus Disease 2019 (COVID19) was first detected in China in late 2019 and has since then caused a global pandemic. While molecular assays to directly detect the viral genetic material are available for the diagnosis of acute infection, we currently lack serological assays suitable to specifically detect SARS-CoV-2 antibodies.

Methods

Here we describe serological enzyme-linked immunosorbent assays (ELISA) that we developed using recombinant antigens derived from the spike protein of SARS-CoV-2. These assays were developed with negative control samples representing pre-COVID 19 background immunity in the general population and samples from COVID19 patients.

Results

The assays are sensitive and specific, allowing for screening and identification of COVID19 seroconverters using human plasma/serum as early as 3 days post symptom onset. Importantly, these assays do not require handling of infectious virus, can be adjusted to detect different antibody types and are amendable to scaling.

Conclusions

Serological assays are of critical importance to determine seroprevalence in a given population, define previous exposure and identify highly reactive human donors for the generation of convalescent serum as therapeutic. Sensitive and specific identification of coronavirus SARS-Cov-2 antibody titers will also support screening of health care workers to identify those who are already immune and can be deployed to care for infected patients minimizing the risk of viral spread to colleagues and other patients.

CT Features of Coronavirus Disease 2019 (COVID-19) Pneumonia in 62 Patients in Wuhan, China

Shuchang Zhou, Yujin Wang, Tingting Zhu, Liming Xia

– *AJR Am J Roentgenol.* 2020 Mar 05 –

Abstract

Background

The purpose of this study was to investigate 62 subjects in Wuhan, China, with laboratory-confirmed coronavirus disease (COVID-19) pneumonia and describe the CT features of this epidemic disease.

Methods

A retrospective study of 62 consecutive patients with laboratory-confirmed COVID-19 pneumonia was performed. CT images and clinical data were reviewed. Two thoracic radiologists evaluated the distribution and CT signs of the lesions and also scored the extent of involvement of the CT signs. The Mann-Whitney U test was used to compare lesion distribution and CT scores. The chi-square test was used to compare the CT signs of early-phase versus advanced-phase COVID-19 pneumonia.

Results

A total of 62 patients (39 men and 23 women; mean [\pm SD] age, 52.8 ± 12.2 years; range, 30–77 years) with COVID-19 pneumonia were evaluated. Twenty-four of 30 patients who underwent routine blood tests (80.0%) had a decreased lymphocyte count. Of 27 patients who had their erythrocyte sedimentation rate and high-sensitivity C-reactive protein level assessed, 18 (66.7%) had an increased erythrocyte sedimentation rate, and all 27 (100.0%) had an elevated high-sensitivity C-reactive protein level. Multiple lesions were seen on the initial CT scan of 52 of 62 patients (83.9%). Forty-eight of 62 patients (77.4%) had predominantly peripheral distribution of lesions. The mean CT score for the upper zone (3.0 ± 3.4) was significantly lower than that for the middle (4.5 ± 3.8) and lower (4.5 ± 3.7) zones ($p = 0.022$ and $p = 0.020$, respectively), and there was no significant difference in the mean CT score of the middle and lower zones ($p = 1.00$). The mean CT score for the anterior area (4.4 ± 4.1) was significantly lower than that for the posterior area (7.7 ± 6.3) ($p = 0.003$). CT findings for the patients were as follows: 25 patients (40.3%) had ground-glass opacities (GGO), 21 (33.9%), consolidation; 39 (62.9%), GGO plus a reticular pattern; 34 (54.8%), vacuolar sign; 28 (45.2%), microvascular dilation sign; 35 (56.5%), fibrotic streaks; 21 (33.9%), a subpleural line; and 33 (53.2%), a subpleural transparent line. With regard to bronchial changes seen on CT, 45 patients (72.6%) had air bronchogram, and 11 (17.7%) had bronchus distortion. In terms of pleural changes, CT showed that 30 patients (48.4%) had pleural thickening, 35 (56.5%) had pleural retraction sign, and six (9.7%) had pleural effusion. Compared with early-phase disease (≤ 7 days after the onset of symptoms), advanced-phase disease (8–14 days after the onset of symptoms) was characterized by significantly increased frequencies of GGO plus a reticular pattern, vacuolar sign, fibrotic streaks, a subpleural line, a subpleural transparent line, air bronchogram, bronchus distortion, and pleural effusion; however, GGO significantly decreased in advanced-phase disease.

Conclusions

CT examination of patients with COVID-19 pneumonia showed a mixed and diverse pattern with both lung parenchyma and the interstitium involved. Identification of GGO and a single lesion on the initial CT scan suggested early-phase disease. CT signs of aggravation and repair coexisted in advanced-

phase disease. Lesions presented with a characteristic multifocal distribution in the middle and lower lung regions and in the posterior lung area. A decreased lymphocyte count and an increased high-sensitivity C-reactive protein level were the most common laboratory findings.

Molecular immune pathogenesis and diagnosis of COVID-19

Xiaowei Li, Manman Genga, Yizhao Peng, Liesu Meng, Shemin Lu

– *Journal of Pharmaceutical Analysis*, <https://doi.org/10.1016/j.jpha.2020.03.001> –

Abstract

Coronavirus disease 2019 (COVID-19) is a kind of viral pneumonia with an unusual outbreak in Wuhan, China, in December 2019, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The emergence of SARS-CoV-2 has been marked as the third introduction of a highly pathogenic coronavirus into the human population after the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV) in the twenty-first century. In this minireview, we provide a brief introduction of the general features of SARS-CoV-2 and discuss current knowledge of molecular immune pathogenesis, diagnosis and treatment of COVID-19 on the base of the present understanding of SARS-CoV and MERS-CoV infections, which may be helpful in offering novel insights and potential therapeutic targets for combating the SARS-CoV-2 infection.

Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis

Giuseppe Lippi, Carl J. Lavie, Fabian Sanchis-Gomar

– *Prog Cardiovasc Dis*. 2020 Mar 10; doi: 10.1016/j.pcad.2020.03.001 –

Introduction

Coronavirus disease 2019 (COVID-19) is an emerging outbreak caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). According to updated statistics released by the World Health Organization (WHO), COVID-19 has already affected over 93,000 people from over 75 countries worldwide, causing >3200 deaths.¹ In up to 15% of infected patients the clinical course of this pathology may be complicated by the onset of a severe form of intestinal pneumonia, which may then progress towards acute respiratory distress syndrome (ARDS) and/or multi organ failure (MOF) and death.² People with underlying cardiovascular disease are among the highest risk individuals for severe disease and death. Importantly, among the COVID-19 knowledge gaps are laboratory and diagnostics issues as well as the clinical management of severe and critically ill patients.³ Since major cardiac complications have been reported to develop in a considerable number of patients with pneumonia,⁴ we performed an analysis of the current scientific literature to investigate whether the measurement of cardiac troponin I (cTnI) or cardiac troponin T (cTnT) may help predict clinical severity in patients with COVID-19.

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