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CLINICAL FINDINGS OF COVID-19 PANDEMIC : A BRIEF REVIEW

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Abstract

A novel coronavirus was identified as the cause of a cluster of pneumonia cases, at the end of 2019, in Wuhan, a city in the Hubei Province of China. The WHO announced the disease was caused by a new corona virus called COVID-19 acronym of corona virus disease 2019. It rapidly spread, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries throughout the world with varying degrees of illness, becoming a pandemic. As the understanding of COVID-19 is evolving, an attempt has been made in this review article to provide an insight into the clinical findings of covid-19. The objective of this brief review is to raise awareness among the healthcare providers for better management and prevention of covid-19 outbreak.

keywords:COVID-19,SARS-CoV-2, Pneumonia, Acute Respiratory Distress Syndrome, Pandemic

Introduction

A cluster of idiopathic pneumonia cases were reported in December2019, in Wuhan, Hubei, China [1]. Scientists employed real-time reverse transcription polymerase chain reaction (RT-PCR), and identified the etiology being a novel corona virus labeled as Severe Acute Respiratory Syndrome Corona virus 2 (SARS-CoV-2). This was later called coronavirus disease 2019 (COVID-19) [2,3].COVID-19 seems to be contagious and spreads rapidly [4]. Transmission is from close contact and droplets produced as a result of coughing or sneezing of infected person. There is scarce evidence to suggest airborne transfer [5].

COVID-19 is a spherical or pleomorphic enveloped particles containing single-stranded (positive-sense) RNA associated with a nucleoprotein within a capsid comprised of matrix protein. The envelope bears club-shaped glycoprotein projections[6].The viral protein binds with the human protein receptor(Angiotensin-Converting Enzyme-2)ACE2 which is a membrane-bound amino peptidase [7]. ACE2 is abundant in lung, heart, kidney, and adipose tissue [8,9]. Binding of viral protein with ACE2 allows for membrane fusion and introduction of COVID-19RNA into the cell. The released RNA genome of the virus is then replicated and translated into various types of viral proteins. The replicated RNA genome and synthesized viral proteins are finally assembled together into new viruses, before they escape and attack other

cells [10,11].It was observed that, slower association between virus and receptor can result in longer incubation period, while still maintaining a relatively higher level of viral concentration in human body.[12] COVID-19 has a longer incubation period and is more contagious, while SARS presents with more symptoms and disease severity [13].

Clinical findings

According to a report from the Chinese Center for Disease Control and Prevention that included approximately 44,500 confirmed infections, 87 percent of patients were between 30 and 79 years old [14]. Recent studies reveal that the clinical characteristics of Covid-19 mimic those of SARS-CoV [15,16,17]. Fever and cough were the dominant symptoms and gastro-intestinal symptoms were uncommon, which suggests a difference in viral tropism as compared with SARS-CoV,MERS-CoV, and seasonal influenza[18,19].COVID-19 manifests with a wide clinical spectrum ranging from asymptomatic patients to septic shock and multi organ dysfunction. Based on the severity of the presentation the disease may be classified into mild, moderate, severe, and critical. Patients with mild illness may present with symptoms of an upper respiratory tract viral infection. These include dry cough, mild fever, nasal congestion, sore throat, headache, muscle pain, and malaise. It is also characterized by the absence of serious symptoms such as dyspnea. The majority (81%) of COVID-19 cases are mild in severity [20]. Furthermore, radiograph features are also absent in such cases [21].

Patients with mild disease can quickly deteriorate into severe or critical cases. Moderate Disease patients present with respiratory symptoms of cough, shortness of breath, and tachypnea. However, no signs and symptoms of severe disease are present. Patients with severe disease present with severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis, or septic shock. Clinical presentations include the presence of severe dyspnea, tachypnea (respiratory rate > 30/minute), respiratory distress. Even in severe forms of the disease, fever can be absent or moderate [20]. In addition, 5% of patients can develop a critical disease with features of respiratory failure, cardiac injury, septic shock, or multiple organ dysfunction [20,21]. Data from the Chinese Centers for Disease Control and Prevention (CDC) suggest that the case fatality rate for critical patients is 49% [20]. Patients with pre- existing co-morbidities have a higher case fatality rate. These co morbidities include diabetes, respiratory disease, cardiovascular disease, hypertension, and oncological complications. Patients without co-morbidities have a lower case fatality rate[21].Organ dysfunction (eg, shock, acute respiratory distress syndrome [ARDS], acute cardiac injury, and acute kidney injury) and death can occur in severe cases [15].

Acute Respiratory Distress Syndrome (ARDS)

The Lung alveolar cells contain abundant amounts of ACE2, thus allowingCOVID-19 to harbor within the alveoli [8]. SARS-CoV-2(severe acute respiratory syndrome coronavirus 2) mainly invades alveolar epithelial cells, resulting in respiratory symptoms. About 41.8 % of patients develop acute

respiratory distress syndrome (ARDS) [22].(COVID-19) represents viral pneumonia from SARS-CoV-2infection leading to ARDS. Its manifestations can be viewed as a combination of the 2 processes, namely viral pneumonia and ARDS [23]. ARDS causes diffuse alveolar damage in the lung. There is hyaline membrane formation in the alveoli in the acute stage, and this is followed by interstitial widening, edema and then fibroblast proliferation in the organizing stage. COVID-19-ARDS causes the typical ARDS pathological changes of diffuse alveolar damage in the lung[24,25]. Pulmonary thrombosis is common in sepsis-induced ARDS. Coagulation dysfunction appears to be common in COVID-19, and is detected by elevated D-dimer. In fatal cases there is diffuse micro vascular thrombosis, suggesting a thrombotic micro-angiopathy, and most deaths from COVID-19 ARDS have evidence of a thrombotic Disseminated intravascular coagulation (DIC)[26].

Mortality increases with the severity of the disease. Patients greater than 65 years of age present with worse degrees of ARDS and have a higher mortality likelihood [27].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 [23].Laboratory findings associated with the development of ARDS include neutrophilia, lymphopenia,elevated C-reactive protein (high-sensitivity and normal),elevated blood urea nitrogen, elevated d-dimer, prolonged PT, and elevated LDH. Laboratory markers predicting mortality of COVID-19 ARDS patients include low albumin, elevated blood urea nitrogen, and elevated LDH [22,27].

Myocardial injury

The mechanism of acute myocardial injury caused by SARS-CoV-2 infection might be related to ACE2. ACE2 is widely expressed not only in the lungs but also in the cardiovascular system and, therefore, ACE2-related signalling pathways might also have a role in heart injury. Other proposed mechanisms of myocardial injury include a cytokine storm triggered by an imbalanced response by type 1 and type 2 T helper cells and respiratory dysfunction and hypoxaemia caused by COVID-19, resulting in damage to myocardial cells[28,29].The most common causes of COVID-19-related death are associated with the lungs and heart [30]. Myocardial injury includes acute coronary syndrome, heart failure,myocarditis, hypotension or shock, and sepsis [31,32].Regardless of previous cardiac history, heart failure is commonly encountered in severe cases of COVID-19[31,33]. In severe cases it is presented with elevated levels of N-terminal pro-B-type natriuretic peptide (NT pro-BNP)and troponin levels,especially[34]. It is suspected that pulmonary hypertension causing right heart failure also contributes to these cases [35,31].Elevated high-sensitivity troponin (HS-troponin) and creatinine kinase–myocardial brand (CK-MB) levels can independently predict severe COVID-19 cases [32,33,36,37]. A recent meta-analysis has shown troponin elevation in severe cases [38]. CK itself does not predict severity [78a]. Also patients with elevated HS-troponin and CK-MB are suspected to have myocarditis or heart failure

[28,36].

Acute kidney injury

Human kidney is a target for novel severe acute respiratory syndrome corona virus 2 [SARS-CoV-2] infection. Acute kidney injury (AKI) is a severe symptom after COVID-19 infection, the incidence of which is second only to respiratory system injuries [24].AKI develops in 40% to 60% of COVID-19 ICU patients, including 20% to 30% who require renal replacement therapy (RRT). Patients may become dehydrated even before hospitalization because they have not been eating or drinking, have diarrhea, and are battling fever. Aggressive di-uresis can induce hypovolemia. “Acute tubular necrosis” (ATN) may ensue from a cytokine storm and respiratory failure.[40]. An important report on autopsy findings from deceased patients with COVID-19demonstrated prominent acute proximal tubular injury [41].

It is one of the most frequent organ damage of corona virus, with a sharp rise in serum creatinine (SCr) level and a sharp decrease in urine output [42].Systematic analysis showed that 75%of MERS-CoV infected patients developed acute renal failure (ARF) with a median interval of 11 days from symptom onset, and 6.7% of SARS-CoV infected patients with ARFwere diagnosed after a median of 20 days from symptom onset [42,43]. The latest epidemiological and clinical characteristics study showed that 3-19%patients with COVID-19 had symptoms of AKI, and about 9% patients with renal failure received continuous blood purification [28]. Acute kidney injury presents with elevated urea and cystatin-C levels in severe COVID-19 infection [22,27,44,45]. There are two postulates concerning the cause of acute kidney injury. One is from kidneys harboring more ACE2 levels than the lung or heart, especially in the proximal convoluted tubules. However, COVID-19 RNA is not encountered in the urine [46]. The other theory relates to injury via acytokine storm [45].But whether the AKI of COVID-19 is caused by a coronavirus-induced cytopathic effect or cytokinestorm-induced systemic inflammatory response remains unclear. Based on kidney injury severity, patients may acquire continuous renal replacement therapy (CRRT). It is presumed hat CRRTpotentially serves as a means of removing large cytokine levels from the system, regardless of kidney injury [44,45].

Conclusions

The COVID-19 pandemic being more infectious than SARS or MERS is spreading across the globe at an alarming rate. From the clinical findings it appears that elderly and immuno compromised patients are at the greatest risk of fatality.Since no confirmed medication or vaccine has been developed, there is a need to closely monitor the vital organ functions in patients with COVID-19 and take early clinical interventions. Current clinical management includes infection prevention and control measures and supportive care, including supplemental oxygen and mechanical ventilatory support when indicated. Prophylactic vaccination is required for the future prevention of CoV-related epidemic or pandemic.

REFERENCES

[1] C. Wang, P.W. Horby, F.G. Hayden, G.F. Gao, A novel coronavirus outbreak of global health concern, Lancet, 2020; 395: 470-473.

[2] N. Zhu, D. Zhang, W. Wang, et al., A novel coronavirus from patients with pneumonia in China, 2019, N. Engl. J. Med. 2020; 382: 727-733.

[3] J. Fang, L. Deng, L. Zhang, Y. Cai, C.W. Cheung, Z. Xia, Review of the clinical characteristics of coronavirus disease 2019 (COVID-19), J. Gen. Intern. Med. 2020; 35: 1545-1549.

[4] C.I. Paules, H.D. Marston, A.S. Fauci, Coronavirus infections—more than just the common cold, JAMA 2020; 323: 707-708.

[5] World Health Organization, Rational Use of Personal Protective Equipment for Coronavirus Disease (COVID-19): Interim Guidance, World Health Organization, 2020.

[6] de Haan C.A.M., Kuo L., Masters P.S., Vennema H., Rottier P.J.M. Coronavirus particle assembly: primary structure requirements of the membrane protein. J Virol. 1998;72(8):6838–6850.

[7] P. Zhou, X.L. Yang, X.G. Wang, et al., A pneumonia outbreak associated with a new coronavirus of probable bat origin, Nature 2020; 597: 270-273.

[8] A.J. Turner, J.A. Hiscox, N.M. Hooper, ACE2: from vasopeptidase to SARS virus receptor, Trends Pharmacol. Sci. 2004; 25: 291–294.

[9] M. Gupte, C.M. Boustany-Kari, K. Bharadwaj, et al., ACE2 is expressed in mouse adipocytes and regulated by a high-fat diet, Am. J. Physiol. Regul. Integr. Comp. Physiol. 2008; 295: 781–788.

[10] Qin, P., et al., Characteristics of the Life Cycle of Porcine Deltacoronavirus (PDCoV) In Vitro: Replication Kinetics, Cellular Ultrastructure and Virion Morphology, and Evidence 18 of Inducing Autophagy. Viruses. 2019; 11(5): 455.

[11] Qinfen, Z., et al., The life cycle of SARS coronavirus in Vero E6 cells. Journal of medical virology, 2004; 73(3): 332-337.

[12] Han, W., et al., The course of clinical diagnosis and treatment of a case infected with coronavirus disease 2019. Journal of medical virology, 2020; 92: 461-463.

[13] Z. Su, Y. Wu, A multiscale and comparative model for receptor binding of 2019 novel coronavirus and the implications of its life cycle in host cells, BioRxiv 2020.

[14] Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020; 323: 1239-1242.

[15] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497-506.

[16] Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N Engl J Med. doi: 10.1056/NEJMoa2001316.

[17]Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395: 391-393.

[18] Leung WK, To KF, Chan PK, et al. Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection. Gastroenterology 2003; 125: 1011-7.

[19]Assiri A, McGeer A, Perl TM, et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. N Engl J Med 2013; 369: 407-16.

[20] Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Napoli RD: Features, Evaluation and Treatment Coronavirus (COVID-19). StatPearls Publishing, Treasure Island, FL; 2020.

[21] Wang Y, Wang Y, Chen Y, Qin Q: Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. J Med Virol. 2020, 10. https://doi.org/10.1002/jmv.25748

[22] C. Wu, X. Chen, Y. Cai, J. Xia, X. Zhou, S. Xu, Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China, JAMA Intern. Med. 2020. doi:10.1001/jamainternmed.2020.0994.

[23] Australian guidelines for the clinical care of people with COVID-19 v2.0 - 4/16/20. National COVID-19 Clinical Evidence Taskforce. www.covid19evidence.net.au

[24] Xu Z, Shi L,Wang Y. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020; doi:10.1016/S2213- 2600(20)30076.

[25] Tian S, Xiong Y, Liu H, et al. Pathological study of the 2019 novel coronavirus disease (COVID-19) through post-mortem core biopsies. Preprints. 2020:2020030311. doi: 10.20944/preprints202003.0311.v1.

[26] Wang J, Hajizadeh N, Moore EE, McIntyre RC, Moore PK, Veress LA, Yaffe MB, Moore HB, Barrett CD. Tissue Plasminogen Activator (tPA) Treatment for COVID-19 Associated Acute Respiratory Distress Syndrome (ARDS): A Case Series. J Thromb Haemost. 2020 Apr 8. doi: 10.1111/jth.14828.

[27] Y. Liu, W. Sun, J. Li, et al., Clinical features and progression of acute respiratory distress syndrome in coronavirus disease 2019, MedRxiv 2020.

[28] Huang, C. et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395: 497–506.

[29] Wong, C. K. et al. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. Clin. Exp. Immunol. 2004; 136: 95–103.

[30] Q. Ruan, K. Yang, W. Wang, L. Jiang, J. Song, Clinical predictors of mortality due to COVID-19 based on analysis of data of 150 patients from Wuhan, China, Intens. Care Med. Exp. 2020; 46: 846-848.

[31] Z.C. Tan, L.H. Fu, D.D. Wang, K. Hong, Cardiac manifestations of patients with COVID-19 pneumonia and related treatment recommendations, Zhonghua Xin Xue Guan Bing Za Zhi. 48,2020.

[32] M. Madjid, P. Safavi-Naeini, S.D. Solomon, O. Vardeny, Potential effects of coronaviruses on the cardiovascular system: a review, JAMA Cardiol. 2020.

[33] T. Guo, Y. Fan, M. Chen, et al., Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19), JAMA Cardiol. 2020.

[34] C. Chen, C. Chen, J.T. Yan, N. Zhou,

J.P. Zhao, D.W. Wang, Analysis of myocardial injury in patients with COVID-19 and association between concomitant cardiovascular diseases and severity of COVID-19, Zhonghua Xin Xue Guan Bing Za Zhi. 48: 2020; e008.

[35] E. Driggin, M.V. Madhavan, B. Bikdeli, et al., Cardiovascular considerations for
patients, health care works, and health systems during the coronavirus disease 2019
(COVID-19) pandemic, J. Am. Coll. Cardiol. 2020; 75: 2352-2371.

[36] C. Wu, X. Hu, J. Song, et al., Heart injury signs are associated with higher and earlier mortality in coronavirus disease 2019 (COVID-19), MedRxiv 2020.

[37] B. Zhou, J. She, Y. Wang, X. Ma, The clinical characteristics of myocardial injury in severe and very severe patients with 2019 novel coronavirus disease, Lancet 2020;doi:https://doi.org/10.1016/j.jinf.2020.03.021

[38] G. Lippi, C.J. Lavie, F. Sanchis-Gomar, Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): evidence from a meta-analysis, Prog. Cardiovasc. Dis. 2020.

[39] Chafekar A, Fielding BC. MERS-CoV: Understanding the Latest Human Coronavirus Threat. Viruses. 2018;10:doi: 10.3390/v10020093.

[40]https://www.renalandurologynews.com/home/news/nephrology/acute-kidney- injury/covid-19-and-acute-kidney-injury-challenges-and-management/

[41] Su H, Yang M, Wan C, Yi LX, Tang F, Zhu HY, et al.: Renal histopathological analysis of 26 postmortem findings of patients with COVID19 in China. Kidney International doi: 10.1016/j.kint.2020.04.003

[42] Eckerle I, Müller MA, Kallies S, Gotthardt DN, Drosten C. In-vitro renal epithelial cell infection reveals a viral kidney tropism as a potential mechanism for acute renal failure during Middle East Respiratory Syndrome (MERS) Coronavirus infection. Virology Journal. 2013; 10: 359.

[43] Chu KH, Tsang WK, Tang CS, Lam MF, Lai FM, To KF, et al. Acute renal impairment in coronavirus-associated severe acute respiratory syndrome. Kidney International. 2005; 67: 698-705.

[44] X.H. Yang, R.H. Sun, D.C. Chen - Zhoughua Yi Xue Za Zhi, Diagnosis and treatment of COVID-19: acute kidney injury cannot be ignored,2020. doi:10.3760/cma.j.cn112137-20200229-00520.

[45] D. Xu, H. Zhang, H.Y. Gong, et al., Identification of a potential mechanism of acute kidney injury during the COVID-19 outbreak: a study based on single-cell transcriptome analysis, Intensive Care Med. 2020;doi: 10.1007/s00134-020-06026-1.

[46] R. Woelfel, V.M. Corman, W. Guggemos, et al., Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster, MedRxiv 2020; doi:
https://doi.org/10.1101/2020.03.05.20030502.