REVIEW ARTICLE

Clinical Characteristics of Covid-19 among Old Adult Patients with Chronic Diseases: A Systematic Review Study

Ogholgol Ghajari[1], MSc;
Farzaneh Kasraie[2], MSc,
Abdolrahim Asadollahi[1], PhD

[1]Department of Health Promotion and Aging, Faculty of Health, Shiraz University of Medical Sciences, Shiraz, Iran;

[2]Infection Control Supervisor, Ibn-e-Sina Hospital, Shiraz, Iran, Shiraz University of Medical Science, Shiraz, Iran

Correspondence:
Abdolrahim Asadollahi, PhD;
Department of Health Promotion and Aging, School of Health, 3rd Floor, Shiraz University of Medical Sciences, Razi Ave. P.O. Box: 7153675541. Shiraz, Iran
Email: a_asadollahi@sums.ac.ir
Received: 6 October 2019
Revised: 12 November 2019
Accepted: 18 December 2019

Abstract

Background: COVID-19 "coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in Wuhan, China" is a new infectious disease that has been declared by World Health Organization (WHO) as a public health emergency worldwide due to its rapid spread to China and then to other parts of the world. The present study was designed to evaluate the clinical manifestations of this disease in the elderly.

Methods: We performed a systematic review on the database of the WHO, Centers for Disease Control and prevention (CDC), PubMed, Google Scholar, Scopus, and lancet. All of the articles published until March 15, 2020, have been extracted from the above articles in English on coronavirus infection, disease, virology, epidemiology, clinical features, treatment, and prevention of the disease. Of the 1376 articles, 5 were selected out of recently published articles focusing on the epidemiological information of the virus, pneumonia caused by new corona virus, and the effects of the disease on different age groups, especially the elderly, and the rest were excluded from the review. The mean age of the patients, the mean age of mortality and the underlying diseases were chosen as the criteria of data extraction.

Results: Based on the researchers' perceptions of the text of the articles, 342 cases were included in these 5 studies. The mean age of the patients was 58.4 and that of the diceased patients was 66.5. More than 50% of the total cases had one or more underlying diseases.

Conclusion: Despite the involvement of various age groups in this infection, the virus is most likely to cause severe complications and fatalities in older people with underlying diseases.

Please cite this article as: Ghajari O, Kasraie F, Asadollahi A. Clinical Characteristics of Covid-19 among Old Adult Patients with Chronic Diseases: A Systematic Review Study. J Health Sci Surveillance Sys. 2020;8(1):2-9.

Keywords: Older Adults, Global Pandemic, COVID-19, New Coronavirus, Vulnerability

Introduction

In late December 2019, following an unusual pneumonia reported in a number of patients in Wuhan, China, extensive studies on the disease were initiated.[1] On January 7, 2020, the new Corona virus was approved by the CDC China Center and named by WHO as COVID-19 since the samples taken from the patients' upper respiratory tract contained a new type of corona virus which was confirmed by Reverse Transcription polymerase chain reaction (RT-PCR) which declared infection with a virus of corona group, but with a new genotype and different characteristics. The disease spread to several other countries within a month.[2] The rapid spread of the disease prompted the WHO to declare a relatively high risk of the disease on 30 January 2020

and warned of an epidemic.[3]

According to coronavirus studies, the elderly people with underlying diseases who have positive history of being physically in high-risk centers or have contacted known patients or carriers are at a higher risk for new corona infection and have higher mortality. Since Iran is one of the countries suffering from this disease and due to several factors such as the increased elderly population, lack of sufficient health care, and the probable outbreak, we need to address the issue in ways to prevent crisis.

Materials and Methods

A systematic review was performed on the database of the World Health Organization, CDC, PubMed, Google Scholar, Scopus and lancet. All of the articles published until March 15, 2020 were extracted from the above articles in English on coronavirus infection, disease, virology, epidemiology, clinical features, treatment, and prevention of the disease. Of the 1376 articles, 5 were selected out of recently published articles focusing on the epidemiological information of the virus, pneumonias caused by new corona virus, and the effects of the disease on different age groups, especially the elderly, and the rest were excluded from the review. The mean age of the patients, the mean age of mortality, and underlying diseases were chosen as the criteria of data extraction (as shown in Figure 1.).

Epidemiology and Transmission

According to recent studies of the virus, although it can affect all age groups and cause severe complications for them, the elderly with multiple concomitant diseases, such as hypertension, diabetes, cardiovascular or brain problems, are more prone to severe complications and death. An epidemiological study of the new coronavirus in China between January 15 and January 20, 2020, estimated such data as the incubation period, transmission interval, and baseline transmission rate using Lognormal, Gamma, and Weibull distribution methods. The Akaike Information Criterion (One of the evaluation indicators of statistical models [AIC]) criterion was also used to determine the optimal distribution. Moreover, between 10 and 31 January 2020, regarding the persistence of the epidemic, growth, and maximum likelihood, SEIR , The SEIR models the flows of people between four states: susceptible (S), exposed (E), infected (I), and resistant (R). Each of those variables represents the number of people in those groups, model were used to fit the data that showed the mean incubation period of 5.01 days (95 % CI: 4.31-5.69) and median time to infection transmission of 6.03 days (95% - CI: 5.20-6.91); the number of infections with the above three methods presented 3.74, 3.16 and 3.91 days, respectively, indicating that the risk of prevalence of virus was serious in all age groups.[1]

In one of the first studies, of 99 patients with

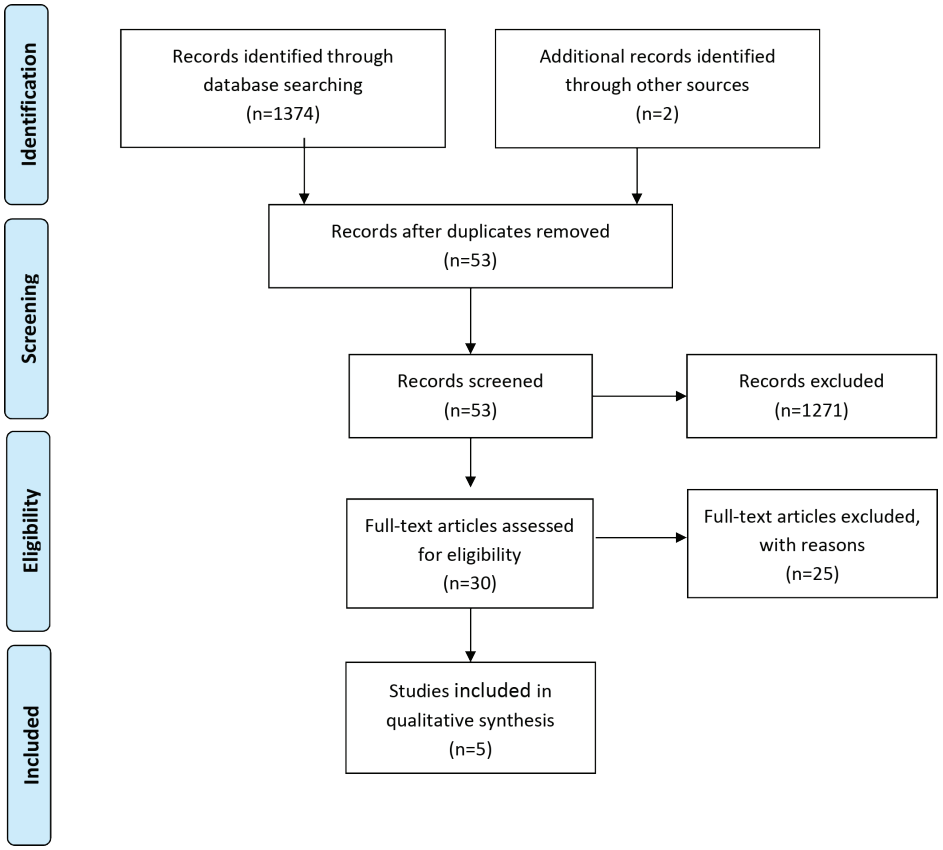

Figure 1: PRISMA Flow Diagram

pneumonia, 49 had a history of being present in the market of animal and marine products and the mean age was 55.5 years, including 67 males and 34 females. All of them were confirmed to be affected by coronavirus. Of the total number, 50 people (51%) had positive history of underlying diseases. Seventeen patients (17%) had severe respiratory distress syndrome and 11 (11%) died due to various internal organ failure. According to the findings of this study, the COVID-19 infection had a cluster onset. In general, the characteristics of patients who died were according to the MuLBSTA (A predictive MuLBSTA score was calculated on the basis of a multivariate logistic regression model in order to predict mortality with a weighted score that included multilobular infiltrates, hypo-lymphocytosis, bacterial coinfection, Smoking history, hypertension, Age) score, an early warning model for predicting mortality in viral pneumonia.[2] In the study of Fei Zhou et al., the potential risk factors for COVID- 19 are older age, high SOFA (The sequential organ failure assessment score) score, and d-dimer (A blood test that can be used to help rule out the presence of a serious blood clot) greater than 1 μg/ml, which can help clinicians identify the patients with poor prognosis in early stage.[3] According to a study by Xiaobo Yang and colleagues on 52 patients with severe COVID-19 infection at critical stages of the disease, older patients (>65 years) with multiple comorbidities and Acute respiratory distress syndrome (ARDS) are at higher risk of death.[4] A study of Yingzhen Du et al. on clinical profiles of 85 people who died of COVID-19 showed the mean age of the patients was 65.8 years (SD,14.2; range, 14-86 years), and 72.9% were male (n=62). Patients had fever (n=78, 91.8%), shortness of breath (n=50, 58.8%), fatigue (50, 58.8%), dyspnea (n=60, 70.6%), anorexia (n=48, 56.6%), expectoration (n=32,), dry cough (n=19, 22.4%), diarrhea (n=16, 18.8%), myalgia (n=14, 16.5%), headache (n=4, 4.7%), vomiting (n=4 4.7%), abdominal pain (n=3, 3.5%), chest pain (n=2, 2.4%) and pharyngalgia (n=2, 2.4%), Hypertension (n=32, 37.6%), diabetes (n=19, 22.4%) and coronary heart disease (n=10, 11.8%) which were the most common accompanying conditions. Significantly, 69 (81.2%) patients had a low eosinophil counts at admission. Complications were notified as respiratory failure (80 [94.1%]), shock (69 [81.2%]), ARDS (63 [74.1%]) arrhythmia (51 [60%]), acute myocardial injury (38 [44.7%]), acute liver injury (30 [35.3%]), and sepsis (28 [32.9%]).[5]

Qionghong Duan and colleagues' study on 116 in-patient cases with Covid-19 infection in China reported that 6.0% of the study population were hospital staff. 10.3% were directly or indirectly exposed to the Huanan seafood market (only one was in the market), while others lived within 1 km distance of the market. 39.7% had visited health centers after the first cluster emerged. 19.0% had exposure to known COVID-19 contaminants. The mean age of 116 patients was 62.62 and 50% were female; 66.4% (77 cases) had one or more underlying diseases. The most common underlying diseases were hypertension (45%), hyperglycemia (27%), cardiovascular and cerebrovascular problems (20.7%), and pulmonary disorders (10.3%).[6]

In a study by Lee et al. on the newly emerging COVID-19 coronavirus, 425 patients with a mean age of 59 years were studied. 56% of the patients were male and 55% had experienced working in the marine raw material market, offering a wide range of domestic or wild, legal or illegal animals. The incubation period was 5.2 days. The reason for the rapid spread and prevalence of the disease was the human-to-human transmission capacity (in cases of animal-to-human transmission, the disease is less widespread and has lower speed of prevalence).[7] In a report in recent studies, a Chinese businessman has indicated that after returning from Germany, he had developed sign and symptoms of the disease and his COVID-19- test was positive. 4-5 days later, his German partner had similar symptoms and the corona test for him and three other employees of the company were also positive. This study strongly supported the assumption of human-to-human transmission,[8] which is consistent with the study of Roujian Lu et al.[9] and Zhang Q et al.[10] Therefore, while the commonality of this virus (and other similar viruses such as MERS and SARS) between humans and animals is a concern for human health, the ease of transmission from publicly polluted environments such as vehicles, elevators, etc. should also be considered.[8] In Kai Liu et al.'s study, from January 15 to February 18, the clinical features of COVID-19 in the elderly patients compared to middle-aged and adolescent patients, which was performed on 56 patients, showed that 18 patients were elderly (32.14%) and 38 were young and middle aged (66.67%); the most common symptoms in both groups were fever, followed by cough and sputum. In the ICU ward, four patients in the elderly group and five patients in the young and middle-aged group received negative pressure for mechanical ventilation. One patient died in the elderly group (5.56%) and two patients in the young and middle-aged group (5.26%). Pneumonia Severity Index score was higher in the elderly group than in the young and middle-aged group ($P < 0.001$). The proportion of patients with PSI grade IV and V was significantly higher than the young and middle-aged group ($P<0.05$). Multi-lobe involvement was higher in the elderly than in the young and middle-aged group ($P<0.001$), and there was no difference in single lobe lesions between the two groups. The lymphocyte ratio was significantly lower in the elderly group than in the young and middle-aged group ($P<0.001$), and CRP

was significantly higher in the elderly group. Based on the above findings, Kai et al. found that older adults were at higher risk of infection,[11] which is consistent with Jin-YanLi's[12] findings and GuanWJ.[13]

In the early days of the outbreak, according to early studies, R0, which is an indicator to show the prevalence and potential of spreading of infectious diseases (indicating the number of people, each person can infect), was considered 2.2 for the new Corona virus 2019. If R0 (The basic reproduction number (R0), also called the basic reproduction ratio or rate or the basic reproductive rate, is an epidemiologic metric used to describe the contagiousness or transmissibility of infectious agents) is <1, the disease is highly self-limiting and will soon disappear spontaneously, and the greater the number, the greater the likelihood of an epidemic. However, R0 is not a fixed number and varies at the community level; with indicators such as public awareness and personal hygiene (It is obvious by measures taken by the Chinese Health Organization to control the outbreak of infection in Wuhan). To substantiate this claim, 24 Chinese provinces with more than 100 definitive and confirmed positive patients were included in a study. At the beginning of the outbreak R0t (The basic reproduction time), higher variances were presented; then, the prevention and control strategies have been declining since January 2020 and stabilized in February, equal to 75% in 18 provinces which was less than 1. This value was 0.925 on 8th of February. This study addressed several important points:

- Given the uncertainty of R0 of COVID-19 which is estimated between 2 and 4, disastrous results will be unavoidable.

- Measures such as banning traffic and reducing physical communication at community level are effective. However, breaking home quarantines and preventive principles can lead to recurrent epidemics.[14] In a study of clinical and epidemiologic features of the disease performed in Beijing on 262 confirmed cases up to 10 February, demographic, epidemiological and clinical and laboratory information was categorized and compared with SARS-2003 specification. Among 262 patients, 17.6% (n=46) had severe symptoms, 73.3% (n=192) had mild symptoms, 4.2% (n=11) had non-pneumonia symptoms, and 5% (n=13) were asymptomatic. 26% (50 people) had traveled to Wuhan and 60.4% (116) had contact with suspicious cases and the rest were from Beijing. The incubation period was 6.7 days and the symptoms started 4.5 days before seeking a physician. The study focused on early isolation and quarantine as a successful way to reduce emissions and mortality.[15] Cheng et al.'s study of 1079 definite cases of coronavirus with regard to regional distribution and severe morbidity and mortality showed that there was a family-centered outbreak and the number of mortality had a higher incidence among the elderly people with underlying disease.[16] A study that considered the mean age of 56 years and mostly men with severe symptoms, given the variety of symptoms, showed that restrictions on partying and city-wide traffic were a major factor in slowing the rate of outbreaks.[17] Also, in a study of 84 patients in Wuhan, the age range was 22 to 88 years, with a mean of 56 years and 47.1% with underlying diseases such as hypertension, hyperglycemia, liver or kidney disease, malignancy, Pulmonary diseases , hyperuricemia, hyperthyroidism, and HIV.[18] In a study presented by late February 2020, up to 14% relapse after completion of hospital treatment and discharge was reported, with probable factors related to underlying diseases such as diabetes, elderly, systemic corticosteroid consumption, and it is still unclear how many percent and how long the antibody-acquired immunity in our body will provide us with immunity.[19]

Clinical Presentation, Pathogenesis and Diagnosis

In their study, Nanshan and colleagues found symptoms such as fever, cough, shortness of breath, muscle pain, dizziness, headache, sore throat, runny nose, chest pain, diarrhea, and nausea and vomiting, respectively. Along with the symptoms, lung imaging studies and related findings have also suggested that the disease is more likely to affect older men with several underlying diseases, and can lead to severe and even fatal respiratory diseases such as Acute respiratory distress syndrome.[2] In a retrospective study 50 patients were enrolled, of whom 9 had mild symptoms, 28 had moderate, 10 were severe, and 3 were very severe. In general, patients with the mild type were significantly younger (mean age 29 years), had a fever less than 39 degrees and had no lesion on CT scan. People with moderate type with a mean age of 44.5, severe form with a mean age of 54.7 and very severe form with a mean age of 65.7 had main changes in blood test findings such as increase in C-reactive (52%), lymphopenia (28 %), visible lesions in the various lobes of lungs, especially the inferior lobes and mainly the lesions were ruggedly in the form of ground-glass opacity and initially with partial consolidation and fibrosis. According to this study, the use of computed tomography (CT) images is an appropriate method for the diagnosis of pulmonary injuries caused by the new coronavirus.[20]

In the study of Xu Zhu et al. from January 20 to February 15, 2020, 114 patients over the age of 70 admitted with a definite diagnosis of COVID-19 showed the most common symptoms such as fever, cough and shortness of breath. Patients with severe disease had more respiratory problems and impaired oxygen delivery than those with non-severe disease. The total

mortality was 23.7%. Multivariate analysis showed that the presence of essential respiratory diseases or lactic dehydrogenase (LDH) was independently associated with the severity of infection. According to the results, elevated white blood cells, neutrophils, aspartate aminotransferase, LDH, creatinine kinase, creatinine, blood urea nitrogen, D-dimmer, and PCT or decreased lymphocytes (especially CD3, CD4, CD19, T cells and CD16 - CD56) were more common in the critically ill group.[21]

Some studies have reported asymptomatic incidence rates for the new coronavirus, which is important because it is inversely correlated with the mortality rates and is a potential risk for the elderly in particular. In a report in Germany as well as in China, the asymptomatic incidence was reported (a 10-year-old Chinese boy whose family and grandparents had symptoms of infection, was asymptomatic, but Real Time - Polymerase Chain Reaction (RT-PCR) testing of the oropharynx and nasopharynx of the boy was positive and had a mild infiltration in the CT scan of the lung).[22] Thus, asymptomatic carriers can be a potential risk for the elderly (Table 1).

In another study on several patients of different age groups, including a 63-year-old man, high-resolution computed tomography showed scans of several pure glass opacities in the lower right lob. Diagnosis with computed tomography is confirmed by other standard methods such as nucleic acid amplification test (NAAT) and real-time fluorescence polymerase chain reaction (RT-PCR) on blood samples, but these two methods have serious limitations, such as:

- Low diagnostic rates and false negative reporting when viral load is low.

- Only reporte positive or negative cases and cannot show the intensity like a CT scan.

- The supply and demand of the kits vary with the quality of their production.

- It takes a day or more to get your test results ready.

- Ttests should be positive two to three times sequentially, so that the doctor can trust them.

The CT scans can detect the following stages of the disease:

- Beginning of the disease with pure GGOs

- In Progressive stage: Seeing multiple GGOs, consolidation in the lesions, crazy-paving pattern

- In advanced stages: diffuse exudative lesions, lung white-out[23]

Table 1: The volume of the proposed sample systematic review study: Clinical characteristics of Covid-19 among old adult patients based on the assumptions/objectives of the study

	Author of the article	Title	Journal title	Type of study	Number of sample	Average age of the patients	Percent of accompanying underlying disease	Mean age of the diceased patients	
1	Chen N, Zhou M	Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China	Lancet	Descriptive study	99	55.5	51% (of total cases)	Non-mentioned (Based on researchers' perceptions of the text of the article: 63.3% un-survived was among aged group_)	SD : 13.1
2	Zhou F	Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study	Lancet	Retrospective cohort study	191	56·0	67% (of elderly) 48%(of total cases)	69.0	P value <0·0001
3	Yang X	Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan	Lancet	Retrospective, observational study	52	59·7	53% (of un-survived)	63.4	SD: 13·3
4	Du Y	Clinical features of 85 fatal cases of COVID-19 from Wuhan	AJRC-CM	Retrospective Observational Study.	85	Non-mentioned	68.2% (of total cases)	65.8	SD: 14.2
5	Duan Q,	Treatment outcomes, influence factors of 116 hospitalized COVID-19 patients with longer/prolonged treatment course in Wuhan, China	SSRN	Retrospective observational study	116	62.5	66.4% (of total cases) %22.7 (of uncured)	68.0 (uncured)	P value: 0.000

Therefore, the diagnostic value of CT-scans is high and can be used to initiate and evaluate the treatment of infection related to new coronavirus 2019.[24] In a study by Ying Xiong and colleagues, it was found that high age and C-reactive protein, ESR or lactate dihydrogenase levels had a significant positive correlation with lesion severity and pneumonia severity on CT scans. Also, fever and opacity severity in primary CT scan correlated significantly with progression of opacity at follow-up.[24] The CT scan results of 62 patients with pneumonia caused by COVID-19, in the study of Shuchang et al., provided a mixed and varied pattern of the lung and interstitial parenchyma. Identification of GGO and a single lesion is usually helpful in identifying the early stages of the disease. Lymphocyte depletion and increased C-reactive protein are commonly seen with CT scans.[25] An elderly couple who traveled from China to Italy and were hospitalized with a diagnosis of COVID-19 in a hospital in Italy showed signs of dyspnea in adults, including pleural effusion, tubular appearance and congestion in the pulmonary arteries with decreased diameter, mediastinal lymphadenopathy as well as a sign namely "feeding vessel sign", which may be helpful in predicting the patient's imminent deterioration.[26]

Treatment

At least four chemical drugs in this study have shown good antiviral properties, including Lupinavir, Ritonavir (both of which are protease inhibitors in SARS corona virus), Chloroquine and Arbidol. At the time of the SARS epidemic, Lupinavir and Ritonavir were used in combination with Ribavirin, which has been described as an effective treatment in China. Ribavirin is a US Food and Drug Administration-approved antiviral drug that is used to treat hepatitis C and viral haemorrhagic fever, such as the Crimean Congo fever and Venezuelan haemorrhagic fever, as well as Hantavirus. According to researchers at the Wuhan Institute of Virology, chloroquine, a drug used to treat malaria, is also effective in controlling the new coronavirus. Arbidol has also been used as a broad spectrum antiviral drug in the treatment and control of coronary-associated pneumonia.[27] In one study, monoclonal antibodies were used as passive immunotherapy to fight the new coronavirus, and it was hypothesized that the knowledge and information summarized in these monoclonal antibodies that neutralize SARS and MERS may be effective in treating new coronary disease. Despite the promising results of this treatment, two problems, i.e. the difficult production of these antibodies and the high cost of the drug, have put the development of this treatment in a relative impasse. However, there is hope in the future for mass and cheap production of the drug.[28] Symptomatic and supportive treatment with acetaminophen, oxygen therapy when needed, Guyafenzine and some antibiotics has also been mentioned.[29]

Prevention and control

Early isolation, diagnosis, and management of the disease have greatly contributed to limiting and preventing the spread of the new Coronavirus-2019.[27] In the management of prevention, all aspects of health and social affairs must be taken into account. In order to prevent the spread of the disease, the overall conclusions emphasized the need for action on world-class activities such as the Japan 2020 Olympics.[30] Priority should also be given to clinical, para-clinical, and hospital activities and medical follow up, virtually, as much as possible.[31]

Conclusion

Studies have shown that the disease is more common in the old people who have underlying illnesses and have been in contact with sick or carriers (including family members, health care providers and visitors), or those who live in high-risk areas. The mean age of the patients was 57.5 and that of deceased patients was 68.1 years. Therefore, it seems that in order to prevent age-related discriminations and ageism with regard to COVID-19 infection, further RCT studies should be performed in order to compare the methods of prevention, incidence of severe complications, and their prognosis in this age group, as well as the appropriate treatment modalities. Our study had several limitations such as unavailable epidemic and social studies findings due to lack of publication to date and some of the archives of articles, and the findings were not yet free.

Acknowledgements

We wish to thank the colleagues and the anonymous referees for their valuable comments. Also, we would like to thank Abedin Bakht Abnoos for assistance.

Conflict of Interest: None declared.

References

1 WHO. Novel coronavirus—China. Geneva: World Health Organization; 2020 Jan 12. Retrieved from: https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china.

2 Song QQ, Zhao H, Fang LQ, Liu W, Zheng C, Zhang Y. [Study on assessing early epidemiological parameters of coronavirus disease epidemic in China]. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(4):461-5. Available from: doi:10.3760/cma.j.cn112338-20200205-00069.

3 Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020;395(10223):507-13. Available from: doi:https://doi.org/10.1016/S0140-6736(20)30211-7.

4 Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical

course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020;395(10229):1054-62. Available from: doi:https://doi.org/10.1016/S0140-6736(20)30566-3.

5 Yang X, Yu Y, Xu J, Shu H, Xia Ja, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020. Available from: doi:https://doi.org/10.1016/S2213-2600(20)30079-5.

6 Du Y, Tu L, Zhu P, Mu M, Wang R, Yang P, et al. Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan: A Retrospective Observational Study. 2020. Available from:

7 Duan Q, Guo G, Ren Y, Shang H, Du J, Li M, et al. Treatment Outcomes, Influence Factors of 116 Hospitalized COVID-19 Patients with Longer/Prolonged Treatment Course in Wuhan, China. Influence Factors of. 2020;116. Available from: doi:https://dx.doi.org/10.2139/ssrn.3550017.

8 Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med. 2020;382(13):1199-207. Available from: doi:10.1056/NEJMoa2001316.

9 Ahmad T, Khan M, Haroon, Musa TH, Nasir S, Hui J, et al. COVID-19: Zoonotic aspects. Travel Medicine and Infectious Disease. 2020:101607. Available from: doi:https://doi.org/10.1016/j.tmaid.2020.101607.

10 Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. The Lancet. 2020;395(10224):565-74. Available from: doi:https://doi.org/10.1016/S0140-6736(20)30251-8.

11 Zhang Q, Pan J, Zhao M-x, Lu Y-q. Clinical value of the emergency department in screening and diagnosis of COVID-19 in China. J Zhejiang Univ Sci B. 2020:1-6. Available from: doi:10.1631/jzus.B2010011.

12 Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. Journal of Infection. 2020. Available from: doi:https://doi.org/10.1016/j.jinf.2020.03.005.

13 Li J-Y, You Z, Wang Q, Zhou Z-J, Qiu Y, Luo R, et al. The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future. Microbes and Infection. 2020;22(2):80-5. Available from: doi:https://doi.org/10.1016/j.micinf.2020.02.002.

14 Guan W-j, Ni Z-y, Hu Y, Liang W-h, Ou C-q, He J-x, et al. Clinical characteristics of 2019 novel coronavirus infection in China. medRxiv. 2020:2020.02.06.20020974. Available from: doi:10.1101/2020.02.06.20020974.

15 Huang LL, Shen SP, Yu P, Wei YY. [Dynamic basic reproduction number based evaluation for current prevention and control of COVID-19 outbreak in China]. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(4):466-9. Available from: doi:10.3760/cma.j.cn112338-20200209-00080.

16 Tian S, Hu N, Lou J, Chen K, Kang X, Xiang Z, et al. Characteristics of COVID-19 infection in Beijing. Journal of Infection. 2020;80(4):401-6. Available from: doi:https://doi.org/10.1016/j.jinf.2020.02.018.

17 Cheng JL, Huang C, Zhang GJ, Liu DW, Li P, Lu CY, et al. [Epidemiological characteristics of novel coronavirus pneumonia in Henan]. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43(0):E027. Available from: doi:10.3760/cma.j.cn112147-20200222-00148.

18 Zumla A, Niederman MS. The explosive epidemic outbreak of novel coronavirus disease 2019 (COVID-19) and the persistent threat of respiratory tract infectious diseases to global health security. Curr Opin Pulm Med. 2020. Available from: doi:10.1097/mcp.0000000000000676.

19 Huang Y, Tu M, Wang S, Chen S, Zhou W, Chen D, et al. Clinical characteristics of laboratory confirmed positive cases of SARS-CoV-2 infection in Wuhan, China: A retrospective single center analysis. Travel Med Infect Dis. 2020:101606. Available from: doi:10.1016/j.tmaid.2020.101606.

20 Zhou L, Liu K, Liu HG. [Cause analysis and treatment strategies of "recurrence" with novel coronavirus pneumonia (covid-19) patients after discharge from hospital]. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43(0):E028. Available from: doi:10.3760/cma.j.cn112147-20200229-00219.

21 Xu Y-H, Dong J-H, An W-M, Lv X-Y, Yin X-P, Zhang J-Z, et al. Clinical and computed tomographic imaging features of novel coronavirus pneumonia caused by SARS-CoV-2. Journal of Infection. 2020;80(4):394-400. Available from: doi:https://doi.org/10.1016/j.jinf.2020.02.017.

22 Zhu X, Yuan W, Huang K, Wang Q, Yao S, Lu W, et al. Clinical Features and Short-Term Outcomes of 114 Elderly Patients with COVID-19 in Wuhan, China: A Single-Center, Retrospective, Observational Study. China: A Single-Center, Retrospective, Observational Study (3/2/2020). 2020. Available from: doi:https://dx.doi.org/10.2139/ssrn.3548774.

23 Al-Tawfiq JA. Asymptomatic coronavirus infection: MERS-CoV and SARS-CoV-2 (COVID-19). Travel Med Infect Dis. 2020:101608. Available from: doi:10.1016/j.tmaid.2020.101608.

24 Dai WC, Zhang HW, Yu J, Xu HJ, Chen H, Luo SP, et al. CT Imaging and Differential Diagnosis of COVID-19. Can Assoc Radiol J. 2020:846537120913033. Available from: doi:10.1177/0846537120913033.

25 Xiong Y, Sun D, Liu Y, Fan Y, Zhao L, Li X, et al. Clinical and High-Resolution CT Features of the COVID-19 Infection: Comparison of the Initial and Follow-up Changes. Invest Radiol. 2020. Available from: doi:10.1097/rli.0000000000000674.

26 Zhou S, Wang Y, Zhu T, Xia L. CT Features of

Coronavirus Disease 2019 (COVID-19) Pneumonia in 62 Patients in Wuhan, China. AJR Am J Roentgenol. 2020:1-8. Available from: doi:10.2214/ajr.20.22975.

27 Albarello F, Pianura E, Di Stefano F, Cristofaro M, Petrone A, Marchioni L, et al. 2019-novel Coronavirus severe adult respiratory distress syndrome in two cases in Italy: An uncommon radiological presentation. International Journal of Infectious Diseases. 2020;93:192-7. Available from: doi:https://doi.org/10.1016/j.ijid.2020.02.043.

28 Liu W, Zhu HL, Duan Y. Effective Chemicals against Novel Coronavirus (COVID-19) in China. Curr Top Med Chem. 2020;20. Available from: doi:10.2174/1568026620999200305145032.

29 Shanmugaraj B, Siriwattananon K, Wangkanont K, Phoolcharoen W. Perspectives on monoclonal antibody therapy as potential therapeutic intervention for Coronavirus disease-19 (COVID-19). Asian Pac J Allergy Immunol. 2020;38(1):10-8. Available from: doi:10.12932/ap-200220-0773.

30 Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). International Journal of Surgery. 2020;76:71-6. Available from: doi:https://doi.org/10.1016/j.ijsu.2020.02.034.

31 Gallego V, Nishiura H, Sah R, Rodriguez-Morales AJ. The COVID-19 outbreak and implications for the Tokyo 2020 Summer Olympic Games. Travel Medicine and Infectious Disease. 2020:101604. Available from: doi:https://doi.org/10.1016/j.tmaid.2020.101604.

32 Chen Y, Pradhan S, Xue S. What are we doing in the dermatology outpatient department amidst the raging of the 2019 novel coronavirus? Journal of the American Academy of Dermatology. 2020;82(4):1034. Available from: doi:10.1016/j.jaad.2020.02.030.