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RESEARCH ARTICLE

Epidemiological and Clinical Characteristics of Patients with COVID-19 in Arak, Iran

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Abstract:

Background:

The number of confirmed cases of COVID-19 is increasing. Here we present the clinical characteristics and outcomes of COVID-19 in Arak, Iran.

Methods:

In this study, 139 COVID-19 confirmed cases from 15 February to 15 March 2020 in Arak, Iran, were investigated. The clinical signs, symptoms, laboratory and radiological findings and outcomes were analyzed.

Results:

The mean age of the patients was 55.41 years (S.D.: 17.11) and 55.40% of them were males. 26.81% of patients had recently traveled to other epidemic cities. The most common clinical manifestations were fever (71.64%), cough (67.16%), shortness of breath (55.22%), muscle ache (50.00%) and the most prevalent complications were taste and smell disruption (29.5%), weakness (22.3%), anorexia (20.1%) and acute respiratory distress syndrome (ARDS) (15.8%). Almost half of the patients had lymphopenia, an elevated level of erythrocyte sedimentation rate (ESR) and C - reactive protein (CRP). In terms of outcome, 9.3% of patients needed an ICU admission as a result of ARDS in which 15.32% were directly admitted to the ICU. 43.2% of patients have been discharged and the case fatality rate (CFR) was estimated as 11.5%.

Conclusion:

COVID-19 pneumonia usually occurred at an age older than 50 years and in the male gender. The most common initial clinical laboratories and radiological presentations are fever, cough, lymphopenia with elevated CRP and ESR and Bilateral mixed ground-glass opacities with consolidation.

Keywords: COVID-19, Epidemiology, Case Fatality Rate, Acute Respiratory Distress Syndrome, ICU, Epidemiology.

1. INTODUCTION

On December 8, 2019, a new virus was detected that led to a cluster of cases of pneumonia with fever, cough and dyspnea in Wuhan, Hubei Province, China [1 - 4]. On January 7, 2020, according to the throat swab sample of patients, the Chinese Center for Disease Control and Prevention (CCDC) identified that the causative organism belonged to the beta-Coronavirus family and the World Health Organization (WHO) named it 2019 novel coronavirus (2019-nCoV or COVID-19) [5]. Considering the worldwide increase in cases, and the fact that cases have been reported from more than 160 countries, WHO announced COVID-19 as a pandemic on 11 March 2020 [6], and until now (August 2020), more than 200 countries or territories have been reported to be infected with COVID-19. The number of confirmed cases reached more than 24 million, with 840,000 deaths worldwide, by 30 August 2020 [7].

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Table 1. The average of vital signs in the first week of admission.

Variables	SBP	DBP	PR	RR	T	O$_2$ saturation
1st day	113.5 (17.4)	73.8 (10.2)	87.5 (11.1)	19.9 (2.7)	37.5 (0.99)	89.6 (8.2)
2nd day	112.8 (11.2)	72.2 (8.4)	88.1 (16.7)	20.7 (6.0)	37.2 (1.9)	92.3 (5.3)
3rd day	112.8 (11.8)	71.6 (8.5)	84.6 (10.9)	20.7 (6.3)	38.5 (7.7)	92.2 (3.9)
4th day	112.5 (12.6)	71.6 (11.3)	84.0 (8.9)	20.0 (1.96)	37.3 (0.68)	92.4 (6.0)
5th day	114.6 (13.4)	74.9 (9.3)	86.13 (10.7)	19.8 (2.4)	37.2 (0.7)	93.4 (3.2)
6th day	110.7 (14.4)	73.2 (9.0)	83.9 (14.0)	21.4 (8.2)	38.1 (6.7)	93.2 (4.8)
7th day	111.3 (11.0)	71.5 (8.7)	85.6 (8.3)	21.3 (8.8)	37.4 (0.65)	92.9 (3.1)

Abbreviations: SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PR: Pulse rate, RR: Respiratory rate: T: Temperature

Outside of China, the spread of the disease in some countries such as European countries (especially Italy, Spain, Germany, France, Switzerland and The United Kingdom), Iran, The United States, Brazil, India, Russia, Peru, South Africa, Colombia, Mexico, Chile, Argentina, *etc.* is higher than the others and is increasing dramatically [7, 8].

Iran had 341,000 confirmed cases with 19,492 deaths (until 31 August, 2020) [7, 8] but the epidemiological and clinical features are not yet clear. Because of the lack of information regarding the COVID-19, this study aimed to describe clinical, epidemiological, laboratory, radiological characteristics and outcomes of patients with COVID-19 infection in Arak, Markazi province, Iran.

2. MATERIALS AND METHODS

In this study, the data were obtained from two hospitals (Khansari and Vali-Asr Hospital) affiliated with Arak University of Medical Sciences. Patients were admitted from 15 February to 15 March, 2020. For confirmation of 2019-nCoV, the oropharengial/ nasopharyngial swab specimens in Viral Transport Media (VTM) were referred to the Specialized Virology laboratory of Emam Reza clinic (Arak University of Medical Sciences, Arak, Iran). Viral RNA was extracted using the QIAamp DSP Virus Kit (Qiagen, Hilden, Germany) in QIAcube extractor machines (Qiagen), based on the standard protocol of the manufacturer. Reverse-transcription Real-time PCR (RT-qPCR) assays were performed using 2019-nCoV Nucleic Acid Diagnostic kit (Sansure biotech, Changsha, China), according to the manufacturer's protocol [4].

The epidemiological and demographic variables, laboratory tests, daily changes of vital signs and outcomes were obtained from patients' medical records. For all patients, the routine supportive care included respiratory support and therapeutic regimes which involved an anti-viral agent, Oseltamivir (75mg/PO/BD), an anti-fungal agent, hydroxy chloroquine (200/PO/BD), and the antibiotic Azithromycin (500mg/PO/daily). In addition, the medications of the patients with the underlying disease were continued. The basis for hospital discharge was the improvement of the clinical symptoms and a negative RT-PCR test. For this purpose, the RT-PCT was repeated every 3 days.

This study was approved by the Ethical Committee of Arak University of Medical Sciences (Code: IR.ARAKMU. REC.1398.333) and an informed consent was obtained from all patients or their guardians. The data were analyzed by Stata statistical software (Stata Corp LP, College Station, TX Stata).

3. RESULTS

3.1. Demographic Characteristics

This epidemiologic study investigated 139 COVID-19 laboratory-confirmed cases. The mean age of the patients was 55.41 years (S.D.: 17.11, range: 23-91) and 55.40% of cases (n= 77) were males. 97.12% of them (n=135) lived in urban areas, and 95.68% (n=133) were Iranian nationals (6 cases were from Afghanistan, India and Pakistan); these cases were acquired in Arak.

26.81% of patients (n=37) have recently traveled to the other epidemic cities in Iran (Qom, Tehran, Rasht, *etc.*), and 20.86% of them (n=29) had contact with other people likely to have been infected with COVID-19. The frequency of COVID-19 among health care providers was 5.07% (n=7), which were identified from all health centers in Arak.

3.2. Clinical Manifestations

On the day of hospitalization, the most common clinical manifestations were fever 71.64% (n=96), cough 67.16% (n=90), shortness of breath 55.22% (n=74), muscle ache 50.0% (n=67), headache 26.87% (n=36), sputum productive 15.67% (n=21), nausea and/or vomiting 12.69% (n=17), pleuritic chest pain 10.37% (n=14), sore throat 8.96% (n=12), and diarrhea 3.73% (n=5).

As shown in Table **1**, the vital signs, including pulse rate, respiratory rate, systolic/diastolic blood pressure, temperature and O$_2$ saturation of patients, were measured every day. Changes in vital signs during the first week of hospitalization have also been observed. During the first week of hospitalization, the mean O$_2$ saturation increased from 82.6 to 92.9 and the mean respiratory rate increased from 19.9 to 21.3.

3.3. Complications

The frequency of the most common complications is reported in Table **2**. The results suggest that the most prevalent complications were taste and smell disorder (29.5%) followed by weakness (22.3%), anorexia (20.1%), acute respiratory distress syndrome (ARDS) (15.8%), dry mouth (11.5%) and acute kidney injury (AKI) (5%).

Table 2. The frequency of complications among COVID-19 confirmed cases in Arak, Iran.

Complications	N (%)	95% CI
Taste disorder	41 (29.5)	22.4-37.7
Smell disorder	41 (29.5)	22.4-37.7
Weakness	31 (22.3)	16.0-30.0
Anorexia	28 (20.1)	14.2-27.7
ARDS	22 (15.8)	10.6-23.0
AKI	5 (3.5)	1.4-8.4
Dry mouth	16 (11.5)	7.1-18.1

Abbreviations: AKI: Acute kidney injury, ARDS: Acute Respiratory distress syndrome

Table 3. The S.D. of CBC, hematology, and serology tests in the first three days of COVID-19 patients, Arak, Iran.

Variables	1st day	2nd day	3rd day
WBC	6.4 (2.8)	5.4 (2.4)	5.8 (2.3)
PMN	69.1 (14.9)	62.2 (17.7)	65.8 (16.2)
Lymph	21.5 (12.0)	28.5 (21.4)	23.2 (14.7)
Hb	13.8 (1.9)	13.3 (2.3)	13.1 (2.04)
Plt	191.7 (68.5)	186.6 (69.3)	223.4 (103.5)
PTT	38.5 (17.6)	31.9 (13.3)	32.7 (14.8)
INR	1.16 (0.2)	1.11 (0.23)	1.18 (0.22)
ESR	31.9 (25.1)	29.8 (25.7)	43.0 (11.3)
BUN	32.6 (15.3)	37.7 (45.5)	35.6 (20.3)
Cr	1.01 (0.27)	1.06 (0.54)	1.09 (0.69)
BS	98.9 (54.3)	-	-
Alb	10.5 (27.9)	-	-
CPK	162.6 (200.9)	-	-
LDH	467.2 (184.2)	-	-

Abbreviations: WBC: white blood cell count, PMN: Neutrophil count, Lymph: Lymphocyte, Hb: hemoglobin, PLT: platelet, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, Cr: creatinine, and BUN: Blood Urea Nitrogen.

3.4. Laboratory Findings

The results of the complete blood count (CBC), hematology and serology tests at admission are presented in Table **3**. Most patients had normal leukocyte counts (78.41%-109/139); however, 9.35% of the patients (n=13/139) showed leukopenia and 12.23% of cases (n=17/139) had leukocytosis (normal range; $3.5-9.5*10^9$/L). While the neutrophil (PMN) level of 8.63% of patients (12/139) was below the normal range, 20.86% of cases (29/139) had a PMN level above the normal range where the normal range is $1.5-6.5*10^9$/L. Furthermore, 48.92% of patients (68/139) showed lymphopenia and only 0.71% of them (2/139) had lymphocytosis where the normal range of lymphocyte is $1.1-3.2*10^9$/L.

Most of the patients had normal hemoglobin (Hb) (63.33% with the normal range of 12-17g/L), platelet (Plt) count (85.83% with the normal range of $125-350*10^9$/L), partial thromboplastin time (PTT) (77.89% with the normal range of 31.5-43.5s), international normalized ratio (INR) (66.31% with the normal range of 0.9-1 index), creatinine (Cr) (84.03% with the normal range of 0.8-1.3mg/l), and blood urea nitrogen (BUN) (70.94% with the normal range of 17-45mg/l). Furthermore, 61.66% and 52.17% of COVID-19 patients had a high erythrocyte sedimentation rate (ESR) (normal range is 0.0-15 mm/hr) and C - reactive protein (CRP) (normal range; 0.0-5.0 mg/L). CRP test results of 91 patients were available,

of which 43 cases (47.2%) were negative, 20 cases (22%) were 1+, 11 cases (12.0%) were 2+, 9 cases (9.9%) were 3+, 3 cases (3.3%) were 4+ and 5 cases (5.5%) were weakly 5+.

3.5. Chest CT Findings

Based on the initial chest thin section results, 78.61% (92/118) and 9.38% (11/118) of patients had bilateral and unilateral pneumonia, respectively. The involvement of chest CT was divided into Pure Ground Glass Opacity (PGGO) and mixed Ground Glass Opacity (GGO) with consolidation or pure consolidation that were unilateral or bilateral.

According to the obtained results, there were 0.85% (1/118) unilateral PGGO, 5.12% (6/118) unilateral consolidation, 3.41% (4/118) unilateral mixed GGO with Consolidation, 25.78% (29/118) bilateral PGGO, 10.25% (12/118) bilateral consolidation, and 43.58% (51/118) bilateral GGO with Consolidation. Furthermore, 11.96% of patients (14/118) had a normal chest CT and 15.10% of cases (21/139) did not have a CT scan.

3.6. Disease Severity

15.8% of the patients (n=22) developed ARDS and were admitted to the intensive-care unit (ICU). 60 patients (43.2%) have been discharged and the case fatality rate (CFR) was estimated as 11.5% (16 cases among 139). The CFR was

25.93% (14 cases) for the patients older than 60 years and 2.4% (2 cases) for those younger than 60 years. Moreover, the CFR was 18.84% (13 patients) in patients with a medical history and 4.3% (3 patients) in patients without a medical history. The youngest patient who died was 53 years old with no medical history, and no deaths have been reported in people under 50 years of age.

4. DISCUSSION

The results of our study showed that the mean age of patients was 55.41 years, most of the patients were male and 5.07% of them were health care providers. The most common symptoms included fever, cough, shortness of breath, muscle ache, and a headache, which is similar to the studies on COVID-19 patients in China [4, 9]. According to this research and other studies which have been done on COVID-19 [4, 9 - 12], the susceptible people for this viral pneumonia, usually were in the average age range of 50-60 years, males, and had at least a chronic underlying disease; furthermore, the most common initial symptoms of pneumonia were fever, cough, shortness of breath and headache.

Most of the complications that occurred during the admission included taste and smell disorders, weakness and anorexia. The other less common complications included ARDS (15.8%), dry mouth (11.5%), and AKI (3.5%). Although the available studies regarding patients with COVID-19 have not addressed any neurological problems in these patients, the loss of taste and smell sense, weakness and anorexia were the most complications in our studied COVID-19 cases. We daily visited patients and asked them about their daily complications; the corresponding results showed that the patients with COVID-19 experienced different neurological problems such as loss of taste and smell sense, weakness and anorexia. The other studies showed that the different strains of HCoV can involve the central nervous system (especially cerebral nerves like vague) [13, 14] and olfactory bulb [15]. The virus has been observed to spread to the central nervous system by reaching the bloodstream [16, 17] or through the olfactory bulb [18, 19] after disruption of the nasal epithelium. In a systematic review and meta-analysis, twenty-four studies were included to estimate the smell and taste dysfunction in patients with COVID-19. The results revealed that the prevalence of olfactory dysfunction and gustatory dysfunction accounted for 41.0% and 38.2%, respectively [20]. However, understanding this problem requires further wide human and pathological studies.

In terms of laboratory evaluation, most of the patients had a normal count of white blood cells (WBC), PMN, Hb, Plt, PTT, INR, BUN, and Cr, but almost half of the patients had lymphopenia and elevated level of ESR and CRP. In recent Chinese studies [4, 21, 22], lymphopenia was a common laboratory abnormality seen in the initial disease like what we observed in our cases. For this reason, lymphopenia, high level of CRP and ESR can help to diagnose COVID-19. As a result, lymphopenia can possibly confirm the previous findings of T-lymphocyte affected by COVID-19 (like SARS-CoV) [9, 23].

Although it was observed that most of the patients in the first seven hospitalization days had stable blood pressure and

pulse rate, 32% of them had RR larger than 20 and 4% of them intubated on admission. Besides that, fever (body temperature ≥37.8°c) has been seen in a few days and the oxygen saturation, which is measured by finger pulse oximeter, was below 90 on the first day of the admission, and on the other days, it was larger than or equal to the 93% in the air for most of the patients. It can be demonstrated that the prescribed treatment was effective in improving the respiratory function.

According to the CT findings, most patients presented the bilateral pneumonia and the most common chest CT abnormality of patients was bilateral mixed ground-glass opacities with consolidation, which was confirmed by Michael Chung [11], Adam Bernheim [24] and other radiological studies regarding COVID-19 [25 - 27].

Overall, 43.2% of patients were treated and discharged, 9.3% needed an ICU admission as a result of ARDS and 15.32% were directly admitted to the ICU. Besides these, the CFR was estimated to be 11.5% (16 cases among 139 patients). CFR was estimated only of patients with COVID-19 who were admitted to the hospitals, whereas in Arak City, many positive cases were quarantined and treated with daily follow up at home. The CFR assessed at the hospital in our study is in line with the Nanshan Chen's study [9], which estimated the CFR of patients with COVID-19 at about 11% and aslo with the study of Chaolin Huang [4]. In another study, the global CFR was estimated as 3.3%, which is lower than that in our study [28]. It should be highlighted that since the probability of hospitalization of severe patients is higher, the CFR in our study is overestimated. Another notable point in our study is that the age and underlying disease in patients with COVID-19 are the mortality factors. It means that the mortality was higher in older patients with underlying disease. Besides that, in our population, no deaths under 50 years old have been observed (it was estimated at 25.93% in older than 60 years and 2.4% for those younger than 60 years and 18.84% in the patients with a medical history and 4.3% in the patients with no medical history).

We acknowledge that our study has the following limitations. First, we investigated the hospitalized patients, and the patients who had been quarantined at home and received treatment at home were not included. Second, the study duration was short (it was only 1 month), which means missing some patients with more detailed information for analysis. It is highly recommended to conduct a larger study to confirm the results. In the end, we recommend future studies to investigate COVID-19 cases (both hospitalized and outpatients) in different epidemic cities of Iran for a longer period of time.

CONCLUSION

In conclusion, the new viral pneumonia has been observed to usually occur in older males and the most common initial clinical symptoms and laboratory abnormalities include fever, cough, and lymphopenia with the elevation of CRP and ESR, respectively. Most of the patients had bilateral mixed ground-glass opacities with consolidation in chest CT and experienced some neurological problems. The CFR was estimated at 11.5%.

LIST OF ABBREVIATIONS

AKI	=	Acute Kidney Injury
ARDS	=	Acute Respiratory Distress syndrome
BUN	=	Blood Urea Nitrogen
Cr	=	Creatinine
CRP	=	C-reactive Protein
DBP	=	Diastolic Blood Pressure
ESR	=	Erythrocyte Sedimentation Rate
Hb	=	Hemoglobin
LYM	=	Lymphocyte
PLT	=	Platelet
PMN	=	Neutrophil Count
PR	=	Pulse Rate
RR	=	Respiratory Rate
SBP	=	Systolic Blood Pressure
T	=	Temperature
WBC	=	White Blood Cell Count

AUTHORS' CONTRIBUTIONS

HS, AAH and MMH designed the study and conducted the literature search. HS and MJ were responsible for disease diagnosis and treatment, and HS, MMH, AAH and FS were responsible for data collection. AAH, MMH and HS analyzed the data. All authors drafted and revised the report.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval for the study was provided by the Ethical Committee of Arak University of Medical Sciences, Iran (IR.ARAKMU.REC.1398.333).

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

The subjects participated in this study after signing the informed consent form.

AVAILABILITY OF DATA AND MATERIALS

The authors confirm that the data supporting the findings of this study are available within the article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

REFERENCES

[1] Zhang L, Jiang Y, Wei M, *et al.* [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. Zhonghua Fu Chan Ke Za Zhi 2020; 55(3): 166-71. [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. [PMID: 32145714]

[2] Lu H, Stratton CW, Tang Y-W. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J Med Virol 2020; 92(4): 401-2.
[http://dx.doi.org/10.1002/jmv.25678] [PMID: 31950516]

[3] Hui DSI, I Azhar E, Madani TA, *et al.* The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis 2020; 91: 264-6.
[http://dx.doi.org/10.1016/j.ijid.2020.01.009] [PMID: 31953166]

[4] Huang C, Wang Y, Li X, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395(10223): 497-506.
[http://dx.doi.org/10.1016/S0140-6736(20)30183-5] [PMID: 31986264]

[5] World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (ý 2019-nCoV)ý infection is suspected: interim guidance, 28 January 2020. World Health Organization 2020.

[6] COVID-19, a pandemic or not? Lancet Infect Dis 2020; 20(4): 383.
[http://dx.doi.org/10.1016/S1473-3099(20)30180-8] [PMID: 32178762]

[7] World Health Organization. Coronavirus disease (COVID-19): Weekly Epidemiological Update 2020. [31 August 2020]. Available from:
https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200831-weekly-epi-update-3.pdf?sfvrsn=d7032a2a_4

[8] Worldometer. COVID-19 CORONAVIRUS PANDEMIC 2020. [August 31, 2020]. Available from:
https://www.worldometers.info/coronavirus/country/iran/

[9] 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(10223): 507-13.
[http://dx.doi.org/10.1016/S0140-6736(20)30211-7] [PMID: 32007143]

[10] Zhu N, Zhang D, Wang W, *et al.* A novel coronavirus from patients with pneumonia in china, 2019. N Engl J Med 2020; 382(8): 727-33.
[http://dx.doi.org/10.1056/NEJMoa2001017] [PMID: 31978945]

[11] Chung M, Bernheim A, Mei X, *et al.* CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology 2020; 295(1): 202-7.
[http://dx.doi.org/10.1148/radiol.2020200230] [PMID: 32017661]

[12] Cao M, Zhang D, Wang Y, *et al.* Clinical features of patients infected with the 2019 novel coronavirus (COVID-19) in Shanghai. China: MedRxiv 2020.

[13] Xu J, Zhong S, Liu J, *et al.* Detection of severe acute respiratory syndrome coronavirus in the brain: potential role of the chemokine mig in pathogenesis. Clin Infect Dis 2005; 41(8): 1089-96.
[http://dx.doi.org/10.1086/444461] [PMID: 16163626]

[14] Gu J, Gong E, Zhang B, *et al.* Multiple organ infection and the pathogenesis of SARS. J Exp Med 2005; 202(3): 415-24.
[http://dx.doi.org/10.1084/jem.20050828] [PMID: 16043521]

[15] Netland J, Meyerholz DK, Moore S, Cassell M, Perlman S. Severe acute respiratory syndrome coronavirus infection causes neuronal death in the absence of encephalitis in mice transgenic for human ACE2. J Virol 2008; 82(15): 7264-75.
[http://dx.doi.org/10.1128/JVI.00737-08] [PMID: 18495771]

[16] Berth SH, Leopold PL, Morfini GN. Virus-induced neuronal dysfunction and degeneration. Front Biosci 2009; 14: 5239-59.
[http://dx.doi.org/10.2741/3595] [PMID: 19482613]

[17] Koyuncu OO, Hogue IB, Enquist LW. Virus infections in the nervous system. Cell Host Microbe 2013; 13(4): 379-93.
[http://dx.doi.org/10.1016/j.chom.2013.03.010] [PMID: 23601101]

[18] Mori I, Nishiyama Y, Yokochi T, Kimura Y. Olfactory transmission of

neurotropic viruses. J Neurovirol 2005; 11(2): 129-37.
[http://dx.doi.org/10.1080/13550280590922793] [PMID: 16036791]

[19] Durrant DM, Ghosh S, Klein RS. The olfactory bulb: an immunosensory effector organ during neurotropic viral infections. ACS Chem Neurosci 2016; 7(4): 464-9.
[http://dx.doi.org/10.1021/acschemneuro.6b00043] [PMID: 27058872]

[20] Agyeman AA, Chin KL, Landersdorfer CB, Liew D, Ofori-Asenso R. Smell and taste dysfunction in patients with COVID-19: A systematic review and meta-analysis. Mayo Clin Proc 2020; 95(8): 1621-31.
[http://dx.doi.org/10.1016/j.mayocp.2020.05.030] [PMID: 32753137]

[21] Song F, Shi N, Shan F, *et al.* Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology 2020; 295(1): 210-7.
[http://dx.doi.org/10.1148/radiol.2020200274] [PMID: 32027573]

[22] Wang D, Hu B, Hu C, *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 2020; 323(11): 1061-9.
[http://dx.doi.org/10.1001/jama.2020.1585] [PMID: 32031570]

[23] Liu WJ, Zhao M, Liu K, *et al.* T-cell immunity of SARS-CoV: Implications for vaccine development against MERS-CoV. Antiviral Res 2017; 137: 82-92.

[http://dx.doi.org/10.1016/j.antiviral.2016.11.006] [PMID: 27840203]

[24] Bernheim A, Mei X, Huang M, *et al.* Chest CT findings in coronavirus disease-19 (COVID-19): Relationship to duration of infection. Radiology 2020; 295(3)200463
[http://dx.doi.org/10.1148/radiol.2020200463] [PMID: 32077789]

[25] Duan YN, Qin J. Pre- and posttreatment chest CT findings: 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology 2020; 295(1): 21.
[http://dx.doi.org/10.1148/radiol.2020200323] [PMID: 32049602]

[26] Kanne JP. Chest CT findings in 2019 novel coronavirus (2019-nCoV) infections from Wuhan, China: key points for the radiologist. Radiology 2020; 295(1): 16-7.
[http://dx.doi.org/10.1148/radiol.2020200241] [PMID: 32017662]

[27] Pan Y, Guan H, Zhou S, *et al.* Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): A study of 63 patients in Wuhan, China. Eur Radiol 2020; 30(6): 3306-9.
[http://dx.doi.org/10.1007/s00330-020-06731-x] [PMID: 32055945]

[28] Almasi-Hashiani A, Doosti-Irani A, Mansournia MA. Case fatality rate of COVID-19: Meta-analysis approach. Arch Iran Med 2020; 23(9): 644-6.
[http://dx.doi.org/10.34172/aim.2020.78] [PMID: 32979914]