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Research Article

Clinical Findings and Related Factors with the Final Outcome in Hospitalized COVID-19 Patients: An Evidence Based Cross-sectional Study

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ABSTRACT

Background: Numerous conventional laboratory diagnostic tests has been developed to diagnose COVID-19 infection. These include but are not limited to measurement of the antibody titer against the viruses, screening the viral antigen and RT-PCR from samples obtained from nasopharynx swaps, sputum, the secretions of the lower respiratory tract, blood, and feces. Infection with SARS-CoV-2 could manifest as nonspecific symptoms such as fatigue, muscle sore, fever, and nonproductive coughs. Recent studies suggest that blood group type might play a role in determining prognosis in COVID-19 patients. Opting for the suitable diagnostic tests is essential in the timely management of these patients. In our study, we aimed at the comparison of distribution patterns of COVID 2019 and estimation of the partial frequency of the clinical findings of COVID 2019 in order to facilitate decision making of the physicians and differentiating the factors having impact on the final outcome of the hospitalized patients

Methods: In a cross-sectional descriptive-analytic study, a total of 350 patients diagnosed with COVID-19 were enrolled. The information on the previous encounters, clinical signs on admission and at the hospitalizations time, and lab results on admission were collected. Radiological findings such as chest X-ray were also collected. The questionnaires were filled out by experienced staff.

Results: A total of 350 patients with the median age of 64 years old, 204 (58.3%) male and 146 (41.7%) female were studied. 110 people (31.4%) were hospitalized in ICU. The most common underlying diseases were hypertension, diabetes, cardiac diseases, renal diseases, and cancer. Blood group types A+ and O+ were the most common blood group types among the ICU hospitalized patients P <0.0001. There was a statistically significant correlation between blood group type and mortality among the studies patients. The highest rate of the mortality was amongst patients with blood group type A+ and O+ P <0.0001.

Conclusion: Fever, fatigue and non-productive coughs, dyspnea, leukopenia, leukocytosis, lymphopenia, thrombocytopenia, thrombocytosis, increased ESR, increased CRP, and increased D-dimer are the most common clinical and laboratory findings in COVID-19 patients. A statistically significant correlation was observed between the patients hospitalized in ICU and the blood group type; the most frequent blood group type was A+ followed by O+.

Introduction

Coronavirus family belongs to a vast virus category of Coronaviridae which can cause wide range of manifestations from common cold to very severe diseases such as SARS, MERS and COVID-19 in both humans and animals. COVID-19 stands for SARS-CoV-2 virus, disease and the year 2019. This type of coronavirus was never seen before the onset of epidemic in humans in 2019. It has an incubation period of 1 to 14 days, but commonly three to seven days. The manifestations are usually fever, fatigue and non-productive coughs, while some of the patients might experience other symptoms such as nasal congestion, rhinorrhea or diarrhea [1-4].

The virus is commonly transmitted through respiratory secretions and direct contact (surfaces or individuals). The complications have been reported to be more severe in the elderly or patients with chronic diseases. Children and infants are also at the risk of transmission [5-9]. The virus can mutiply efficiently in the respiratory tract and it has been shown to be transmitted through respiratory droplets, near contact, aerosols and probably oral fecal axis. The patients can transmit the virus to the others within the incubation period. Angiotensin Converting Enzyme 2 (ACE2) has been introduced as a key necessary factor for COVID-19 multi-organ infection as it allows the entrance of the virus into different cells such as alveolar, upper esophageal compartment, and epithelial and enterocytes ileum and colon cells [6].

The conventional laboratory diagnostic tests, such as measurement of the antibody titer against the viruses or screening the viral antigen has been developed and are being used. Novel diagnostic tests such as RT-PCR are also effective in follow-up of the epidemiological measures. Nucleic acids of SARS-CoV-2 can be detected in samples from nasopharynx swaps, sputum, the secretions of the lower respiratory tract, blood, and feces. Infection with SARS-CoV-2 in the preliminary phase could be associated with nonspecific symptoms such as fatigue, muscle sore, fever, and nonproductive coughs. Some might only experience a slight headache or even some could be asymptomatic [10-15].

Recent studies suggest that group A blood type might be a risk factor for poor prognosis in COVID-19 patients; whereas, the patients with group O blood type might have a better prognosis [11-14]. The correlation of ABO blood group types with venous thromboemboli (VTE) has been studied and a correlation between groups B and A blood type with the incidence of VTE has been suggested [12]. Current studies suggest that the blood group type, especially ABO blood group type, is not only an important factor in the blood transfusion and tissue transplantation, but also it can be accounted for the incidence and severity of different diseases. Therefore, it could be considered as a facilitating tool in predicting the incidence and improvising prophylactic measures in some diseases. Administering the appropriate diagnostic tests enables the physicians to perform the required measurements for the patients in a timely manner. Therefore, selection of an appropriate laboratory method, correct sampling and transportation of the samples are of great importance. Although molecular diagnostics are the best options inn diagnosing COVID-19, recent studies suggest that it is better not to confine in the results obtained from a single test and rather to use a combination of methods composed of different diagnostic and clinical approaches. The current study was designed aiming at the comparison of distribution patterns of COVID 2019 and estimation of the partial frequency of the clinical findings of COVID 2019 in order to facilitate decision making of the physicians and also differentiating the factors having impact on the final outcome of the hospitalized patients in the hospitals affiliated to Tabriz university of Medical Sciences.

Methods

The current study is a cross-sectional descriptive-analytic study. A total of 350 patients diagnosed with COVID-19 in August 2020 were enrolled into the study. Diagnosis of COVID-19 was performed using WHO guidelines. Positive COVID-19 was defined as a positive result of a PCR test obtained from the nasopharyngeal swap test. The information on the previous encounters, clinical signs on admission and at the hospitalizations time, and lab results on admission were collected. Radiological findings such as chest X-ray were also collected. Inclusion criteria to this study were the COVID-19 patients hospitalized in Tabriz hospitals. The exclusion criteria from the study were incomplete data unwillingness to participate in the study. Sampling was performed in a simple randomized method. The questionnaires were filled out by experienced staff. Nevertheless, the collected data were reevaluated after final collection for a qualitative control.

Radiological findings were reported by radiologists or infectious disease specialists in accordance with the charts and instructions of the health ministry. Laboratory evaluations including blood cell count, biochemical analysis of the blood, coagulation parameters, liver function test, kidney function tests, electrolytes, C-reactive protein, procalcitonin, dihydrogen lactate, and creatinine kinase were collected.

Recovery or death were set as the final outcomes in this study. Fever was checked with axillary thermometer and it was defined by temperature ≥37.5 ºC. Lymphocytopenia was defined as lymphocyte count of less than 1500 cells/ml3. Thrombocytopenia was defined as platelets less than 150000 cells/ml^3.

The collected data were analyzed using SPSS ver. 22. The obtained results were reported as numbers, percentage and median (considering the heterogeneous nature of the data). To test the distribution normality of the data Kolmogorov–Smirnov test were used. To analyze the data Fisher's exact test and Wilcoxon test were used. $P<0.05$ was considered statistically significant. This study was approved by Ethics Committee under the number: IR.TBZMED.REC.1399.529.

Results

A total of 350 patients with the median age of 64 years old, 204 (58.3%) male and 146 (41.7%) female. The demographic and clinical characteristics of the patients have been presented in (Table 1). The most common clinical findings were fatigue in 214 people (61.1%), cough in 207 people (59.1%), dyspnea in 202 people (57.7%). The median of the hospitalized days was four days with one day being the least and 60 days being the most days registered for hospitalization duration. 110 people (31.4%) were hospitalized in ICU. 208, 47, and 95 people were reported to be of mild, severe and critical conditions, respectively. The most common underlying diseases were hypertension, diabetes, cardiac diseases, renal diseases, and cancer in 105, 104, 72, 24, end 11, respectively. All 350 patients (100%) were reported to have positive findings for COVID-19 at their first and second CT scans and PCR tests.

Table 1- Demographic and clinical characteristics of the patients

Characteristics		Frequency (percent)
Age year median (IQR)		64 (76 – 52.75)
Sex	Male	204 (58.3)
	Female	146 (41.7)
Signs and symptoms	Cough	207 (59.1)

	Dyspnea	202 (57.7)
	Fatigue	214 (61.1)
	Rhinorrhea	74 (21.1)
	Sore throat	94 (26.9)
	Vomiting	106 (30.3)
	Respiratory tract complications	85 (24.3)
	Murmur	62 (17.7)
Hospitalization length per day (IQR)		4 (7 – 3)
Severity of the disease	0	208 (59.4)
	1	47 (13.4)
	2	95 (27.1)
PCR test	Yes	350 (100)
	No	0 (0)
CT scan	Yes	350 (100)
	No	0 (0)
Second CT scan	Yes	350 (100)
	No	0 (0)
Hospitalized in Ward		350 (100)
Hospitalized in ICU		110 (31.4)
Encounter	Yes	93 (26.6)
	No	257 (73.4)
Risk factor	Hypertension	155 (44.3)
	Diabetes Mellitus	104 (29.7)
	Cancer	11 (3.1)
	Renal diseases	24 (6.9)
	Cardiac diseases	72 (20.6)
Blood group	A	111 (31.7)
	B	49 (14)
	O	165 (47.1)
	AB	25 (7.1)
RH	Positive	321 (91.7)
	Negative	29 (8.3)
Mortality	Yes	109 (31.1)
	No	241 (68.9)

(Table 2) shows the paraclinical findings of the patients on admission and discharge. 98 (54.7%) of the patients had imbalanced WBC, 38 with leukopenia and 60 with leukocytosis. 54 patients (30.2%) had lymphopenia. 64 people (35.8%) had imbalanced platelets count: 26 people with thrombocytopenia and 38 people with thrombocytosis. 78 people (43.6%) were reported to have elevated CRP.

(Table 3) shows the distribution of the different blood group and Rh types among patients. The most common blood group type among the patients was blood group type O in 165 people (47.1%) followed by blood group type A in 111 people (31.7%). Rh+ was more frequent than Rh-.

(Figure 1) illustrates the distribution of different blood group types among studied COVID-19 patients. A mortality of 31.1% (109 people) was reported among the studied patients.

Table 2- Paraclinical findings of the patients on admission and discharge

Variable			Normal range	Median (IQR)	Patients	P value*
CBC	Hb (g/dL)	On admission	≥ 12	12.5 (13.5 – 11.8)	95 (27.1)	0.911
		At discharge		12.5 (13.5 – 11.8)	95 (27.1)	
	Lymph	On admission	> 1500	1082 (1371 – 707.5)	283 (85.9)	<0.0001
		At discharge		1283 (1614 – 740)	229 (65.4)	
	Plt	On admission	>150000	173000 (228250 – 141500)	229 (65.4)	0.007
		At discharge		181000 (245000 – 134750)	228 (65.1)	

Coagulation(s)	PT	On admission	≤ 16	14 (15 – 13.5)	42 (12)	<0.0001
		At discharge		15 (16.5 – 13.8)	100 (28.6)	
	BT	On admission	>37.5	37 (38 – 36.8)	123 (35.1)	<0.0001
		At discharge		36.8 (37 – 36.6)	21 (6)	
Biochemical		LDH	<245	764 (949.25 – 623)	86 (24.6)	---
	ALT	On admission	M: 29 -33	24 (28 – 19.75)	286 (81.7)	0.747
		At discharge	F: 29 -25-	21 (36.5 – 17)	307 (87.7)	
	Cr	On admission	<1.33	1.2 (1.5 – 1)	121 (34.6)	<0.0001
		At discharge		1 (1.41 – 0.9)	103 (29.4)	
		Na	135 - 145	138 (140 – 136)	4 (1.1)	---
		K	3.5 – 4.5	3.8 (4 – 3.6)	4 (1.1)	----
		CK	<185	124.5 (184 – 84)	86 (24.6)	---
		CRP	0	---	350 (100)	---
Blood Pressure (mmHg)		SBP	100 - 120	110 (120 – 110)	20 (5.7)	---
		PR	60 - 100	82 (88 – 76)	14 (4)	---
		RR	12 - 20	20 (22 – 18)	92 (26.3)	---

Table 3- Distribution of the blood group and Rh type among all and ICU patients

Blood group	All patients (%)	ICU patents (%)
A^+	103 (29.4)	51 (46.4)
A^-	8 (2.3)	1 (0.9)
B^+	44 (12.6)	14 (12.7)
B^-	5 (1.4)	1 (0.9)
O^+	155 (44.3)	33 (30)
O^-	10 (2.9)	4 (3.6)
AB^+	19 (5.4)	3 (2.7)
AB^-	6 (1.7)	3 (2.7)

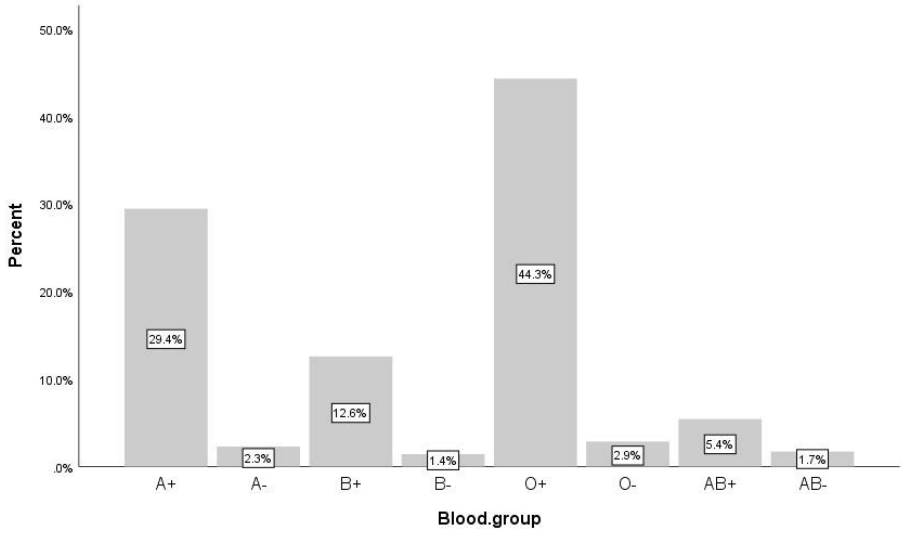

Figure 1- Distribution of different blood

(Table 4) shows the correlation of the blood group and mortality among all and ICU patients. There was a statistically significant correlation between blood group type and hospitalization in ICU. Blood group types A+ and O+ were the most common blood group types among the ICU hospitalized patients P<0.0001. There was a statistically significant correlation between blood group type and mortality among the studies patients. The highest rate of the mortality was amongst patients with blood group type A+ and O+ P <0.0001.

Table 4- Correlation of the blood group and mortality among all and ICU patients

Outcome		Blood group								P value*
		A^+	A^-	B^+	B^-	O^+	O^-	AB^+	AB^-	
ICU hospitalization	Yes	51 (46.4)	1 (0.9)	14 (12.7)	1 (0.9)	33 (30)	4 (3.6)	3 (2.7)	3 (2.7)	<0.0001
	No	52 (21.7)	7 (2.9)	30 (12.5)	4 (1.7)	122 (50.8)	6 (2.5)	16 (6.7)	3 (1.3)	
Mortality	Yes	50 (45.9)	1 (0.9)	13 (11.9)	1 (0.9)	34 (31.2)	3 (2.8)	4 (3.7)	3 (2.8)	0.001
	No	53 (22)	7 (2.9)	31 (12.9)	4 (1.7)	121 (50.2)	7 (2.9)	15 (6.2)	3 (1.2)	

Discussion

Similar to our study, most studies reported the following common clinical findings in COVID-19 patients: fever, cough, fatigue, muscles sore, dyspnea, lymphocytopenia, elevated liver enzymes, elevated cardiac enzymes and ground glass like consolidations in lungs [15-18]. In most studies, it has been suggested that the deceased COVID-19 patients had one or multiple underlying diseases such as hypertension, diabetes or cardiovascular diseases which could have contributed to immune dysregulation [19-26]. These findings are in line with the findings of our study.

In a similar study by Nasrollahzadeh et al., 1408 patients were studied from which 27% required mechanical ventilation and ultimately 9.21% deceased. The severe manifestations of the disease and its associated high mortality rate in studied COVID-19 patience was contributed to the underlying cardiovascular diseases and diabetes [23]. These findings are In line with our study. In another study by Talebi et al., 43.8% of all patients and 71.9% of the deceased patients suffered from at least one underlying disease. The increased level of WBC, lymphocytopenia and neutrophilia were significantly more frequent in the deceased patients. The findings of this study are also in line with the findings of our study. In our study, a significant correlation was observed between the blood group type and the probability of ICU hospitalization in the studied patients. Among the patients hospitalized in ICU, the most frequent blood group type was A+ followed by O+. The results of the current studies indicate that blood Group type A and O might be considered as a poor and good prognostic factors in COVID-19 patients, respectively [11].

The correlation between ABO group type and VTE has been studied in numerous studies and it seems there to be a correlation between blood group types A and B and the incidence of VTE [12]. Studies show that the topic of blood group and especially ABO blood group type is no more only a parameter to be solely used in transfusion or tissue graft; whereas, it might play a major role in the incidence and severity of numerous diseases. Therefore, one might be hypothesize that blood group type could be used as a prognostic risk factor in some diseases and consequently appropriate prophylactic measures could be taken, especially in the elderly and the patients with underlying diseases. Furthermore, the clinical manifestation of the disease on admission of the patients, for instance leukocytosis and lymphocytopenia might be useful in the stratification and prognosis of the patients.

Conclusion

Fever, fatigue and non-productive coughs, dyspnea, leukopenia, leukocytosis, lymphopenia, thrombocytopenia, thrombocytosis, increased ESR, increased CRP, and increased D-dimer are the most common clinical and laboratory findings in COVID-19 patients. A statistically significant correlation was observed between the patients hospitalized in ICU and the blood group type; the most frequent blood group type was A+ followed by O+.

List of abbreviations

ICU: Intensive Care Unit
ARDS: Acute respiratory distress syndrome

Declarations

Ethics approval and consent to participate:

This study was approved by the regional ethics committee with No. IR.TBZMED.REC.1399.529. Written informed consent was obtained from patient and so each patient' relatives. I confirm that all methods were carried out in accordance with relevant guidelines and regulations. All procedures in the study involving human participants were performed in accordance with the ethics standards of the institutional and national research committee and with the Helsinki Declaration and its later amendments or comparable ethics standards.

Consent for publication:

The data presented in the manuscript and its supplemental files do not contain any details relevant to any individual patient and thus, no consent for publication was required.

Availability of data and materials:

The datasets generated during and analyzed during the current study are not publicly available due to restriction

of ethic committee of Tabriz University of Medical Sciences but are available from the corresponding author on reasonable request.

Authors' contributions:

"SEJ G, NHK, ES, ZT, SGF, AA, AO, RME, SS and HS performed the data collection, literature review, and drafting of the manuscript. HS, ZT and ES undertook the major parts of the study design and performed the statistical analysis. All authors reviewed the manuscript."

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Data Reproducibility

The dataset presented in the study is available on request from the corresponding author during submission or after publication

References

[1] Liu W, Tao ZW, Wang L, Yuan ML, Liu K, Zhou L, Wei S, Deng Y, Liu J, Liu HG, Yang M. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J. 2020;133(09):1032-8.

[2] Soleimanpour H, Sarbazi E, Esmaeili ED, Mehri A, Fam SG, Nikbakht HA, Saadati M, Sedighi S, Vali M, Azizi H. Predictors of receiving COVID-19 vaccine among adult population in Iran: an observational study. BMC Public Health. 2023;23(1):490.

[3] Bagi HM, Soleimanpour M, Abdollahi F, Soleimanpour H. Evaluation of clinical outcomes of patients with mild symptoms of coronavirus disease 2019 (COVID-19) discharged from the emergency department. PloS one. 2021;16(10):e0258697.

[4] Shahsavarinia K, Ghojazadeh M, Ghabousian A, Hatefnia F, Soleimanpour M, Soleimanpour H. An umbrella review of clinical efficacy and adverse cardiac events associated with hydroxychloroquine or chloroquine with or without azithromycin in patients with COVID-19. Anesth Pain Med. 2021;11(4).

[5] Shadvar K, Tagizadiyeh A, Gamari AA, Soleimanpour H, Mahmoodpoor A. Hemoperfusion as a potential treatment for critically ill COVID-19 patients with cytokine storm. Blood Purif. 2021;50(3):405-7.

[6] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P. A novel coronavirus from patients with pneumonia in China, 2019. New England J Med. 2020;382(8):727-33.

[7] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DS, Du B. Clinical characteristics of coronavirus disease 2019 in China. New England J Med. 2020;382(18):1708-20.

[8] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L. 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.

[9] Sun P, Qie S, Liu Z, Ren J, Xi J. Clinical characteristics of 50404 patients with 2019-nCoV infection. MedRxiv. 2020:2020-02.

[10] Zu ZY, Jiang MD, Xu PP, Chen W, Ni QQ, Lu GM, Zhang LJ. Coronavirus disease 2019 (COVID-19): a perspective from China. J Radiol. 2020;296(2):E15-25.

[11] Zhao J, Yang Y, Huang H, Li D, Gu D, Lu X, Zhang Z, Liu L, Liu T, Liu Y, He Y. Relationship between the ABO blood group and the coronavirus disease 2019 (COVID-19) susceptibility. Clin Infect Dis. 2021;73(2):328-31.

[12] Zhan Y. ABO blood type and ARDS. Chest. 2015;147(2):e67.

[13] Deschasaux-Tanguy M, Szabo de Edelenyi F, Druesne-Pecollo N, Esseddik Y, Allègre J, Srour B, Galan P, Hercberg S, Severi G, Zins M, Wiernik E. ABO blood types and SARS-CoV-2 infection assessed using seroprevalence data in a large population-based sample: the SAPRIS-SERO multi-cohort study. Scientific Reports. 2023;13(1):4775.

[14] Ijaz S, Cheema AH, Rafiq A, Asghar A, Shah Syed AR, Syed AA, Eqbal F, Mumtaz H. Relationship between the ABO blood group and Rhesus factors with COVID-19 susceptibility. Expert Rev Hematol. 2023;16(4):297-303.

[15] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.

[16] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DS, Du B. Clinical characteristics of 2019 novel coronavirus infection in China. MedRxiv. 2020.

[17] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Yu T. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13.

[18] Ozcan E, Yavuzer S, Borku Uysal B, Islamoglu MS, Ikitimur H, Unal OF, Akpinar YE, Seyhan S, Koc S, Yavuzer H, Cengiz M. The relationship between positivity for COVID-19 RT-PCR and symptoms,

clinical findings, and mortality in Turkey. Expert Rev Mol Diagn. 2021;21(2):245-50.

[19] Jaillon S, Berthenet K, Garlanda C. Sexual dimorphism in innate immunity. Clin Rev Allergy Immunol. 2019; 56:308-21.

[20] Libert C, Dejager L, Pinheiro I. The X chromosome in immune functions: when a chromosome makes the difference. Nat Rev Immunol. 2010;10(8):594-604.

[21] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-62.

[22] Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. International J Antimicrob Agents. 2020;55(3):105924.

[23] Nasrollahzadeh Sabet M, Khanalipour M, Gholami M, Sarli A, Rahimi Khorrami A, Esmaeilzadeh E. Prevalence, clinical manifestation and mortality rate in COVID-19 patients with underlying diseases. J Arak Uni Med Sci. 2020;23(5):740-9.

[24] Akhavizadegan H, Aghaziarati M, Roshanfekr Balalemi MG, Arman Broujeni Z, Taghizadeh F, Akbarzadeh Arab I, Janani M. Relationship between comorbidity, chronic diseases, ICU hospitalization, and death rate in the elderly with Coronavirus infection. Iran J Ageing. 2021;16(1):86-101.

[25] Mohammadi M, Amini Nasab Z, Bajdi Gezik F, Lashkari R, Rastin T, A review of the effect of coronary heart disease on the care of hypertensive patients in South Khorasan, the second national conference on new biological findings, Zahedan. 2020.

[26] Talebi S, Nematshahi M, Tajabadi A, Khosrogerdi A. Comparison of clinical and epidemiological characteristics of deceased and recovered patients with COVID-19 in Sabzevar, Iran. J Mil Med 2022;22(6):509-16.