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Original research

Clinical characteristics and laboratory findings of patients with COVID-19 in Rasht, Iran

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Abstract

In December 2019, a pandemic of an unknown respiratory virus emerged in Wuhan, China, putting the whole world in crisis; a newly emerged coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In this study, we evaluated the clinical characteristics and laboratory findings of patients with coronavirus disease 2019 (COVID-19) in the North of Iran. Demographical data and clinical characteristics of 126 patients with COVID-19 in Razi Hospital, Rasht, Iran, were recorded. The mean age of patients was 62 years old and 57.1% of cases were male. About 17.5% of patients had direct contact with a SARS-CoV-2-infected patient. The most common underlying diseases were lung diseases (11.9%), diabetes (11.9%), cardiovascular disease (CVD) (7.1%), and hypertension (4.8%). The mean levels of lactate dehydrogenase (LDH), creatine phosphokinase (CPK), creatine kinase MB (CK-MB), serum glutamic oxaloacetic transaminase (SGOT), and erythrocyte sedimentation rate (ESR) (1231.79±866.48 U/L, 766.88±2288.68 U/L, 59.2±55.18 U/L, 112.28±213.07 U/L, and 67.61±31.07 mm/hr, respectively) were remarkably higher than the normal ranges. Also, the average O2 Saturation (O2Sat) was 61.42±26.37%. Male gender, advanced age, a history of underlying diseases, higher level of cardiac enzymes, and lower level of O2Sat were associated with severity in patients with COVID-19.

Keywords: SARS-CoV-2, COVID-19, Laboratory findings, Clinical characteristics

1. Introduction

Coronaviruses, belonging to the family Coronaviridae, are enveloped single-stranded RNA viruses that are widely spread in mammals including humans [1]. Despite mild infections caused by coronaviruses, a novel coronavirus was found as the cause of a new emerging worldwide pandemic after testing the lower respiratory tract samples, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2]. The coronavirus disease 2019

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(COVID-2019) is announced as a worldwide concern by the World Health Organization (WHO). Patients with COVID-19 have some clinical manifestations such as fever and cough as primary clinical presentations, and shortness of breath and myalgia as the following manifestation [3]. Due to the wide spectrum of SARS-CoV-2 symptoms, some patients may have serious and extensive complications such as acute respiratory distress syndrome (ARDS) and cytokine storm, which may result in organ failure and death [4, 5]. Some circumstances lead to susceptibility of being fatal cases of COVID-19, such as middle and upper age with a history of pre-existing underlying diseases (lung diseases, cardiovascular diseases (CVD), kidney and liver diseases, hypertension, and diabetes) [6, 7]. Among underlying diseases, lung and cardiac complications are strongly related to higher in-hospital mortality in patients with COVID-19. The mechanisms of SARS-CoV-2, which causes this acute heart complication, include direct and indirect damage to cardiomyocytes and systemic inflammation [8]. A study demonstrated that the mortality was associated with an increased level of C-reactive protein (CRP), serum glutamic oxaloacetic transaminase (SGOT), potassium (K), neutrophils count, white blood cell (WBC) count, and prothrombin time (PT) in COVID-19 patients with abnormal chest computed tomography (CT)-scan results. Additionally, in these patients, a decrease in lymphocytopenia and O2 saturation (O2Sat) levels is associated with severe conditions [9]. Some laboratory findings such as lymphocytopenia, thrombocytopenia, elevated CRP, and ESR can also be helpful for clinicians to predict the patient's condition [10]. The higher neutrophil to lymphocyte ratio (NLR) and upper age can be used as independent biomarkers indicators of poor clinical outcomes [11], in which NLR greater than 6.5 may reflect the progression of the disease toward an unfavorable clinical outcome; with this notion, the ratios higher than 9 may result in death [12]. In addition, in COVID-19 patients with mild to severe conditions, the average level of lactate dehydrogenase (LDH), creatine phosphokinase (CPK), SGOT, serum glutamic pyruvic transaminase (SGPT), and CRP, are higher than the normal range [13].

Since the evaluation of clinical and laboratory findings are more accessible and valuable for the diagnosis of infections such as SARS-CoV-2 [14]; we aimed to evaluate demographical data, clinical characteristics, and laboratory findings of patients with COVID-19 in the North of Iran.

2. Materials and Methods

2.1 Data collecting

This retrospective study was conducted from February to May 2020, on the 126 cases of COVID-19, referring to Razi Hospital, Rasht, Iran. All cases were confirmed for SARS-CoV-2 infection via using the real-time polymerase chain reaction (RT-PCR) test on nasopharyngeal swabs specimens from the upper respiratory tract. Demographic data and clinical characteristics of patients including age, gender, history of smoking, history of opium consumption, direct contact with COVID-19 patients, history of underlying diseases, and symptoms at the time of admission were collected from the patient's medical records. Laboratory variables including complete blood count (CBC), ESR, coagulation profile (PT and partial thromboplastin time (PTT)); arterial blood gases (ABG); and biochemical parameters such as alkaline phosphatase (ALP), SGPT, SGOT, total protein, albumin, CPK, creatine kinase MB (CK-MB), calcium (Ca), phosphorous, magnesium (Mg), direct and indirect bilirubin, uric acid, blood urea nitrogen (BUN), creatinine, amylase, blood sugar, LDH, sodium (Na), and K were analyzed on blood samples of the patients with COVID-19. The patients with incomplete data were excluded from the study.

2.2 Statistical analysis

The variables were represented by mean ± standard deviation (SD), median and interquartile range (IQR). The Shapiro-Wilk test was used to test the normality of data distribution. The categorical variables were presented in numbers and percentages. All statistical data were analyzed using IBM SPSS, version 24.0.

3. Results

A total number of 126 patients with COVID-19 were included in this study, of which the median age of patients was 62 years, ranging from 28 to 92 years old. Overall, 57.1% of cases were male and 42.9% were female. According to Table 1, 17.5% of patients had direct contact with COVID-19 patients. The most common underlying diseases were lung diseases (11.9%), diabetes (11.9%), CVD (7.1%), and

hypertension (4.8%). Fever (80.2%), cough (80.2%), myalgia (50%), and dyspnea (40.5%) were the most common symptoms, while digestive symptoms were rare. Also, 81% of patients experience an O2Sat level <93%, and 13.5% of patients were intubated. The mean levels of some laboratory findings represented abnormalities in ESR (67.61±31.07 mm/hr), CK-MB (59.2±55.18 U/L), CPK (766.88±2288.68U/L), LDH (1231.79±866.48 U/L), SGOT (112.28±213.07 U/L) and SGPT (90.33±209.47 U/L). The mean of lymphocyte, neutrophil, and O2Sat were 20.03±14.05%, 76.56 ±15.5%, and 61.42±26.37%, respectively. O2Sat was critically lower than the normal range, Table 2.

Table 1. Demographical data and clinical characteristics of patients with COVID-19

Demographical data	n (%)
Gender	
Male	72 (57.1)
Female	54 (42.9)
Contact with COVID-19 cases	17 (13.5)
History of smoking	2 (1.6)
History of opium consumption	2 (1.6)
Clinical characteristics	
Fever	101 (80.2)
Cough	101 (80.2)
Myalgia	63 (50.0)
Dyspnea	51 (40.5)
Loss of consciousness	8 (6.3)
Anosmia	4 (3.2)
Ageusia	3 (2.4)
Gastrointestinal manifestation	2 (1.6)
Nausea	1 (0.8)
Vomiting	1 (0.8)
Seizure	1 (0.8)
Po_2	
Less than 93%	102 (81.0)
Upper than 93%	24 (19.0)
Intubation	17 (13.5)
Underlying disease	
Lung diseases	18 (11.9)
Diabetes	15 (11.9)
Cardiovascular diseases	9 (7.1)
Hypertension	6 (4.8)
Chronic kidney disease	4 (3.2)
Chronic neurological disorders	4 (3.2)
Other chronic diseases	4 (3.2)
Chronic liver disease	2 (1.6)
Immunodeficiencies	2 (1.6)
Patients undergoing hemodialysis	2 (1.6)
Chronic hematologic diseases	2 (1.6)
Cancer	1 (0.8)

4. Discussion

At the beginning of the COVID-19 pandemic, the diagnosis of the disease was complicated by various symptoms, abnormal chest CT-scan results, abnormal laboratory findings, and the severity of the disease at the time of onset. Due to our results, males were the majority of hospitalized patients, similar to some other reports, which consequences in severe complications [15–18]. Gender differences in the frequency and outcomes of infectious diseases are reported at all ages in males [19–21]. These data represented that, while environmental factors may be affecting various aspects of the pandemic, fundamental differences in the immune response among males and females are possibly a factor behind the notably observed gender bias in the COVID-19 pandemic. Various studies reported the genetic differences among genders in their innate and adaptive immune system function [22–25].

The most common underlying diseases were lung diseases, diabetes, and CVD. In several studies, lung diseases and CVD were reported as frequently associated factors with SARS-CoV-2 infection and the severity condition in these patients [26–28]. In addition, pre-existing CVD upsurges the rate of COVID-19 morbidity and mortality and is closely related to poor disease outcomes [8]. A cohort study in China illustrated that cardiac injury is frequent among hospitalized patients with COVID-19, and is associated with a higher risk of in-hospital mortality [29]. Along with age and CVD, one of the most common comorbidities associated with a poor prognosis in COVID-19 patients is diabetes. People with diabetes and lung complications are more susceptible to get infections, and they tend to develop more severe conditions with a significantly higher mortality rate than those without diabetes [30]. Fever, cough, dyspnea, and myalgia were the most reported symptoms among patients with COVID-19. Chen et al. reported that the majority of patients with COVID-19 were males, and common symptoms were fever and cough [31].

The hematological analysis demonstrated a lower level of O2 Sat, lymphocytopenia, and a higher level of ESR and neutrophil count. Several studies have illustrated a lower level of lymphocytes and a higher level of neutrophils in COVID-19 cases with severe conditions, which were consistent with our results. The NLR can be useful in the clinical management of

Table 2. Laboratory findings of patients with COVID-19

Laboratory Index	Tested	Median	IQR1	IQR3	Mean	SD	Min	Max	Normal Range
WBC	122	9.5	6.2	11.6	10.04	5.86	2.5	48.1	4-10 x 10^3 /CUMM
RBC	122	4.7	4.1	5.1	4.61	0.84	82	6.69	4.5-6 x 10^6 mIu/L
Hb	122	13.2	11.5	14.4	12.85	2.34	6	19.1	12-16 g/dL
HCT	122	41.3	36.3	44.4	40.10	7.08	8.4	61.4	35.5-48 %
MCH	122	28.4	27	29.5	28.23	4.94	17.9	73.2	27-32 pg
MCHC	122	32.1	30.9	33.4	32.28	3.98	26.8	71.4	31-37 gr/dl
MCV	122	87.5	84.7	91.2	87.29	7.46	61.4	107.9	80-100 FL
RDW	121	13.6	12.5	15.1	14.04	2.15	10.8	24.2	11-16 %
Platelet	122	203	147.5	268.5	224.16	113.19	40	812	140-450 x 10^3 U/L
Lymphocyte	36	17.5	10.25	25	20.03	14.05	5	80	25-40%
Neutrophil	36	80	72	85.75	76.56	15.52	15	95	40-60%
Eosinophil	33	2	2	2	2.58	4.192	1	26	1-4%
Monocyte	13	2	1	3	2.23	1.013	1	4	2-8%
ESR	38	70	44.25	88.25	67.61	31.07	10	138	0-22 mm/hr Male 0-29 mm/hr Female
PTT	49	32	29	36.5	33.55	5.96	28	54	30-45 Second
PT	49	12	12	12.75	12.85	2.20	12	25	10-2-12 Second
INR	50	1	1	1.08	1.11	0.30	1	2.85	0.8-1.1
O_2Sat	55	68	38.5	83.3	61.42	26.37	6.8	98.8	>95%
HCO_3	55	22.1	18.5	25.6	23.17	8.76	9.6	54.7	22-26 mEq/L
PO_2	55	36.2	24.5	48.3	43.62	30.47	8.1	148.8	80-100 mmHg
PCo_2	55	41.1	35.7	49	43.39	14.27	20.3	96.4	35-45 mmHg
pH	55	7.4	7.3	7.4	7.33	0.08	6.99	7.517	7.35-7.45
LDH	68	951	735.8	1398.3	1231.79	866.48	7	4247	230-460 U/L
CPK	72	183.5	94.5	461.5	766.88	2288.68	35	18000	10-120 mcg/L
CPK-MB	69	46	31	64.5	59.28	55.18	13	350	<24 U/L or 6-25% of total CPK
ALP	62	183.5	138.5	276.3	223.65	125.28	79	702	20-140 U/L
SGPT	61	32	23	60	90.33	209.47	11	1404	7-56 U/L
SGOT	61	49	30	90.5	112.28	213.07	12	1377	8-45 U/L
K	119	4.2	4	4.4	4.20	0.48	2.6	5.7	3.5-5 mEq/L
Na	120	134	131	137	134.56	4.93	125	149	135-145 mEq/L
Ca	46	8.4	8.2	8.6	8.40	0.49	6.7	9.5	8.5-10.5 mg/dl
Phosphorus	48	3	2.5	3.4	3.23	1.55	1.5	10.9	2.6-4.5 mg/dl
Mg	49	1.9	1.8	2.1	1.98	0.25	1.4	2.8	1.8-2.4 mg/dl
BS	96	155	115.5	202	180.89	92.30	75	582	<140 mg/dl
BUN	124	21	14	29.8	27.07	22.26	8	159	7-21 mg/dl
Creatinine	123	1.1	0.9	1.4	1.37	1.10	0.70	10.10	0.6-1.2 mg/dl
Uric Acid	42	6	4	8.5	6.58	2.96	2.2	15	2.6-8.2 mg/dl
Total protein	47	6.5	5.7	7	6.31	0.93	3.80	8	6-8.3 g/dl
Albumin	49	3.6	3.3	3.9	3.60	0.47	2.60	4.50	3.5-5.2 g/dl
Bilirubin Total	59	0.7	0.5	0.9	0.78	0.57	0.30	4.40	0.3-1.2 mg/dl
Bilirubin Direct	59	0.2	0.2	0.4	0.30	0.25	0.10	1.90	<0.2 mg/dl
Amylase	38	60	41.8	91.3	78.89	74.97	16	454	40-140 U/L

Abbreviations: CBC (complete blood count), WBC (white blood cell), RBC (red blood cell), Hb (hemoglobin), HCT (hematocrit), MCH (mean corpuscular hemoglobin), MCV (mean corpuscular volume), MCHC (mean corpuscular hemoglobin concentration), RDW (red cell distribution width), EER (*e*rythrocyte sedimentation rate), PT (prothrombin time), PTT (partial thromboplastin time), INR ($PTtest/PT_{Normal})^{ISI}$, O_2Sat (O_2 Saturation), HCO_3 (hydrochloric acid), PO_2 (arterial partial pressure of oxygen), PCo_2 (arterial partial pressure of carbon dioxide), pH (potential of hydrogen), LDH (lactate dehydrogenase), CPK (creatine phosphokinase), CK-MB (creatine kinase MB), K (potassium), Na (sodium), Ca (calcium), Mg (magnesium), BS (blood sugar), ALP (alkaline phosphatase), SGPT (serum glutamic pyruvic transaminase), SGOT (serum glutamic oxaloacetic transaminase), SD (standard deviation), IQR (interquartile range).

SARS-CoV-2 infection in the early stages [32–35]. Besides, hypoxia and dyspnea are both reported as a sign of lung involvement. The lower level of O2Sat predisposes patients with COVID-19 to intensive care unit (ICU) admission [36, 37]. Pu et al. suggested that SARS-CoV-2 might trigger the changes in the form of erythrocytes or plasma characteristics through an unknown mechanism by elevating the level of ESR [38]. A sustained high level of ESR may lead to adverse effects on the prognosis status of patients with COVID-19 because a higher ESR level can damage the joint and lead to joint complications such as osteoarthritis, which may be a precursor of liver and kidney damage [39–42]. The biochemical analysis reported an elevated level of SGOT, SGPT, LDH, CPK, and CK-MB in patients with COVID-19. Due to our results, liver enzymes including, SGOT and SGPT were remarkably higher than the normal range in patients with COVID-19 at the time of admission to the hospital, which was associated with the severity of conditions in these patients. Interestingly, a study demonstrated the association between liver enzymes and severity conditions in patients with COVID-19. They observed that SGOT elevated first, followed by SGPT which was associated with the highest mortality [43, 44]. As SGOT is found in various tissue, the elevated level of this enzyme results in multiorgan failure [45]. An investigation demonstrated that along with lymphocytopenia, elevated levels of LDH were more frequently seen in severe COVID-19 illnesses [46]. Furthermore, the evaluation of CK-MB in patients with COVID-19 might provide specific clinical data for early risk factors in these patients [47–49]. Similar to our study, it was reported that age, pre-existing underlying diseases, low O2Sat, decreased lymphocyte count, and elevated levels of CRP, SGOT, LDH, and CK-MB can be used as predictors of the severity of COVID-19 conditions [50, 51]. Another study revealed that CK-MB, LDH, and SGOT were higher in patients with COVID-19 compared to the control group; moreover, in these patients, the levels of mentioned enzymes were higher in patients with death outcomes than in survivors [52].

According to our investigation, advanced age, male gender, a history of underlying disease, and abnormal laboratory findings predispose patients with COVID-19 to severe conditions.

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Authors' contributions

Concept and Study design: TY, SM, AA. Methods, data collection, and experimental work: EH, LM, DA, SN, VS, ZG, RE, NF. Results analysis and interpretation: AA, EH, LM, DA, SN, VS, ZG, RE, SM. Manuscript preparation: TY, SM, NF. All Authors read and approved the final version of the manuscript.

Conflict of interests

The authors reported no potential conflict of interest.

Ethical declarations

The study design was approved by the ethical committee at the Guilan University of Medical Sciences (IR.GUMS.REC.1399.022).

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References

1. Pal M, Berhanu G, Desalegn C, Kandi V. Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2): An Update. Cureus. 2020; 12(3):e7423.
2. She J, Jiang J, Ye L, Hu L, Bai C, Song Y. 2019 novel coronavirus of pneumonia in Wuhan, China: emerging attack and management strategies. Clin Transl Med. 2020; 9(1):19.
3. Halaji M, Heiat M, Faraji N, Ranjbar R. Epidemiology of COVID-19: An updated review. J Res Med Sci. 2021; 26:82.
4. Lechien JR, Chiesa-Estomba CM, Place S, Van Laethem Y, Cabaraux P, Mat Q, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. J Intern Med. 2020; 288(3):335–44.
5. Pan Y, Li X, Yang G, Fan J, Tang Y, Zhao J, et al. Serological immunochromatographic approach in diagnosis with SARS-CoV-2 infected COVID-19 patients. J Infect. 2020; 81(1):e28–32.
6. Adhikari SP, Meng S, Wu Y-J, Mao Y-P, Ye R-X, Wang Q-Z, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infect Dis poverty. 2020; 9(1):29.
7. Mansury D, Moghim S. Coronavirus disease 2019 (COVID-19): A New Pandemic and its Challenges. J Curr Biomed Rep. 2022; 1(2):52-57.
8. Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. Nat Rev Cardiol. 2020; 17(9):543–558.
9. Bairwa M, Kumar R, Beniwal K, Kalita D, Bahurupi Y.

Hematological profile and biochemical markers of COVID-19 non-survivors: A retrospective analysis. Clin Epidemiol Glob Heal. 2021; 11:100770.
10. Ghahramani S, Tabrizi R, Lankarani KB, Kashani SMA, Rezaei S, Zeidi N, et al. Laboratory features of severe vs. non-severe COVID-19 patients in Asian populations: A systematic review and meta-analysis. Eur J Med Res. 2020;25(1):30.
11. Vafadar Moradi E, Teimouri A, Rezaee R, Morovatdar N, Foroughian M, Layegh P, et al. Increased age, neutrophil-to-lymphocyte ratio (NLR) and white blood cells count are associated with higher COVID-19 mortality. Am J Emerg Med. 2021; 40:11-4.
12. Pirsalehi A, Salari S, Baghestani A, Vahidi M, Khave LJ, Akbari ME, et al. Neutrophil-to-lymphocyte ratio (NLR) greater than 6.5 May reflect the progression of COVID-19 towards an unfavorable clinical outcome. Iran J Microbiol. 2020; 12(5):466–474.
13. Gholizadeh P, Safari R, Marofi P, Zeinalzadeh E, Pagliano P, Ganbarov K, et al. Alteration of liver biomarkers in patients with SARS-CoV-2 (COVID-19). J Inflamm Res. 2020; 13:285–92.
14. Zeinali T, Faraji N, Joukar F, Khan Mirzaei M, Kafshdar Jalali H, Shenagari M, et al. Gut bacteria, bacteriophages, and probiotics: Tripartite mutualism to quench the SARS-CoV2 storm. Microb Pathog. 2022; 170:105704.
15. 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):1199–1207.
16. 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. Lancet. 2020; 395(10223):507–513.
17. Zhang J-J, Dong X, Cao Y-Y, Yuan Y-D, Yang Y-B, Yan Y-Q, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020; 75(7):1730–1741.
18. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020; 323(11):1061–1069.
19. Klein SL, Flanagan KL. Sex differences in immune responses. Nat Rev Immunol. 2016; 16(10):626–38.
20. Schröder J, Kahlke V, Staubach KH, Zabel P, Stüber F. Gender differences in human sepsis. Arch Surg. 1998; 133(11):1200–5.
21. Flanagan KL, Fink AL, Plebanski M, Klein SL. Sex and Gender Differences in the Outcomes of Vaccination over the Life Course. Annu Rev Cell Dev Biol. 2017; 33:577–599.
22. Laffont S, Rouquié N, Azar P, Seillet C, Plumas J, Aspord C, et al. X-Chromosome complement and estrogen receptor signaling independently contribute to the enhanced TLR7-mediated IFN-α production of plasmacytoid dendritic cells from women. J Immunol. 2014; 193(11):5444–52.
23. Ziegler SM, Altfeld M. Human Immunodeficiency Virus 1 and Type I Interferons-Where Sex Makes a Difference. Front Immunol. 2017; 8:1224.
24. Meier A, Chang JJ, Chan ES, Pollard RB, Sidhu HK, Kulkarni S, et al. Sex differences in the Toll-like receptor-mediated response of plasmacytoid dendritic cells to HIV-1. Nat Med. 2009; 15(8):955–9.
25. Berghöfer B, Frommer T, Haley G, Fink L, Bein G, Hackstein H. TLR7 ligands induce higher IFN-alpha production in females. J Immunol. 2006; 177(4):2088–96.
26. Imazio M, Klingel K, Kindermann I, Brucato A, De Rosa FG, Adler Y, et al. COVID-19 pandemic and troponin: indirect myocardial injury, myocardial inflammation or myocarditis? Heart. 2020; 106(15):1127–1131.
27. Tavazzi G, Pellegrini C, Maurelli M, Belliato M, Sciutti F, Bottazzi A, et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. Eur J Heart Fail. 2020; 22(5):911-915.
28. Das BB, Sexon Tejtel SK, Deshpande S, Shekerdemian LS. A Review of the Cardiac and Cardiovascular Effects of COVID-19 in Adults and Children. Texas Hear Inst J. 2021; 48(3):e207395.
29. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol. 2020; 5(7):802–810.
30. Mazucanti CH, Egan JM. SARS-CoV-2 disease severity and diabetes: why the connection and what is to be done? Immun Ageing. 2020; 17:21.
31. 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. Lancet. 2020; 395(10223):507-513.
32. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, et al. Covid-19 in Critically Ill Patients in the Seattle Region — Case Series. N Engl J Med. 2020; 382(21):2012–2022.
33. Curbelo J, Luquero Bueno S, Galván-Román JM, Ortega-Gómez M, Rajas O, Fernández-Jiménez G, et al. Inflammation biomarkers in blood as mortality predictors in community-acquired pneumonia admitted patients: Importance of comparison with neutrophil count percentage or neutrophil-lymphocyte ratio. PLoS One. 2017; 12(3):e0173947.
34. Liu X, Shen Y, Wang H, Ge Q, Fei A, Pan S. Prognostic Significance of Neutrophil-to-Lymphocyte Ratio in Patients with Sepsis: A Prospective Observational Study. Mediators Inflamm. 2016; 2016:8191254.
35. Berhane M, Melku M, Amsalu A, Enawgaw B, Getaneh Z, Asrie F. The Role of Neutrophil to Lymphocyte Count Ratio in the Differential Diagnosis of Pulmonary Tuberculosis and Bacterial Community-Acquired Pneumonia: a Cross-Sectional Study at Ayder and Mekelle Hospitals, Ethiopia. Clin Lab. 2019; 65(4).
36. Kashani KB. Hypoxia in COVID-19: Sign of Severity or Cause for Poor Outcomes. Mayo Clin Proc. 2020; 95(6):1094–1096.
37. Xie J, Covassin N, Fan Z, Singh P, Gao W, Li G, et al. Association Between Hypoxemia and Mortality in Patients With COVID-19. Mayo Clin Proc. 2020; 95(6):1138–1147.
38. Pu S-L, Zhang X-Y, Liu D-S, Ye B-N, Li J-Q. Unexplained elevation of erythrocyte sedimentation rate in a patient recovering from COVID-19: A case report. World J Clin cases. 2021; 9(6):1394–1401.
39. Hanada M, Takahashi M, Furuhashi H, Koyama H, Matsuyama Y. Elevated erythrocyte sedimentation rate and high-sensitivity C-reactive protein in osteoarthritis of the knee: relationship with clinical findings and radiographic severity. Ann Clin Biochem. 2016; 53(Pt 5):548–53.
40. Atzeni F, Talotta R, Masala IF, Bongiovanni S, Boccassini L, Sarzi-Puttini P. Biomarkers in Rheumatoid Arthritis. Isr Med Assoc J. 2017; 19(8):512–516.
41. Brouillard M, Reade R, Boulanger E, Cardon G, Dracon M, Dequiedt P, et al. Erythrocyte sedimentation rate, an underestimated tool in chronic renal failure. Nephrol Dial Transplant. 1996; 11(11):2244–7.
42. Hess CT. Monitoring laboratory values: transferrin, C-reactive

protein, erythrocyte sedimentation rate, and liver function. Adv Skin Wound Care. 2009; 22(2):96.
43. Lei F, Liu Y-M, Zhou F, Qin J-J, Zhang P, Zhu L, et al. Longitudinal Association Between Markers of Liver Injury and Mortality in COVID-19 in China. Hepatology. 2020; 72(2):389–398.
44. Shokri Afra H, Amiri-Dashatan N, Ghorbani F, Maleki I, Rezaei-Tavirani M. Positive association between severity of COVID-19 infection and liver damage: a systematic review and meta-analysis. Gastroenterol Hepatol from bed to bench. 2020; 13(4):292–304.
45. Téllez L, Martín Mateos RM. COVID-19 and liver disease: An update. Gastroenterol Hepatol. 2020; 43(8):472–480.
46. 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. Lancet . 2020; 395(10229):1054–1062.
47. Bansal A, Kumar A, Patel D, Puri R, Kalra A, Kapadia SR, et al. Meta-analysis Comparing Outcomes in Patients With and Without Cardiac Injury and Coronavirus Disease 2019 (COVID 19). Am J Cardiol. 2021; 141:140–146.
48. Walker C, Deb S, Ling H, Wang Z. Assessing the Elevation of Cardiac Biomarkers and the Severity of COVID-19 Infection: A Meta-analysis. J Pharm Pharm Sci. 2020; 23:396–405.
49. Parohan M, Yaghoubi S, Seraji A. Cardiac injury is associated with severe outcome and death in patients with Coronavirus disease 2019 (COVID-19) infection: A systematic review and meta-analysis of observational studies. Eur Heart J Acute Cardiovasc Care. 2020; 9(6):665–677.
50. Zheng F, Tang W, Li H, Huang YX, Xie YL, Zhou ZG. Clinical characteristics of 161 cases of corona virus disease 2019 (COVID-19) in Changsha. Eur Rev Med Pharmacol Sci. 2020; 24(6):3404–3410.
51. Wang JT, Sheng WH, Fang CT, Chen YC, Wang JL, Yu CJ, et al. Clinical Manifestations, Laboratory Findings, and Treatment Outcomes of SARS Patients. Emerg Infect Dis. 2004;10(5):818–24.
52. Guan Y, Tang X, Yin C, Hong W, Lei C. Study on the myocardiac injury in patients with severe acute respiratory syndrome. Zhonghua nei ke za zhi. 2003; 42(7):458–60.