Annals of Medicine and Surgery 67 (2021) 102519

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Experimental Research

Alkaline phosphatase and score of HRCT as indicators for predicting the severity of COVID-19

Ali Sharifpour [a,b], Sepideh Safanavaei [a,b], Rabeeh Tabaripour [a], Fatemeh Taghizadeh [c,**], Maryam Nakhaei [a], Atikeh Abadi [a], Mahdi Fakhar [a,***], Elham Sadat Banimostafavi [a,d,*], Eisa Nazar [e], Masoud Aliyali [a,b], Siavash Abedi [a,b], Hossein Mehravaran [a,b], Zakaria Zakariaei [a,f], Hossein Azadeh [a,g]

[a] Toxoplasmosis Research Center, Communicable Diseases Institute, Iranian National Registry Center for Lophomoniasis (INRCL), Mazandaran University of Medical Sciences, Sari, Iran
[b] Pulmonary and Critical Care Division, Imam Khomeini Hospital, Iranian National Registry Center for Lophomoniasis (INRCL), Mazandaran University of Medical Sciences, Sari, Iran
[c] Student Researches Committee, Psychiatry and Behavioral Sciences Centre, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran
[d] Department of Radiology, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran
[e] Student Research Committee, Department of Epidemiology and Biostatistics, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran
[f] Toxicology and Forensic Medicine Division, Orthopedic Research Center, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran
[g] Department of Internal Medicine, Orthopedic Research Center, Mazandaran University of Medical Sciences, Sari, Iran

ARTICLE INFO

Keywords:
COVID-19
Clinical symptoms
Blood laboratory data
HRCT

ABSTRACT

Background: The clinical symptoms, blood laboratory data, O2 saturation and high-resolution computed tomography (HRCT) findings are critical factors in diagnosis of COVID-19 infection.

Methods: In this study, 105 hospitalized patients suspected of having COVID-19 were evaluated. Finally, the laboratory and HRCT and related factors data of 83 confirmed cases by HRCT and RT-PCR were analyzed. To compare the median of quantitative variables in the two groups, the Mann-Whitney *U* test was used. Also, to determine the factors associated with the positiveness of the HRCT result, a univariate logistic model was fitted. Moreover, receiver operating characteristic (ROC) curves were constructed to test the ability of the final model to predict the positiveness of HRCT result.

Results: 61.40% of the patients had a comorbidity disease. 89.20% had fever, 92.00% cough, 91.40% dyspnea. Abnormal CRP was seen in 77.80% of the patients, followed by 66.70% lymphopenia, and 60.30% neutrophilia. Also, ALP (abnormal vs. normal) and score of HRCT assessment variables had a significant effect on the positiveness of HRCT findings. 87.95% had abnormal HRCT with 41% bilateral multi lobar patchy ground glass opacity (GGO). Moreover, there was a statistically significant association between the level of O2 saturation and HRCT results.

Conclusion: Our findings showed that male patients with middle age and comorbidity disease were more susceptible to the COVID-19 infection. Additionally, clinical features, blood laboratory findings, O2 saturation and HRCT findings are critical factors in the prognosis of COVID-19 infection.

* Corresponding author. Toxoplasmosis Research Center, Communicable Diseases Institute, Iranian National Registry Center for Lophomoniasis (INRCL), Mazandaran University of Medical Sciences, Sari, Iran.
** Corresponding author.
*** Corresponding author.
E-mail addresses: asharifpour0209@yahoo.com (A. Sharifpour), sepidehjana@gmail.com (S. Safanavaei), r.tabaripour69@gmail.com (R. Tabaripour), Fatemehtaghizadeh93@gmail.com (F. Taghizadeh), maryamnakhaei1396@gmail.com (M. Nakhaei), atikeh.abadi1992@gmail.com (A. Abadi), mahdifakhar53@gmail.com (M. Fakhar), razavi109@yahoo.com (E.S. Banimostafavi), Nazari951@mums.ac.ir (E. Nazar), Masoud-aliyali@yahoo.com (M. Aliyali), Siavash.abedi0@gmail.com (S. Abedi), lab2002b@yahoo.com (H. Mehravaran), ali.zakariaei@yahoo.com (Z. Zakariaei), Hosein.Azade@gmail.com (H. Azadeh).

https://doi.org/10.1016/j.amsu.2021.102519
Received 17 May 2021; Received in revised form 18 June 2021; Accepted 18 June 2021
Available online 24 June 2021

1. Background

Abbreviations

HRCT	high-resolution computed tomography
GGO	ground glass opacity
CRP	Abnormal C-reactive protein
LDH	lactate dehydrogenase
ESR	erythrocyte sedimentation rate
SGOT	serum glutamic-oxaloacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
PMH	past medical history

A current outbreak of pneumonia related to a novel coronavirus, termed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was reported in Wuhan, Hubei province, China in December 2019. The infection spread across other countries around the world [1]. The World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern on January 30, 2020 [2]. Symptoms of COVID-19 can be fever, dry cough, fatigue, shortness of breath, myalgia or even no symptoms [3–7]. Likewise, the studies revealed that older age, male gender, leukocytosis, and blood laboratory findings, also, comorbidities such as high lactate dehydrogenase level, cardiac injury, hypertension, diabetes mellitus, hypothyroidism, coronary artery disease, smoking and hyperglycemia, were related to weak prognosis in COVID-19 patients [8–10]. However, information concerning the clinical features of COVID-19 is still making it difficult for physicians to distinguish the causative agents without related laboratory analysis [11–13]. Furthermore, reverse transcription-polymerase chain reaction (RT-PCR), the gold standard for confirming diagnosis of COVID-19, has some restrictions, such as false negative results and limited sampling method and the rate of high false negative and unavailability of in the early stage of the outbreak restricted fast diagnosis of infection in patients [14]. The high resolution computed tomography (HRCT) of the chest is progressively recognized as a strong indicator for early diagnosis, and can be the key to the evaluation of COVID-19 suspected patients because the changes in chest imaging sometimes may be earlier than symptoms [15]. HRCT is strongly recommended because it is very sensitive to detecting early disease, assessing the nature and extent of lesions [16]. Other investigators examined chest HRCTs in infected patients and found high rates of ground-glass opacities and consolidation, sometimes with a rounded morphology and peripheral lung distribution [17,18]. Chest HRCT can identify the early phase lung infection [19] and prompt larger public health surveillance and response systems [20]. Currently, chest HRCT has been recommended as main evidence for confirmed clinical and laboratory diagnosis. Considering the previous studies, the purpose of the study is to make an early diagnosis, by describing the complete chest HRCT appearances, related laboratory analysis and clinical features of patients with COVID-19, who were hospitalized at the Imam Khomeini Hospital.

2. Methods

In this cross-sectional study, 105 patients suspected of having COVID-19 hospitalized in Imam Khomeini Hospital, during February 2020, were enrolled. Finally, the data of 83 confirmed cases by HRCT was analyzed. Demographic, clinical, HRCT features and laboratory data of the patients were extracted and analyzed. All HRCT images were blindly reviewed by two radiologists with clinical evidence experience. The severity of lung involvement was scored and classified into 3 categories (category 0: negative findings, category 1: less than 50% of the lung involvement, and category 2: up to 50%) of the lung involvement. The current study was reviewed and approved by the Research Ethical Committee (IR.MAZUMS. REC.1399.102). The work has been reported in line with the STROCSS criteria [21]. This study is registered with the Research Registry, and the UIN is researchregistry6824 (https://www.researchregistry.com/browse-the-registry#home/registrationdetails/60a18e6c9b22fb001bde9e86/).

2.1. Statistical analysis

Quantitative variables as mean ± SD and qualitative variables also were reported as frequency (%). Chi-square and Fisher's exact tests were used for categorical variable comparison. In addition, to compare the median of quantitative variables in the two groups, the Mann-Whitney *U* test was used. Then, first to determine the factors associated with the positiveness of the HRCT result, a univariate logistic model was fitted, and those variables which had $P < 0.25$ were entered into the multiple model. Receiver operating characteristic (ROC) curves were constructed to test the ability of the final model to predict the positiveness of HRCT result. All analysis was carried out in the SPSS version 20.0 and STATA Release version 12. $P < 0.05$ was considered statistically significant.

3. Results

The mean age of the patients was 58.12 ± 17.19, and 46 (55.40%) were males. There was not a statistically significant difference between the mean age of men and women ($p > 0.05$). 33 (89.20%) of the patients had fever, 46 (92.00%) cough, and 53 (91.40%) had dyspnea. In addition, 6 (7.23%) had a cold, and 9 (10.84%) had myalgia (Table 1). As well, analysis of the laboratory results showed that abnormal WBC was seen in 34 (42.00%) of the patients, 54 (66.70%) lymphopenia, 47 (60.30%) neutrophilia, 56 (77.80%) abnormal C-reactive protein (CRP), 18 (22.00%) abnormal platelet count test (PLT), 40 (66.70%) abnormal lactate dehydrogenase (LDH), and 53 (80.30%) had abnormal erythrocyte sedimentation rate (ESR). Moreover, the mean of O2 saturation was 93.89 ± 4.77, while, 37 (44.60%) of them had insufficient O2 saturation. Furthermore, 32 (54.20%) of cases had abnormal serum glutamic-oxaloacetic transaminase (SGOT), and 22 (37.30%) of cases had abnormal serum glutamic-pyruvic transaminase (SGPT), and 27 (46.60%) of them had abnormal Alkaline phosphatase (ALP) (Table 2, Table 3). Analysis of the HRCT results showed that 73 (87.95%) had abnormal HRCT as follows: bilateral multilobar patchy ground glass opacities (GGO) 16 (19.30%), bilateral multilobar patchy ground glass opacities and bilateral alveolar consolidations 18 (21.70%), Pleural effusion 7 (8.40%), bilateral alveolar consolidations 6 (7.20%), unilateral/single lobar ground glass opacities 2 (2.40%), unilateral/single lobar alveolar consolidation 2 (2.40%), centrilobular nodules/tree in bud opacities 1 (1.20%), other mixed disease 13 (15.60%) and any other findings 3 (3.60%).

Furthermore, 22 (42.30%) of women and 30 (57.70%) of men tested positive for HRCT, with no statistically significant association between gender and HRCT result based on chi-square test results ($p > 0.05$). The mean age of the patients with negative and positive HRCT was 58.1318.26 and 58.1216.70. The Mann-Whitney test showed that there was not a statistically significant difference between the median age in the two groups of HRCT results ($p > 0.05$). So that, 16 (30.80%) patients were under 50% lung involvement and 36 (69.20%) were over 50% lung involvement (Table 1). Distribution dotplot of HRCT assessment of patients based on the HRCT result presented in Fig. 1. The mean W.B.C of the patients with negative and positive HRCT was 16.9034.70 and 10.9620.36. The Mann-Whitney test showed that there was a statistically significant difference between the median of W.B.C in the two groups of HRCT results ($p < 0.05$) (Table 2). The mean O2 saturation of the patients with negative and positive HRCT tests was 95.034.49 and 93.214.85, respectively. Based on the results from Mann-Whitney, there was a statistically significant difference between the median of O2

Table 1
Comparison of the frequency distribution of demographical, clinical, and radiographical characteristics of patients with suspected COVID-19 based on the HRCT result (n = 83).

Characteristics	Total	HRCT		P
		Negative	Positive	
Gender				
Female	37 (44.60)	15 (48.40)	22 (42.30)	0.59
Male	46 (55.40)	16 (51.60)	30 (57.70)	
Age				
Mean ± SD	58.12 ± 17.19	58.13 ± 18.26	58.12 ± 16.70	0.73
≤ 50 y	25 (30.10)	9 (29.00)	16 (30.80)	0.86
> 50 y	58 (69.90)	22 (71.00)	36 (69.20)	
Fever				
No	4 (10.80)	1 (12.50)	3 (10.30)	0.99
Yes	33 (89.20)	7 (87.50)	26 (89.70)	
Cough				
No	4 (8.00)	1 (8.30)	3 (7.90)	0.99
Yes	46 (92.00)	11 (91.70)	35 (92.10)	
Dyspnea				
No	5 (8.60)	1 (5.30)	4 (10.30)	0.99
Yes	53 (91.40)	18 (94.70)	35 (89.70)	
PMH[a]				
No	32 (38.60)	10 (32.30)	22 (42.30)	0.46
DM[b]/HTN[c]/ Asthma	14 (16.90)	6 (19.40)	8 (15.40)	
Other disease	20 (24.10)	10 (32.30)	10 (19.20)	
Mix	17 (20.50)	5 (16.10)	12 (23.10)	
HRCT[d] Finding				
No pathologic finding	10 (12.00)	9 (29.00)	1 (1.90)	<0.001*
One disease	37 (44.60)	14 (45.20)	23 (44.20)	
Mix	36 (43.40)	8 (25.80)	28 (53.80)	
HRCT Assessment (%)				
Negative	12 (14.50)	12 (38.70)	0 (0.00)	<0.001*
Normal	7 (8.40)	7 (22.60)	0 (0.00)	
≤ 50	23 (27.70)	10 (32.30)	13 (25.00)	
> 50	41 (49.40)	2 (6.50)	39 (75.00)	

*Significant at level of 0.05, Values are reported as frequency (percent) and mean ±*sd*

[a] Past medical history
[b] Diabetes Melitus
[c] Hypertension
[d] High-resolution computed tomography.

saturation in the two groups of HRCT results ($p < 0.05$). Out of a total of 52 positive cases, 23 (44.20%) positive cases at the level of normal oxygen and 29 (55.80%) positive cases occurred at the level of abnormal oxygen. Based on the results from the chi-square test, there was a statistically significant association between the level of O2 saturation and HRCT results ($p < 0.05$). The mean ALP of the patients with negative and positive HRCT tests was 544.67516.51 and 313.84227.36, respectively. Results from the Mann-Whitney test showed that there was not a statistically significant difference between the median of ALP in the two groups of HRCT results ($p > 0.05$). In patients with normal ALP, 24 (64.90%) of the cases had a positive HRCT and in abnormal ALP patients, 13 (35.10%) of cases had a positive HRCT, which there was a statistically significant association between the level of ALP and HRCT result based on the results from the chi-square test ($p < 0.05$) (Table 3). Frequency distribution of past medical history (PMH) among patients with suspected COVID-19 under study presented in Table 4, in which 51 (61.40%) of patients had PMH.

Multiple logistic regression showed that ALP (abnormal vs. normal) and score of HRCT assessment variables had a significant effect on the positiveness of HRCT result ($P < 0.05$). So, after controlling for other variables, the odds of a positive HRCT result with abnormal ALP were 0.04 times higher than those with normal ALP, and this difference is statistically significant (P 0.05). Furthermore, after controlling for the effects of other variables, each unit increase in the HRCT assessment

Table 2
Comparison of the frequency distribution of laboratory experiments of patients with suspected of COVID-19 based on the HRCT result (n = 83).

Characteristics	Total	HRCT		P
		Negative	Positive	
W.B.C (10^3)				
Mean ± SD	13.16 ± 26.53	16.90 ± 34.70	10.96 ± 20.36	0.01*
Normal	47 (58.00)	17 (56.70)	30 (58.80)	0.84
Abnormal	34 (42.00)	13 (43.30)	21 (41.20)	
Lymph (%)				
Mean ± SD	20.47 ± 14.70	18.77 ± 15.04	21.52 ± 14.53	0.29
Normal	27 (33.30)	8 (25.80)	19 (38.00)	0.25
Abnormal	54 (66.70)	23 (74.20)	31 (62.00)	
Neut (%)				
Mean ± SD	71.28 ± 16.71	72.55 ± 17.21	70.45 ± 16.51	0.41
Normal	31 (39.70)	10 (32.30)	21 (44.70)	0.27
Abnormal	47 (60.30)	21 (67.70)	26 (55.30)	
CRP				
Mean ± SD	57.26 ± 61.14	64.88 ± 59.77	52.96 ± 62.14	0.28
Normal	16 (22.20)	6 (23.10)	10 (21.70)	0.89
Abnormal	56 (77.80)	20 (76.90)	36 (78.30)	
PLT (10^3)				
Mean ± SD	236.82 ± 118.59	254.06 ± 136.00	226.33 ± 106.71	0.35
Normal	64 (78.00)	23 (74.20)	41 (80.40)	0.51
Abnormal	18 (22.00)	8 (25.80)	10 (19.60)	
LDH				
Mean ± SD	599.72 ± 577.10	710.45 ± 968.74	544.35 ± 192.89	0.49
Normal	20 (33.30)	9 (45)	11 (27.50)	0.17
Abnormal	40 (66.70)	11 (55)	29 (72.50)	
ESR				
Mean ± SD	49.36 ± 25.50	49.05 ± 30.18	49.51 ± 23.37	0.62
Normal	13 (19.70)	5 (23.80)	8 (17.80)	0.56
Abnormal	53 (80.30)	16 (76.20)	37 (82.20)	

*Significant at level of 0.05, Values are reported as frequency (percent) and mean±*sd*, Normal range for W.B.C: 4.50–11, Normal range for Lymph: 20–50, Normal range for Neut: 37–72, Normal range for CRP: ≤ 10, Normal range for PLT: 130–400, Normal range for LDH: 23–400, Normal range for ESR: (*Female* & Age≤ 50 : ≤ 20, *Female* & Age> 50 : ≤ 30, *Male* & Age≤ 50 : ≤ 15, *Male* & Age> 50 : ≤ 20).

Table 3
Comparison of the frequency distribution of O2 saturation and other Laboratory experiments of patients with suspected COVID-19 based on the HRCT result (n = 83).

Characteristics	Total	HRCT		P
		Negative	Positive	
O2 SAT (%)				
Mean ± SD	93.89 ± 4.77	95.03 ± 4.49	93.21 ± 4.85	0.02*
Normal	46 (55.40)	23 (74.20)	23 (44.20)	0.008*
Abnormal	37 (44.60)	8 (25.80)	29 (55.80)	
SGOT				
Mean ± SD	61.12 ± 54.71	63.71 ± 72.98	59.68 ± 42.51	0.35
Normal	27 (45.80)	12 (57.10)	15 (39.50)	0.19
Abnormal	32 (54.20)	9 (42.90)	23 (60.50)	
SGPT				
Mean ± SD	44.92 ± 42.62	41.38 ± 39.58	46.87 ± 44.60	0.43
Normal	37 (62.70)	13 (61.90)	24 (63.20)	0.92
Abnormal	22 (37.30)	8 (38.10)	14 (36.80)	
ALP				
Mean ± SD	397.41 ± 372.53	544.67 ± 516.51	313.84 ± 227.36	0.07
Normal	31 (53.40)	7 (33.30)	24 (64.90)	0.02*
Abnormal	27 (46.60)	14 (66.70)	13 (35.10)	

*significant at level of 0.05, Values are reported as frequency (percent) and mean±*sd*, Normal range for O2 saturation: 95–99, Normal range for SGOT: 2–38, Normal range for SGPT: 2–38, Normal range for PLT: 130–400, Normal range for ALP: 80–306.

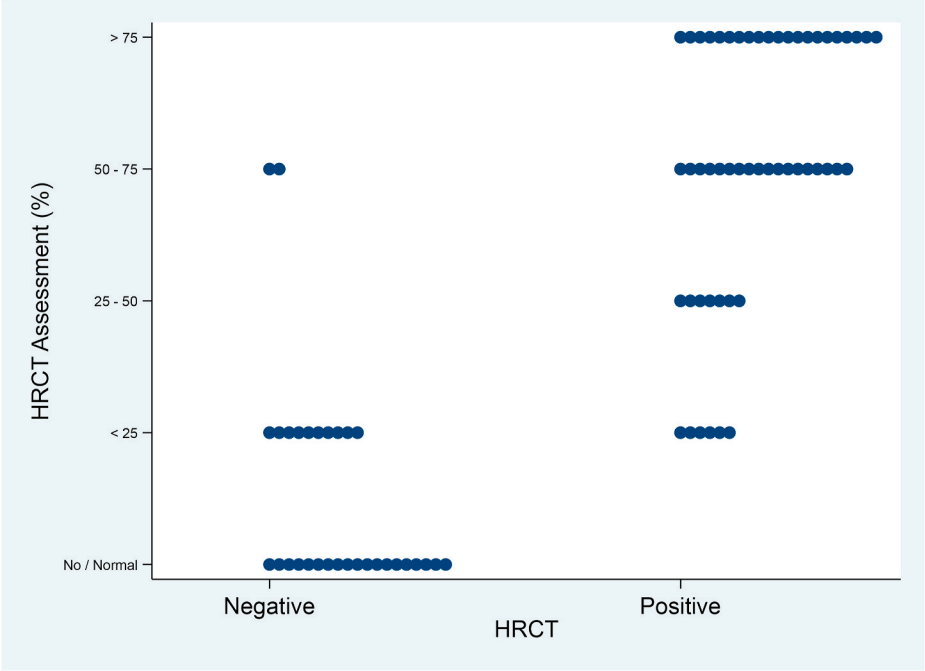

Fig. 1. Distribution plot of HRCT assessment based on the HRCT results.

Table 4
Frequency distribution of PMH among patients with suspected of COVID-19 under study (n = 83).

PMH	N (%)
No	32 (38.60)
DM/HTN/Asthma	14 (16.90)
CKD	4 (4.80)
HTN and DM	8 (9.60)
Cancer	7 (8.40)
DM with other disease	4 (4.80)
DM with other disease	1 (1.20)
CKD with other disease	2 (2.40)
Other disease[a]	11 (13.30)
Total	83 (100)

[a] Other disease including: Anemia, R.A, HepB, Minor Thalassemia, DI, Thyroid, Alergy, DLP, Liver cirrhosis.

score increased the patients' odds of having a positive HRCT result 5.17 times more than those who did not have an increase (P 0.05). But other variables had no significant effect on the positiveness of the HRCT result (P > 0.05) (Table 5). The area under the ROC curve of the model was 0.96, which indicates the good predictive power of the model (Fig. 2).

Table 5
The adjusted odds ratios of risk factors for the positiveness of HRCT result based on multiple logistic regression models.

Characteristics (Reference)	Odds Ratio (%95 CI)	P
Score of HRCT assessment[a]	5.17 (1.71,15.60)	0.004
ALP (normal) abnormal	0.04 (0.003,0.83)	0.03
SGOT (normal) abnormal	1.67 (0.11,25.39)	0.70
LDH (normal) abnormal	1.19 (0.07,19.03)	0.90
O2 (normal) abnormal	2.00 (0.12,31.32)	0.62
HRCT Finding (no pathologic) at least one disease	8.41 (0.005,15509.16)	0.57

[a] Score HRCT assessment: 0 = no/normal, 1= < 25%, 2 = 25%–50%, 3 = 50%–75%, 4= > 75%.

4. Discussion

COVID-19 infection was seen typically in middle-aged, male gender and elderly patients, and patients with other diseases were more susceptible to the disease. A greater number of men was found than that of women, which was similar to previous studies [22,23]. Women have a humoral immune response and a stronger innate immune response than men, making them less susceptible to many parasitic, fungal, bacterial, and viral diseases while being more susceptible to developing malignancies or autoimmune disease [24]. While these sex differences in rates of mortality may be due to sex-specific life styles (smoking, alcohol etc.) [9,25,26]. Cough, fever, and dyspnea were the main symptoms. Abnormal lymphocyte, neutrophil, PLT, SGOT, and SGPT, increased CRP concentration and increased LDH concentration were the laboratory features of COVID-19 infection in the present study. According to other researchers [8] abnormal HRCT was seen in 88% of the patients as the main indicator to evaluate the COVID-19 disease severity. Furthermore, WBC count, O2 saturation, and ALT were associated with lung involvement significantly, statically.

4.1. Other studies in clinical and laboratory findings

According to a meta-analysis, the main clinical manifestations of COVID-19 were fever, cough, and dyspnea [22]. In a study with 208 patients, the median age was 50.5 years, 51.4% of them were men and 48.6% were women. 7.7% of the patients had pulmonary diseases, 19.7% hypertension, and 6.3% diabetes. In our study, 26.5% of the patients had diabetes, hypertension and Asthma. Among all symptoms, 70.2% and 55.3% belonged to fever and cough respectively. In compatible cases, 20.2% had a lower white blood cell count and 29.3% had a lower lymphocyte count.74% of them had elevated CRP, and 11.1% had elevated LDH in the present study [8]. In a retrospective cohort study, the mean age of the patients was 59.5 years and 67% of patients were male [27]. In a study, of 138 hospitalized patients, the median age was 56 years and 54.3% were men. Common symptoms included fever 98.6%, and dry cough 59.4%. Lymphopenia occurred in 70.3% of patients. HRCT showed bilateral patchy shadows or ground glass opacity in the lungs of all patients [28]. In a meta-analysis study,

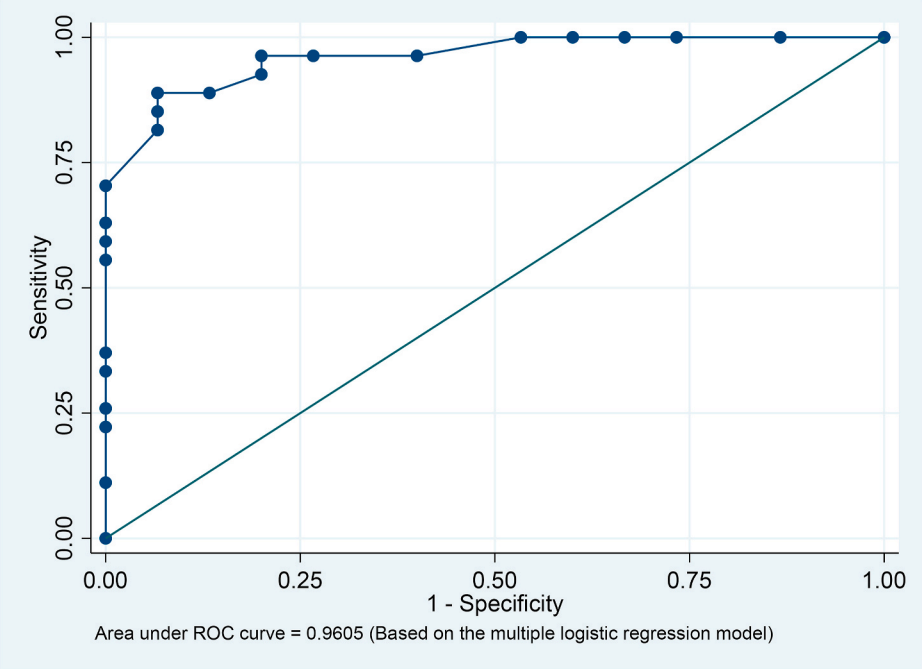

Fig. 2. The receiver operating characteristic curve for score of HRCT assessment, ALP, SGOT, LDH, HRCT Finding and O2 Saturation to predict the HRCT results.

including a total of 50,404 patients with 2019-nCoV infection, the incidence of fever was 90.9%, and cough was 70.8%. Moreover, the incidence of abnormal chest CT was 95.6% [23], abnormal HRCT in our study was 88%. In a study in Beijing of 262 patients, the median age of patients was 47.5 and 48.5% of them were men. The most common symptoms at the onset of illness were fever (82.1%), cough (45.8%), dyspnea (6.9%) [29], compatible with our study. In the other study [30] of 140 hospitalized COVID-19 cases, a 1:1 ratio of men and women COVID-19 patients was found (50.7%), with a median age of 57.0. Fever (91.7%), cough (75.0%) were the most common clinical manifestations, whereas hypertension (30.0%) and diabetes mellitus (12.1%) were the most common comorbidities [30]. Bilateral patchy opacity or ground glass (89.6%) was the most common radiological finding. Lymphopenia (75.4%) and eosinopenia (52.9%) were seen in most cases. Eosinopenia with lymphopenia may be an indicator for diagnosis. Allergic diseases, asthma, and COPD are not risk factors for SARS-CoV-2 infection [30]. The most common comorbidities in our study were hypertension, diabetes mellitus and asthma. Also, bilateral multilobar patchy ground glass opacities, bilateral multilobar patchy ground glass opacities and bilateral alveolar consolidations were the most common radiological findings in the present study. Another study showed that of 1099 patients, the median age of the patients was 47 years; 41.9% of the patients were female. The common symptoms were fever and cough. Ground-glass opacity was the most common radiologic finding on chest CT (56.4%). 83.2% of the patients had lymphocytopenia. Patients often presented without fever, and many did not have abnormal radiologic findings [31]. Ground-glass opacity in the present study was the most common finding. Similar to our study, lymphocytopenia in COVID-19 patients was seen in the other studies [3,32]. The most common manifestations in a metha analysis of 656 patients were fever (88.7%), cough (57.6%), and dyspnea (45.6%) [33]. Of 99 patients with 2019-nCoV pneumonia, the average age of the patients was 55·5 years, including 67 men and 32 women. 83% of the patients had fever, 82% cough, 31% shortness of breath, and 11% myalgia. According to imaging findings, 75% of patients showed bilateral pneumonia, 14% of patients showed multiple mottling and ground-glass opacity, and 1% of patients had pneumothorax [34]. Of the 10 cases, the average age was 56.5 years. 60% of the patients were males. A dry cough was the main symptom, followed by fever and fatigue. Chest computed tomography results were nonspecific, mainly with ground-glass attenuation and/or shadow images [35]. A study found that 72% of people had a fever, and 83% had a cough.33% of them had an abnormal chest radiograph finding or lung crepitation. Lymphopenia was present in 39% [36]. A total of 5700 patients were included with a median age of 63 years, and 39.7% were female. The most common comorbidities were hypertension 56.6%, and diabetes 33.8% [37]. During the course of a study, 21 COVID-19 positive patients were admitted to S.M.S Hospital, Jaipur. 66.66% of the patients were men and 80.90% were less than 60 years old. Almost 33.33% of patients were asymptomatic and of those who were symptomatic, cough was seen in 85.71%, followed by myalgia (64.28%), fever (78.57%), and dyspnea (28.57%). 14.28% of the cases had co morbidities in the form of diabetes mellitus, hypertension, hypothyroidism, or coronary artery disease. Moreover, 52.38% of the patients had lymphopenia [38]. These patterns in comorbidities and lymphopenia were seen in our study, too.

4.2. *Other studies in HRCT findings*

Chest CT is an important component in the diagnostic procedure for patients with suspected COVID-19 infection. Chest CT has limited sensitivity and negative predictive value early after symptom onset, and has little weakness in diagnosis of COVID-19 combined with personal history, clinical symptoms, and initial laboratory findings, and may therefore serve as a standard method for diagnosis of COVID-19 based on its features and transformation rule, the limited number of RT-PCR kits in some centers before initial RT-PCR screening [34,39]. Although 12% of patients were without abnormal lung changes on initial CT images in the present study.

In a study, the most HRCT findings were bilateral parenchymal ground-glass opacities, without or with consolidation in the lung periphery. In particular, 75% of patients with chest HRCT findings related to COVID-19 pneumonia had negative results of concurrent nucleic acid tests [40]. Then, 21.70% of positive chest HRCT patients in the present study had normal CRP. According to imaging examination in a study, 75% of patients showed bilateral pneumonia, 14% of patients showed multiple mottling and ground-glass opacity, and 1% of patients had pneumothorax [34].

In a study, the CRP, ESR, and LDH presented a significantly positive correlation with the pneumonia severity on CT. The highest temperature and the severity of opacifications assessed on initial CT were significantly related to the progression of opacifications on follow-up CT [41]. In the present study, LDH had a significantly positive correlation with HRCT. In a study, GGO was the most common manifestation of COVID-19 pneumonia, which could be followed by consolidation and fibrosis. The Total CT score, GGO score and fibrosis score of male patients were significantly higher than females in the second week. Male patients had higher consolidation scores and fibrosis scores than females in the third week. The total CT score and GGO score had a weak to moderate correlation with arterial blood gas indices [5]. In our study, 42.30% of women and 57.70% of men had positive HRCT for COVID-19. In a meta-analysis of 40 studies with 4183 COVID-19 patients, the rate of positive CT scan in COVID-19 patients was 94.5%. Bilateral lung involvement, GGO pulse consolidation or reticular, consolidation, reticular, presence of nodule findings and GGO, in CT scan of COVID-19 pneumonia patients were respectively estimated to be 64.9%, 49.2%, 30.3%, 17.0%,16.6%, 94.5%. The lung lesions distribution in patients with COVID-19 was 70.0% peripheral, 3.9% central, and 31.1% peripheral and central [42]. In a study, of 1014 patients, 59% had positive RT-PCR results, and 88% had positive chest CT scans. The sensitivity of chest CT in suggesting COVID-19 based on positive RT-PCR results was 97%. In patients with negative RT-PCR results, 75% had positive chest CT findings; 48% were categorized as highly likely cases, with 33% as probable cases. 60%–93% of cases had positive CT consistent with COVID-19 prior to the initial positive RT-PCR results [43].

A total of 14 articles, including 1115 patients, pure GGO 69%, consolidation 47% and "air bronchogram sign" 46% were more common than the atypical lesion of "crazy-paving pattern" 15%. While 67% of patients showed a predominant peripheral distribution [4]. In a study, 52% of the participants were men, with a mean age of 495 years. The major pattern of abnormality observed was bilateral 79%, peripheral 54%, and GGO 65%. A weak relevance was between the fibrosis score and the value of PaO2 and SpO2 [44]. There was a statistically significant association between the level of O2 saturation and HRCT results in the present study. In a study, with a median age of 45, 98% of patients had evidence of abnormal CT compatible with viral pneumonia at baseline [14].

It suggested the critical importance of combining the two methods in the early stage of the disease to exclude the SARS-CoV-2 infection. These CT performances of COVID-19 were similar to previous studies. Patients' O2 saturation decreased, which corresponded to changes in indices in patients with lung involvement. Bilateral GGO was higher in the present study. Our results support the use of chest CT for screening for COVD-19 for patients with clinical and laboratory features compatible with COVID-19 infection [27]. Additionally, a positive relevance was found between the HRCT score and O2 saturation. That was, a patient with a higher CT score tended to have lower O2 saturation.

5. Conclusion

In the present study, middle-aged, male gender and elderly patients, and patients with comorbidity were more susceptible to the COVID-19 infection. W.B.C count, O2 saturation, and ALP were related to lung involvement significantly. Cough, fever, and dyspnea were the main symptoms. Abnormal HRCT was a main indicator for evaluating the COVID-19 disease. As a whole, clinical features, blood laboratory findings, O2 saturation and HRCT findings are critical factors in the prognosis of COVID-19 infection. There were several limitations in this study. First, none of the patients underwent a lung biopsy or autopsy, because of the comparatively better outcomes of the patients in this study. Therefore, the HRCT findings of the lung could not be verified by histopathology. Finally, this was a study with initial HRCT images during hospitalization, mainly demonstrated the early pulmonary lesions in patients with COVID-19. Further longitudinal research was needed to focus on the long-term follow-up, to provide dynamic HRCT evaluation for pulmonary lesions and to obtain the data of long-term pulmonary function changes.

Availability of data and material

The raw data belonged to the present study cannot be made publicly available, because the disclosure of personal data was not included in the research protocol of the present study.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Conflicts of interest

None.

Acknowledgements

The authors would like to thank the patients and Nurses for their kind assistance in achieving data. This study was supported by Mazandaran University of Medical Sciences, Iran.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102519.

Funding

This study was financially supported (in Data collection) by the Vice chancellor of Research and Technology (Mazandaran University of Medical Sciences) (Grant no: 7536).

Ethical approval

The study was approved by our local ethics committee.

Consent

The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. Committee of Mazandaran University of Medical sciences, Approval No. IR.MAZUMS.REC.1399.102. written informed consent was obtained from all participants.

Author contribution

AS, ESB and SS contributed conception and design of the study; EN contributed analysis and interpretation of the data; FT wrote the first draft of the manuscript; MF, ESB, MA, SA, HM,ZZ, HA wrote sections of the manuscript. RT, MN and AA extracted data from the patient's sheets. All authors contributed to critical manuscript revision, read and approved the submitted version.

Registration of research studies

6824.

Guarantor

Elham Sadat Banimostafavi.

References

[1] N. Zhu, D. Zhang, W. Wang, X. Li, B. Yang, J. Song, X. Zhao, B. Huang, W. Shi, R. Lu, I. China Novel Coronavirus, T. Research, A novel coronavirus from patients with pneumonia in China, 2019, N. Engl. J. Med. 382 (8) (2020) 727–733.

[2] C. Sohrabi, Z. Alsafi, N. O'Neill, M. Khan, A. Kerwan, A. Al-Jabir, C. Iosifidis, R. Agha, World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19), Int. J. Surg. (2020).

[3] K. Diao, P. Han, T. Pang, Y. Li, Z. Yang, HRCT imaging features in representative imported cases of 2019 novel coronavirus pneumonia, Precis. Clin. Med 3 (1) (2020) 9–13.

[4] S. Wan, M. Li, Z. Ye, C. Yang, Q. Cai, S. Duan, B. Song, CT manifestations and clinical characteristics of 1115 patients with coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis, Acad. Radiol. (2020).

[5] Y. Shang, C. Xu, F. Jiang, R. Huang, Y. Li, Y. Zhou, F. Xu, H. Dai, Clinical characteristics and changes of chest CT features in 307 patients with common COVID-19 pneumonia infected SARS-CoV-2: a multicenter study in Jiangsu, China, Int. J. Infect. Dis. (2020).

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

[7] M. Zarghami, F. Taghizadeh, M. Moosazadeh, M. Kheradmand, K. Heydari, Validity of self-reporting depression in the Tabari cohort study population, Neuropsychopharmacol. Rep. 40 (4) (2020) 342–347.

[8] R. Zhang, Z. Wang, X. Chen, P. Chen, D. Djakpo, Y. Lin, Clinical Characteristics of 208 Patients with COVID-19 in a Surrounding City of Wuhan, 2020. China.

[9] M. Zarghami, F. Taghizadeh, A. Sharifpour, A. Alipour, Efficacy of guided self-change for smoking cessation in chronic obstructive pulmonary disease patients: a randomized controlled clinical trial, Tob. Induc. Dis. 17 (December) (2019).

[10] F. Elyasi, F. Taghizadeh, M. Zarghami, M. Moosazadeh, S. Abdollahi Chirani, M. Babakhanian, Cognitive-behavioral therapy and hypnosis intervention on anxiety, depression, and quality of life in patients with breast cancer undergoing chemotherapy: a clinical trial, Middle East J. Canc. (2020).

[11] Z. Wu, J.M. McGoogan, Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention, J. Am. Med. Assoc. 323 (13) (2020) 1239–1242.

[12] F. Taghizadeh, H. Taghizadeh, Naso-pharyngeal discharge: the first symptom of COVID-19 infection: report two cases from Iran, Clin. Case Rep. 8 (12) (2020).

[13] Z. Abdollahi, F. Taghizadeh, M. Zarghami, The epidemiology of phosphine self-poisoning in Sari, Iran 2008–2010, Middle East J. Sci. Res. 14 (9) (2013) 1180–1183.

[14] Y. Fang, H. Zhang, J. Xie, M. Lin, L. Ying, P. Pang, W. Ji, Sensitivity of chest CT for COVID-19: comparison to RT-PCR, Radiology (2020) 200432.

[15] G. Pontone, S. Scafuri, M.E. Mancini, C. Agalbato, M. Guglielmo, A. Baggiano, G. Muscogiuri, L. Fusini, D. Andreini, S. Mushtaq, et al., Role of computed tomography in COVID-19, J. Cardiovasc. Comput. Tomogr. (2020) 30436. S1934-5925(1920.

[16] M. Carotti, F. Salaffi, P. Sarzi-Puttini, A. Agostini, A. Borgheresi, D. Minorati, M. Galli, D. Marotto, A. Giovagnoni, Chest CT features of coronavirus disease 2019 (COVID-19) pneumonia: key points for radiologists, Radiol. Med. 125 (7) (2020) 636–646.

[17] X. Yang, Y. Yu, J. Xu, H. Shu, H. Liu, Y. Wu, L. Zhang, Z. Yu, M. Fang, T. Yu, Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study, Lancet Respir. Med. (2020).

[18] D. Ippolito, C. Maino, A. Pecorelli, P. Allegranza, C. Cangiotti, C. Capodaglio, I. Mariani, T. Giandola, D. Gandola, I. Bianco, et al., Chest X-ray features of SARS-CoV-2 in the emergency department: a multicenter experience from northern Italian hospitals, Respir. Med. 170 (2020) 106036.

[19] J.P. Kanne, Chest CT findings in 2019 novel coronavirus (2019-nCoV) infections from Wuhan, China: key points for the radiologist, in: Radiological Society of North America, 2020.

[20] L. Wu, Q. Jin, J. Chen, J. He, D.M. Brett-Major, J.J. Dong, Diagnostic accuracy of chest computed tomography scans for suspected patients with COVID-19: receiver operating characteristic curve analysis, JMIR Publ. Health Surveill. 6 (4) (2020), e19424.

[21] R. Agha, A. Abdall-Razak, E. Crossley, N. Dowlut, C. Iosifidis, G. Mathew, for the STROCSS Group, The STROCSS 2019 guideline: strengthening the reporting of cohort studies in surgery, Int. J. Surg. 72 (2019) 156–165.

[22] F. Jiang, L. Deng, L. Zhang, Y. Cai, C.W. Cheung, Z. Xia, Review of the clinical characteristics of coronavirus disease 2019 (COVID-19), J. Gen. Intern. Med. 35 (5) (2020) 1545–1549.

[23] B. Li, X. Li, Y. Wang, Y. Han, Y. Wang, C. Wang, G. Zhang, J. Jin, H. Jia, F. Fan, et al., Diagnostic value and key features of computed tomography in Coronavirus Disease 2019, Emerg. Microb. Infect. 9 (1) (2020) 787–793.

[24] H. Schurz, M. Salie, G. Tromp, E.G. Hoal, C.J. Kinnear, M. Möller, The X chromosome and sex-specific effects in infectious disease susceptibility, Hum. Genom. 13 (1) (2019) 2.

[25] D. Wrapp, N. Wang, K.S. Corbett, J.A. Goldsmith, C.L. Hsieh, O. Abiona, B. S. Graham, J.S. McLellan, Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation, Science 367 (2020) 1260–1263.

[26] F. Taghizadeh, J.Y. Cherati, Procrastination and self-efficacy among intravenous drug users on a methadone maintenance program in Sari city, Iran, Iran. J. Psychiatr. Behav, Sci. 9 (4) (2013).

[27] H. Shi, X. Han, N. Jiang, Y. Cao, O. Alwalid, J. Gu, Y. Fan, C. Zheng, Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study, Lancet Infect. Dis. (2020).

[28] D. Wang, B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, B. Wang, H. Xiang, Z. Cheng, Y. Xiong, Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China, JAMA 323 (11) (2020) 1061–1069.

[29] S. Tian, N. Hu, J. Lou, K. Chen, X. Kang, Z. Xiang, H. Chen, D. Wang, N. Liu, D. Liu, Characteristics of COVID-19 infection in beijing, J. Infect. (2020).

[30] J-j Zhang, X. Dong, Y-y Cao, Y-d Yuan, Y-b Yang, Y-q Yan, C.A. Akdis, Y-d Gao, Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China, Allergy (2020).

[31] W-j Guan, Z-y Ni, Y. Hu, W-h Liang, C-q Ou, J-x He, L. Liu, H. Shan, C-l Lei, D. S. Hui, Clinical characteristics of coronavirus disease 2019 in China, N. Engl. J. Med. 382 (18) (2020) 1708–1720.

[32] V. Surveillances, The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020, China CDC Weekly 2 (8) (2020) 113–122.

[33] A.J. Rodriguez-Morales, J.A. Cardona-Ospina, E. Gutiérrez-Ocampo, R. Villamizar-Peña, Y. Holguin-Rivera, J.P. Escalera-Antezana, L.E. Alvarado-Arnez, D.K. Bonilla-Aldana, C. Franco-Paredes, A.F. Henao-Martinez, Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis, Trav. Med. Infect. Dis. (2020) 101623.

[34] N. Chen, M. Zhou, X. Dong, J. Qu, F. Gong, Y. Han, Y. Qiu, J. Wang, Y. Liu, Y. Wei, Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, Lancet 395 (10223) (2020) 507–513.

[35] X-y Xia, J. Wu, H-l Liu, H. Xia, B. Jia, W-x Huang, Epidemiological and initial clinical characteristics of patients with family aggregation of COVID-19, J. Clin. Virol. (2020) 104360.

[36] B.E. Young, S.W.X. Ong, S. Kalimuddin, J.G. Low, S.Y. Tan, J. Loh, O.-T. Ng, K. Marimuthu, L.W. Ang, T.M. Mak, Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore, JAMA 323 (15) (2020) 1488–1494.

[37] S. Richardson, J.S. Hirsch, M. Narasimhan, J.M. Crawford, T. McGinn, K. W. Davidson, D.P. Barnaby, L.B. Becker, J.D. Chelico, S.L. Cohen, Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area, JAMA (2020).

[38] S. Bhandari, A. Bhargava, S. Sharma, P. Keshwani, R. Sharma, S. Banerjee, Clinical profile of covid--19 infected patients admitted in a tertiary care hospital in north India, J. Assoc. Phys. India 68 (2020) 13.

[39] A. Bernheim, X. Mei, M. Huang, Y. Yang, Z.A. Fayad, N. Zhang, K. Diao, B. Lin, X. Zhu, K. Li, Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection, Radiology (2020) 200463.

[40] X. He, J. Zheng, J. Ren, G. Zheng, L. Liu, Chest high-resolution computed tomography imaging findings of coronavirus disease 2019 (Covid-19) pneumonia, Int. J. Radiat. Res. 18 (2) (2020) 343–349.

[41] Y. Xiong, D. Sun, Y. Liu, Y. Fan, L. Zhao, X. Li, W. Zhu, Clinical and high-resolution CT features of the COVID-19 infection: comparison of the initial and follow-up changes, Invest. Radiol. (2020).

[42] M. Karimian, M. Azami, Computed tomography scan findings in patients with COVID-19: a systematic review and meta-analysis, 2020. Available at SSRN 3571539.

[43] T. Ai, Z. Yang, H. Hou, C. Zhan, C. Chen, W. Lv, Q. Tao, Z. Sun, L. Xia, Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases, Radiology (2020) 200642.

[44] H. Dai, X. Zhang, J. Xia, T. Zhang, Y. Shang, R. Huang, R. Liu, D. Wang, M. Li, J. Wu, High-resolution chest CT features and clinical characteristics of patients infected with Covid-19 in Jiangsu, China, Int. J. Infect. Dis. (2020).