Dicle Tıp Dergisi / Dicle Med J (2022) 49 (2) : 287-296

www.diclemedj.org

Original Article / Özgün Araştırma

Risk factors for intensive care unit need in patients with COVID-19: An analysis of 368 cases

Filiz Koc[1], Emine Firat Göktas[1], Pinar Firat[1], Zehra Nur Sesen[1], Aslı Burcu Yikilgan[1], İsmail Demirkale[2], Davut Akduman[3]

1 Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences Keçiören Education and Training Hospital, Ankara, Turkey

2 Department of Orthopedics and Traumatology, University of Health Sciences Keçiören Education and Training Hospital, Ankara, Turkey

3 Department of Ear, Nose, and Throat Diseases, University of Health Sciences Keçiören Education and Training Hospital, Ankara, Turkey

Received: 14.01.2022; Revised: 26.04.2022; Accepted: 28.04.2022

Abstract

Objective: Covid-19 is a global epidemic that predominantly affects the respiratory system, in which about 20% of patients are severe and about 10-15% of mild cases become severe. The clinical and laboratory findings in the course of the disease are mild in the first week and may become more severe in the following days, also the possibility false negativity of the tomography in the first 24-48 hours, making it difficult to select patients in triage. Being able to detect cases that may have a serious course in the Covid-19 pandemic will help health systems to function without interruption. In our study, we tried to identify cases that may need intensive care in triage.

Methods: Medical records and radiological findings of 368 patients with laboratory-confirmed Severe-Acute-Respiratory-Syndrome Coronavirus-2 infection who were hospitalized between March and June 2020 were reviewed. The patients were analyzed by dividing into two groups; group 1; critically ill patients with severe pneumonia who need intensive care during treatment. Approximately 8% of all patients are in this group. Group 2; non-critical patients who do not need intensive care followed in the clinic.

Results: It was determined that the mean age of the patients in Group 1, the rate of being over 50 years old and the male gender ratio were higher than Group 2.

Conclusion: Although there are low oxygen saturation, tachypnea and comorbid diseases in critically ill patients in triage, advanced age and male gender were found to be the most important risk factors for intensive care need.

Key Words: COVID-19, Intensive Care Unit, Risk Factors, Triage

DOI: 10.5798/dicletip.1128905

Correspondence / Yazışma Adresi: *Filiz Koç, University of Health Sciences Keçiören Education and Training Hospital, 06280 Ankara, Turkey e-mail: filizdabak@yahoo.com*

COVID-19 Hastalarında Yoğun Bakım İhtiyacı için Risk Faktörleri: 368 Vaka Analizi

Öz

Amaç: Covid-19, hastaların yaklaşık %20'sinin şiddetli olduğu ve hafif vakaların yaklaşık %10-15'inin şiddetli hale geldiği, ağırlıklı olarak solunum sistemini tutan küresel salgına neden olmuş bir hastalıktır. Hastalığın seyrindeki klinik ve laboratuvar bulguları ilk hafta hafif olup ilerleyen günlerde daha şiddetli hale gelebilir, ayrıca ilk 24-48 saat içinde tomografinin yanlış negatif olabilmesi triyajda hasta seçimini zorlaştırır. Covid-19 pandemisinde ciddi seyir izleyebilecek vakaların tespit edilebilmesi, sağlık sistemlerinin kesintiye uğramadan işlemesine yardımcı olacaktır. Çalışmamızda triyajda yoğun bakım gerektirebilecek olguları tespit etmeye çalıştık.

Yöntemler: Mart-Haziran 2020 tarihleri arasında hastaneye yatırılan RT-PCR ile doğrulanmış Covid-19 enfeksiyonu olan 368 hastanın tıbbi kayıtları ve radyolojik bulguları incelendi. Hastalar iki gruba ayrılarak analiz edildi; grup 1; tedavi sırasında yoğun bakıma ihtiyaç duyan ciddi pnömonisi gelişen kritik hastalar, tüm hastaların yaklaşık %8'i bu gruptadır. Grup 2; yoğun bakıma ihtiyacı olmayan kritik olmayan klinikte takip edilen hastalar.

Bulgular: Triajda Grup 1'deki hastalarda erkek cinsiyet ve yaş ortalamalarının, 50 yaş üstü olma oranı Grup 2'ye göre daha yüksek olduğu belirlendi. Hastaların yaş, cinsiyet dışında vucut kitle endeksi,ek hastalıklar,kullanılan ilaçlar açısından fark tespit edilmedi.

Sonuç: Triyajdaki kritik hastalarda düşük oksijen satürasyonu, takipne ve eşlik eden hastalıklar olmasına rağmen, ileri yaş ve erkek cinsiyet yoğun bakım ihtiyacı için en önemli risk faktörleri olarak bulundu.

Anahtar kelimeler: COVID-19, Yoğun Bakım Ünitesi, Risk Faktörleri, Triyaj.

INTRODUCTION

As a member of the Coronaviridae family, a typical Coronavirus (CoV), which is a beta coronavirus, is an evolution of the Severe Acute Respiratory Syndrome (SARS) virus in 2003 and named as SARS-CoV-2. It is a single-stranded RNA (+ssRNA) virus that is enclosed in nucleocapsid (N) protein, while its outer shell is made up from envelop (E), membrane (M), and spike (S) proteins[1]. The disease that caused by the virus is named as The Coronavirus disease 2019 (COVID-19) and virus can be described as "unique", shows no symptoms in some people, and can be fatal in especially advanced aged patients. It is known that more than one million people have lost their lives to date. However, in addition to supportive treatments or treatments for inflammation and coagulation disorders caused by the virus, it is also important to identify patients at risk who are likely to progress with severe pneumonia since according to Wu and McGoonan, approximately 10-15% of mild cases are likely to develop into a severe disease that may require intensive care[2].

According to the reported basic reproduction number (Ro), the COVID-19 carrier infects an average of 2.2 people, while the incubation period and average series interval are 5.2 days and 7.5 days, respectively[3]. To date, two commercially available diagnostic tests are in use; one is reverse transcription-polymerase chain reaction (RT-PCR) which detects part of the viral genome from swab specimens and the other is an antibody test that detects SARS-CoV-2 specific Ig G and Ig M antibodies in serum. The main objective of these diagnostic tests is to avoid false-negative or false-positive results for molecular or serological tests, respectively. According to Sethuraman et al., more than 8 days should be passed after initial symptoms appear to detect serum antibodies, thus molecular tests have gained priority[4]. Along with other molecular tests including clustered regularly interspaced short palindromic repeats (CRISPR) and loop-mediated isothermal amplification (LAMP) RT-PCR has been accepted as the gold standard so far[5]. However, especially in patients with low viral loads, the false-negativity of RT-PCR may reach up to 16.7%; that's why repeated testing is undertaken for symptomatic patients who had negative RT-PCR tests upon admission[6].

Besides molecular and serological testing, computed tomography (CT) examination is a very important diagnostic step especially in symptomatic but RT-PCR false-negative patients[7,8]. According to Wung et al. reported the

ground glass opacities (GGO) with or without consolidation in posterior and peripheral lungs as a cardinal hallmark of COVID-19 pneumonia observed on CT[9]. Despite all these relatively valuable diagnostic tests and advanced treatment methods, the infection process can be bothersome in some patients. Therefore, this study endeavors to determine the risk factors that may predict a severe course of the disease with particular emphasis on symptoms, laboratory, and CT findings on admission.

METHODS

This single-center, retrospective, observational study was done at the University of Health Sciences affiliated hospital of Keçiören and the study was approved by the institutional review boards and the ethics committee of the hospital with the decision numbered 2012-KAEK-15/ 2129. We reviewed clinical electronic medical records and radiological examinations of 402 patients with laboratory-confirmed SARS-CoV-2 infection who were hospitalized in the period between March and June. The diagnosis of SARS-CoV-2 infection was based on the criteria published by the Republic of Turkey Ministry of Health as the cases who meet the criteria of a probable case definition and have SARS-CoV-2 detected by molecular methods. Laboratory confirmation of SARS-CoV-2 infection was performed by RT-PCR of samples taken from upper nasopharyngeal swabs. RT-PCR assay based on oral swabs was held on General Directorate of Public Health (HSGM) Microbiology Reference Laboratory. We contacted discharged patients, healthcare providers, and/or patients' families to clarify any missing or uncertain records via telephone calls. Patients who were <18 years of age (n=20), pregnant patients (n=4), and patients with missing data (n=10) were excluded from the study.

We evaluated demographic data including age, gender, and BMI as well as exposure history, the time elapsed since the start of the complaints on admission, chronic medical comorbidities, presence of pregnancy, medicines received regularly (angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), statins, fibrates), symptoms and vital signs, laboratory findings, chest CT scan findings on admission and during the hospital stay. The clinical management was reviewed. The length of stay intensive care unit (ICU), the applied respiratory supportive strategies including oxygen therapy, high-flow nasal cannula, and noninvasive ventilation, mechanical ventilation, prone positioning ventilation) and absence/presence of therapeutic plasma exchange application was recorded. Coexisted infections, subsequent organ involvements, complications, living, and discharge status of the patients were analyzed. Outpatient continuum of care management after discharge of the patients recruited in the study was also evaluated. The data were reviewed by two physicians for each patient to ensure objectivity. The primary outcome measures were the composite of all-cause mortality.

High-resolution transverse CT images were obtained from xxxx (GE Medical System, Milwaukee, USA). Tube voltage 100 or120 kV, and automatic tube current modulation was100-400 mA. All images are rebuilt with a slice thickness of 1.0mm or 1.25mm and reviewed by two radiologists (xy and yz) who were blind to the final result of patients. Prediction of the extent of lung opacification by region was scored by the system of Chung Y-C[10]. Each of the five lung lobes were visually scored from 0 to 5: 0, when no involvement; 1, <5% involvement; 2, 5 to 25% involvement; 3, 26 to 49% involvement; 4, 50 to 75% involvement and finally 5 when > 75% involvement. The total severity score was the sum of each lobe point, changing from 0 (no involvement) to 25 (maximum involvement).

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS v.22 software at a confidence interval (CI) of 95%. Qualitative data were stated as frequency distribution and quantitative data were stated as mean, minimum, and maximum values. Continuous variables were evaluated using Mann Whitney U-test. Patients

were classified according to ICU need as Group 1 (needed) and Group 2 (not needed). In these patients, the relationship between each outcome measure and ICU need was evaluated by using univariate analysis. Multivariate analysis was used to assess factors independently associated with ICU need. Only factors (p <0.100) that show some correlation with ICU need were included in this second phase of the analysis. In the final model, a backward selection procedure was used to remove non-meaningful variables sequentially until only significant variables remained. Proportional hazards were controlled for significant individual variables and the multivariate model. Also, patients with confirmed clinical pneumonia were classified as severe when having a respiratory rate of 30 breaths per minute or greater and a finger oxygen saturation of 90% or less or mild when having respiratory symptoms with fever and CT manifestations of pneumonia. Categorical variables were compared using the X2 test between clinical pneumonia and CT findings. A value of p< 0.05 was considered statistically significant.

RESULTS

There were 368 patients and the mean age of them was 47.2 ± 11.66 years (range, 18-91) and 188 were male and 180 were female. The overall mortality rate was 9 (2.5%). Group 1 composed of 29 patients (7.9%) and 339 patients (Group 2) were hospitalized for COVID-19.

The detailed information of demographic variables is shown in Table 1 whereas history and physical examination findings are shown in Table 2. There were 147 (40%) patients with an age of >50, however, 17.8% (n=65) of them were already using the ACE inhibitor, ARB, or statins. Close contact tracing workflow revealed 53.7% (n=191) of contact with a positive case. 16% of patients with COVID-19 positivity were smokers. Of them, 211 had at least one comorbidity. The most common comorbidity was hypertension with a frequency of 24.5% (n=90). On admission, 89 patients did not have any complaints. The most common complaint was cough (n=172; 47.8%). Only 12.8% (n=47) of patients had a fever greater than 38.3 degrees Celsius. Also, 37 (10.1%) had a mean finger oxygen saturation of less than %90.

Table I: Demographic variables and baseline characteristics of the patients

	n=368	Range or %
Age	47.2 ± 11.66	18-91
<50	221	%60%
>50	147	40%
BMI	27.7±4.7	17-44%
Gender		
Female	188	51.2%
Male	180	48.8%
Close contact	191	53.7%
Smoker	59	16.5%
ICU need	29	7.9%
Comorbidity		
DM	53	14.4%
HT	90	24.5%
CRF	6	1.5%
CHF	26	7.1%
COLD	26	7.1%
Cancer	6	1.5%
Pregnancy	4	1%
Medication		
ACEI	27	7.4%
ARB	23	6.3%
Statin	15	4.1%

Abbreviations: DM, diabetes mellitus; HT, hypertension; CRF, chronic renal failure; CHF, congestive heart failure; COLD, chronic obstructive lung disease

Table II: Clinical findings on admission

Without complaint	89	25%
With complaint	270	75%
Fever	154	40.5%
Cough	172	47.8%
Dispne	67	18.7%
Diarrehea	15	4.2%
Nausea	24	6.7%
Sore throat	53	14.4%
Headache	30	8.4%
Fatigue	119	32.2%
Myalgia	77	21.6%
Loss of smelling/taste	25	7%
Fever		
<37.5	87	22%
37.5-38.3	46	12.5%
>38.3	47	12.8%
Tachycardia >100	67	18.8%
Tachypnea >22	110	29.9%
Oxygen saturation<90	37	10.1%
Pneumonia		
No	121	34%
Mild	204	54%
Severe	44	11%

Radiological and laboratory findings are shown in Table 3 in detail. The most common CT finding was ground-glass opacity (62.4%; n=199). While 342 patients had complete CT examinations, 111 of them had not any lung involvement and almost all (59%) that had any lung injury had a score of 0-21%.

Of them, 248 had displayed clinical pneumonia findings whereas 121 (34%) had respiratory symptoms with fever and CT manifestations of pneumonia without clinical pneumonia. The rate of severe and mild clinical pneumonia was 44 (11%) and 204 (54%), respectively (Table 4). According to national guidelines for treatment nearly all patients (98.8%) were routinely given hydroxychloroquine. Due to the high incidence of clinical pneumonia in this cohort, 218 (60.4%) of them received azithromycin. The rate of favipiravir usage was 11.8% (n=42). The contemporary treatment modalities such as plasma exchange or stem cell therapy application were very low (3.2%, 0.5%, respectively) (Table 5).

Table III: Radiological examination and laboratory findings

Available CT findings (n=342)	n	%
Ground glass opacity	199	% 62.4
Consolidation	100	%32.5
Crazy-paving pattern	47	%14.6
Reversed halo sign	28	%9
Centrilobular nodule	6	%2
Extent of involvement (%)		
0	111	%35
0-21	185	%59
25-50	13	%4
50-75	4	%2
75-100	2	%1
Laboratory findings		
WBC	5916±2441	2300-26700
Platelets	217±67	98-616
AST	30.2±40.6	2-639
ALT	29.9±40	3-417
LDH	795±8875	102-138000
D-dimer	585±627	0-4800
Creatine	0.94±0.44	0.53-6.4
Urea	29±14	2.5-188
CRP	18.5±31.5	0.2-222
Sedimentation	18.2±26.8	1-107
Treatment		
Oseltamir	97	26.7%
Hydroxychloroquine	355	98.2%
Azithromycin	218	60.4%
Enoxaparin	278	76%
Favipravir	42	11%
Antibiotic	60	16.5%
Plasma exchange	13	3.5%
Tocilizumab	12	3.2%
Stem cell therapy	2	0.5%

Table IV: Comparison of demographic findings

	ICU needed	Not needed ICU	P value	Odd ratio
Patient	27	341		
Age	63.4 14.6 (36-91)	44.3 15.5(18-85)	<0.001	1.082
Age <50//>50	23/4	124/214	<0.001	
BMI	20-44 (30.5 6.1)	26 9.8 16-40	0.393	1.009
Gender Male/Female	17/10	158/177	0.046*	2.340
Direct contact with (+) case	11/16	179/146	0.393	1.492
Smokers			0.927	0.944
Comorbidity				
DM	9/18	44/291	0.157	0.448
HT	7/20	20/314	0.432	0.668
KBY			0.132	0.231
CHF	6/21	19/316	0.104	0.381
Cancer	1/26	5/329	0.781	1.407
Medication				
ACE	7/20	20/314	0.008*	0.221
ARB	3/24	20/3134	0.171	0.399
Statin	4/23	10/325	0.605	0.402

Univariate analysis found that age, gender, chronic obstructive lung disease, ACE inhibitor usage, tachypnea, finger oxygen saturation at admission, the existence of clinical pneumonia, and severity of lung involvement were all significantly associated with ICU need. After adjusting for the effects of these variables multivariate analysis revealed that extent of lung involvement (OR 3.379; p<0.001), >50 years of age (OR 1.082; p<0.001) and male gender (OR 2.340; p=0.046) were significant risk factors for ICU need (Table 6 and 7). Also, the extent of lung involvement (OR 3.379) and crazy-paving pattern (OR 0.41) were strongly associated with the severity of clinical pneumonia.

Table V: Comparison of clinical and physical examination findings of patients with regard to ICU need

	In ICU	Not needed ICU	P value	Odd ratio
Complaint				
Fever			0.179	4.561
Cough	17/10	153/176	0.215	3.191
Dyspnea	15/12	51/277	0.466	0.507
Nausea	2/25	23/302	0.145	0.10
Headache	3/24	27/299	0.633	0.522
Fatigue	11/16	104/225	0.278	3.577
Myalgia	6/21	71/255	0.234	1.607
Fever (>38.3 vs <38.3)	12 vs 15	32 vs 303	0.122	0.568
Tachycardia (>100 vs <100)	11 vs 16	53 vs 282	0.399	0.631
Tachypnea (>22 vs <22)	20 vs 7	87 vs 248	0.010*	0.466
Oxygen saturation (<90 vs >90)	16 vs 11	19 vs 316	0.006*	0.268
Severity of clinical pneumonia (severe vs mild)	26 vs 1	16vs 196	<0.001	0.126

Table VI: Comparison of radiological examination and laboratory findings of the groups

	In ICU	Not needed ICU	P value	OR
Radiological findings				
Ground glass opacity	23/2	172/117	0.234	4.153
Consolidation	13/12	87/197	0.107	2.7
Crazy-paving pattern	12/13	31/253	0.023*	0.296
Reversed halo sign	5/20	21/263	0.420	0.527
Centrilobular nodule	2/25	6/277	0.999	206,6
Extent of lung involvement	1/14/5/3/2	108/167/8/1/0	0.02*	0.756
Laboratory findings				
WBC	5843.8 2092	5843.8 2092	0.060*	1.010
Platelet	197.8 77.8	218.2 66	0.090*	1.033
AST	63.4 126.8	27.8 23.4	0.354	0.959
ALT	46.8 84.2	28.5 35	0.205	0.948
LDH	429.8 366.3	824.4 9206	0.211	0.986
D-dimer	842.1 783.1	565.4 612.6	0.287	0.995
Creatine	1.29 0.97	0.92 0.37	0.463	10.986
Urea	45.3 38.3	28.8 10.5	0.615	1.054
CRP	70.1 60.9	14.3 23.9	0.478	1.027
Sedimentation	46.9 21.1	25.4 17.2	0.253	1.067

Table VII: The effect of radiological CT findings on clinical pneumonia

	Severe Pneumonia	Mild Pneumonia	P value	Odd ratio
Patients	37	197		
Radiological findings				
Ground glass opacity	33/4	138/44	0.529	0.683
Consolidation	19/18	75/104	1	1
Crazy-paving pattern	17/20	24/155	<0.001	0.410
Reversed halo sign	6/31	20/159	0.686	0.789
Centrilobular nodule	5/37	6/173	0.999	215.4
Extent of lung involvement	3/25/4/3/2	37/134/7/1/0	<0.001	3.379

DISCUSSION

The most important finding of this study is that advanced age and male gender are the most important risk factors for ICU monitoring and treatment. In this retrospective comparative study, approximately 8% of all patients needed intensive care treatment and %31 died.

According to sequence analysis, its genome has many open reading frames and especially the first frame makes up the majority of the whole genome length[11]. Although the genome length of RNA viruses is short, the genome length of CoV is three times longer and mutation rates are higher than DNA viruses. Six CoVs that are known to cause upper respiratory diseases were identified prior to the COVID-19 pandemic. It is known that SARS-CoV and Middle East Respiratory Syndrome-CoV(MERS-CoV) can cause severe lower respiratory tract disorders[12]. This seventh coronavirus infection, which was first detected in Wuhan, China in December, turned into a pandemic in about 2 months. Although it causes mild flu-like complaints such as fever, dry cough, and fatigue in most patients, it can cause respiratory failure, especially in elderly patients[13].

Although most patients show minor symptoms, identifying risk factors at an early stage will support efforts to prevent the progression of the disease by giving chance to more appropriately refer clinicians who meet patients admitted with suspected COVID-19, as it can lead to severe lower respiratory problems and lead to mortality. Clinical signs such as high fever and cough, as well as an increase in blood infection markers, have been identified as risk factors for the need for intensive care in previous studies[14,15]. Hou et al., in their retrospective study involving 101 patients hospitalized and treated in Beijing, China, found that advanced age and high C-REACTIVE PROTEIN (CRP) at presentation and low lymphocyte count were directly related to disease progression[13]. In their systematic review and meta-analysis, Jain V and Yuan J-M found that although male gender is only a risk factor for ICU application, dyspnea is a risk factor for both severe disease and ICU application[16].

The results of our investigation are consistent with data from previous studies confirming older age and male gender are obvious risk factors for severe pneumonia. Advanced age has been identified as a serious risk factor in more than 5300 of the studies published on the COVID-19 pandemic so far. Although the most common complaints in the general population are reported as fever (98%), cough (76%), dyspnea (55%), and fatigue (44%), elderly

patients often present with shortness of breath[15,18]. While the potency of each additional disease is not known exactly, it is believed that the multiple comorbidities of advanced age patients explain why severe pneumonia and death are higher in this age group[18]. Although Jain V and Yuan JM compared the patients in the ICU with the inpatients in their systematic review and found that fever, cough, and especially dyspnea were common in patients hospitalized in the ICU, in this study, patients' complaints, blood values , and their demographic data were compared with patients who were directly hospitalized in intensive care[16]. Similar to other studies, although advanced age and male gender have serious risk factors in terms of the need for intensive care, along with low saturation and severity of clinical pneumonia, tachypnea as a symptom was the leading complaint in this study. We are certainly not stating that dyspnea and low oxygen saturation rate, which can be objectively calculated, less important findings in this population rather tachypnea should be considered as a simple reference finding.

At the time of writing this study, 1.3 RT-PCR tests per thousand were being done in our country and 76.8 test per confirmed case was obtained as positive rate[19]. Due to the relatively high false negativity of PCR tests, general practice is CT imaging at the time of admission and test repetition while the patient is hospitalized. In most radiological studies, GGO and consolidation and less likely interlobular septal thickening, reticular pattern, crazy paving, bronchial wall, and/or pleural thickening were shown to be CT imaging characteristics in these patients[20,21]. Although our results do not dispute these data, the extent of lung involvement together with crazy-paving pattern are the main CT findings that may indicate a severe disease and ICU need.

This study has some limitations. First, as our sample was obtained retrospectively, a priori power analysis could not be performed. Hence, a post hoc power analysis was not performed because this study was undertaken as a retrospective review of all eligible patients hospitalized in the aforesaid period. Second, symptoms such as loss of taste and smell sensation that may be important in terms of virus tropism, could not include in this comparison due to inadequate data. Finally, patients hospitalized during the alleged first peak period were included. The characteristics of the fluctuation in the number of patients and the severity of the disease after this period will be presented in future studies.

In conclusion, our results agree with those of previous studies that have shown that advanced age and male gender are important risk factors for patients that may need ICU. In addition to these demographic features, we believe that the prevalence and pattern of pulmonary involvement in CT with tachypnea and low oxygen saturation at the time of admission may resemble warning signs for physicians working in triage. Genetic-based research that can be done in future studies will provide more objective information in determining which patients are at risk.

We thank: Emre Apaydın, Alper Batak, Sevinç Bayrak, Veciha Özlem Bozkaya, Yunsur Çevik, Kürşat Dal, Yavuz Selim Erkoç, Derun Taner Ertuğrul, Mehmet Enes Gökler, Gülsüm Biten Güven, Hakan Bahadır Haberal, Fatih Mehmet Kışlal, Mehmet Fatih Kocamaz, Şahbender Koç, Mesut Koçak, Faik Köse, Aysun Aybal Kutlugün, Zeliha Asiltürk Lülleci, Esra Özayar, Burak Pasinlioğlu, Ferdane Sapmaz, Tijen Şengezer, Gülçin Şimşek, Canan Tapkan, Aslı Çelebi Tayfur, Özlem Tekin, Veysel Barış Turhan, Gülsüm Feyza Türkeş, Erbil Türksal, Öznur Ünal, Uğur Yaradılmış, Derya Yenibertiz, Mustafa Yordam for their contributions.

Ethics Committee Approval: This single-center, retrospective, observational study was done at the University of Health Sciences affiliated hospital of Keçiören and the study was approved by the institutional review boards and the ethics committee of the hospital with the decision numbered 2012-KAEK-15/ 2129.

Conflict of Interest: The authors declared no conflicts of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Afzal A. Molecular diagnostic technologies for COVID-19: Limitations and challenges. J Adv Res. 2020; 26: 149-59.

2. Wu Z, McGoogan JM. 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 2020; 323(13): 1239-42.

3. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med 2020; 382: 1199–207.

4. Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. JAMA 2020; 323: 2249-51.

5. Mori Y, Notomi T. Loop-mediated isothermal amplification (LAMP): a rapid, accurate, and cost-effective diagnostic method for infectious diseases. J Infect Chemother 2009; 15: 62–9.

6. Procop GW, Brock JE, Reineks EZ, et al. A Comparison of Five SARS-CoV-2 Molecular Assays with Clinical Correlations. Am J Clin Pathol.2021; 155(1): 69-78.

7. Xie X, Zhong Z, Zhao W, et al. Chest CT for Typical Coronavirus Disease 2019 (COVID-19) Pneumonia: Relationship to Negative RT-PCR Testing. Radiology 2020; 296(2): E41-E45.

8. Huang P, Liu T, Huang L, et al. Use of Chest CT in Combination with Negative RT-PCR Assay for the 2019 Novel Coronavirus but High Clinical Suspicion. Radiology 2020; 295(1): 22-3.

9. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020; 323(11): 1061-9.

10. Chang YC, Yu CJ, Chang SC, et al. Pulmonary sequelae in convalescent patients after severe acute respiratory syndrome: evaluation with thin-section CT. Radiology 2005; 236(3): 1067-75.

11. Chen Y, Liu Q, Guo D. Emerging coronaviruses: Genome structure, replication and pathogenesis. J Med Virol. 2020 92(4): 418-23.

12. Su S, Wong G, Shi W, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends Microbiol 2016; 24(6): 490-502.

13. Hou W, Zhang W, Ronghua J, et al. Risk factors for disease progression in hospitalized patients with COVID-19: a retrospective cohort study. Infectious Diseases 2020; 0: 1-8.

14. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395(10223): 497–506.

15. Sun Y, Koh V, Marimuthu K, et al. Epidemiological and clinical predictors of COVID-19. Clin Infect Dis 2020; 28; 71(15): 786-92.

16. Jain V, Yuan J-M. Predictive symptoms and comorbidities for severe COVID-19 and intensive care unit admission: a systematic review and meta-analysis. Int J of Public Health 2020; 65(5): 533-46.

17. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA 2020; 28; 323(16): 1612-4.

18. Famularo G. Comment on: COVID-19 and Older Adults: What We Know. J Am Geriatr Soc 2020; 68(10): 2197.

19. Chung M, Bernheim A, Mei X, et al (2020) CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology. 2020; 295(1): 202-207.

20. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol 2020; 30(8): 4381-9.

21. Özmen C A. The Radiology of COVID-19 Pneumonia. Dicle Med J 2021; 48 (Special Issue): 5-14.