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Research Article / Araştırma Makalesi

Investigation of Clinical, Laboratory and Radiological Results of Novel Coronavirus Disease (Covid-19)

Yeni Koronavirüs Hastalığının (Covid-19) Klinik, Laboratuvar ve Radyolojik Sonuçlarının İncelenmesi

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Abstract

Covid-19, which emerged in China in December 2019 and spread to the whole world in a short time, has been a serious public health problem threatening humanity. In this study, we aimed to reveal demographic, clinical, laboratory and radiological features of patients diagnosed with Covid-19. The study is a retrospective cross-sectional study consisting of patients who were hospitalized in health institutions in Bolu, Turkey between 11.03.2020 and 19.04.2020 with a definitive or probable diagnosis of Covid-19. The number of patients in the study was 262. The mean age of the patients participating in the study was 57.39 ± 19.85, the youngest patient was 19 and the oldest was 94 years old. Of the patients, 40.1% was between the ages of 18-50, 59.9% were over 50 years old. 55.3% of the patients were women and 44.7% were men. Most common symptoms were fever (75.6%), cough (71.8%) and dyspnea (46.9%). Elevated CRP (in 71.3%), elevated LDH (in 56.9%), elevated D-DIMER (in 56.4%) and lymphopenia (in 30.5) were most detected laboratory abnormalities. The result of the real-time reverse-transcription polymerase chain reaction (RT-PCR) test was positive in 35.5% of 262 patients. 88.5% of the patients had chest CT findings compatible with Covid-19. Additionally, 24% had both positive RT-PCR results and CT findings compatible with Covid-19. Expected findings were found to be in older patients more than younger ones. We suggest that clinical features, laboratory abnormalities and radiological findings can be used to provide an early diagnosis and treatment of Covid-19.

Keywords: Covid-19, clinical features, radiological findings, laboratory findings.

Özet

Aralık 2019'da Çin'de ortaya çıkan ve kısa sürede tüm dünyaya yayılan Covid-19, insanlığı tehdit eden ciddi bir halk sağlığı sorunu olmuştur. Bu çalışmada Covid-19 tanısı alan hastaların demografik, klinik, laboratuvar ve radyolojik özelliklerini ortaya çıkarmayı amaçladık. Çalışma, 11.03.2020 ile 19.04.2020 tarihleri arasında Bolu ilindeki sağlık kuruluşlarında kesin veya olası Covid-19 tanısı ile hastaneye yatırılan hastalardan oluşan retrospektif kesitsel bir çalışmadır. Çalışmaya katılan hasta sayısı 262 idi. Çalışmaya katılan hastaların yaş ortalaması 57.39 ± 19.85, en genç hasta 19 ve en yaşlı hasta 94 idi. Hastaların% 40.1'i 18-50 yaş aralığında,% 59.9'u 50 yaşın üzerindeydi. Hastaların% 55,3'ü kadın,% 44,7'si erkekti. En sık görülen semptomlar ateş (% 75,6), öksürük (% 71,8) ve nefes darlığı (% 46,9) idi. Yüksek CRP (% 71.3'te), yüksek LDH (% 56.9'da), yükselmiş D-DIMER (% 56.4'te) ve lenfopeni (30.5'te) saptanan laboratuar anormallikleriydi. Gerçek zamanlı ters transkripsiyon polimeraz zincir reaksiyonu (RT-PCR) testinin sonucu 262 hastanın% 35,5'inde pozitifti. Hastaların% 88,5'inde Covid-19 ile uyumlu göğüs BT bulguları vardı. Ek olarak,% 24'ü hem pozitif RT-PCR sonuçlarına hem de Covid-19 ile uyumlu BT bulgularına sahipti. Beklenen bulguların, gençlere göre yaşlı hastalarda daha fazla olduğu bulundu. Covid-19'un erken tanı ve tedavisi için klinik özelliklerin, laboratuvar anormalliklerinin ve radyolojik bulguların kullanılabileceğini önermekteyiz.

Anahtar Kelimeler: covid-19, klinik özellikler, radyolojik bulgular, laboratuvar bulguları

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1. Introduction

In December 2019, a group of pneumonia cases with unknown etiology were detected in Wuhan, China. After investigating these cases, it was concluded that there might a common agent. Thereafter, it was found to be a new type in the coronavirus family (1). On February 11 2020, this disease caused by novel coronavirus was named Covid-19 by the World Health Organization (WHO) (2). The first death due to Covid-19 occurred in China on January 9, 2020 and within weeks following, deaths were reported in Thailand, Japan and Europe. Since Covid-19 started to be seen all over the world, WHO defined it as a pandemic on March 11, 2020 and determined its center as Europe (3,4).

Before December 2019, 6 subtypes of coronavirus were known to infect humans, causing respiratory diseases. 4 of those are HCoV - 229E, HCoV - OC43, HCoV - NL63 and HKU1 and they mostly cause mild upper respiratory tract infections. However, despite occurring rarely, they can cause serious respiratory system infections in infants, children and the elderly (5). SARS-CoV and MERS-CoV, other types of coronavirus, cause more serious and dangerous infections (6). It is thought that the nucleotide structure of SARS-CoV2, which is the cause of Covid-19, is similar to that of bats and the origin of the disease may be bats (7).

The course of Covid-19 is defined in 5 groups according to its clinical severity. As for these groups; asymptomatic cases are patients who do not show any clinical symptoms and are positive for the SARSCoV-2 RT-PCR test. In mild clinical cases, there are signs of acute upper respiratory tract infection such as fatigue, muscle pain, cough, sore throat, sneezing and runny nose. In the group with moderate clinical course, the clinical presentation is pneumonia accompanied by fever, cough and sometimes wheezing, but dyspnea and noticeable hypoxemia aren't expected. In severe clinical cases, there are signs and symptoms such as dyspnea, central cyanosis, oxygen saturation less than 92% and hypoxemia which progress rapidly in one week. In critical cases, clinical pictures such as acute respiratory distress syndrome (ARDS), respiratory failure, shock, and multiple organ disorders may appear. [8, 9]

In previous studies, it is not known how long SARS-CoV-2 can survive on the surfaces, but it is thought it may remain alive for a few hours on inanimate surfaces. (10) According to the studies, it is estimated that the incubation period is considered as 5.2 days (1-12.5), but it can last up to 14 days. (11) In our study, clinical, laboratory and radiological results of both definitive and probable cases of Covid-19 were compiled. Those who have a positive RT-PCR test were defined as definitive cases. Some cases had very typical clinical and particularly radiological findings although their RT-PCR results weren't positive, they were assumed as probable case.

Our aim in this study is to show that assessment of clinical, laboratory and radiological findings together may help for providing an early diagnosis and treatment of Covid-19.

2. Materials and Methods

This is a retrospective, cross-sectional study consisting of patients who were hospitalized in health institutions affiliated to City Health Administrative of Bolu, Turkey between 11.03.2020 and 19.04.2020 with a definitive or probable diagnosis of Covid-19. Ethical approval of the study was obtained from Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (Date: 12.05.2020, Number: 2020/93).

The number of participants in the study was 262. Written informed consent was obtained from all the patients. Data was collected by scanning the patients retrospectively from the Public Health Management System of City Health Administrative and Hospital Information Management System. Data concerning the patients consisted of age, gender, results of RT-PCR samples, results of laboratory parameters such as white blood cell (WBC), red blood cell (RBC), lymphocyte (LYM), hemoglobin (HGB),

basophile (BASO), platelet (PLT), plateletcrit (PCT), neutrophil (NEU), monocyte (MONO), D-DIMER, C-reactive protein (CPR) and lactate dehydrogenase (LDH), chest computerized tomography (CT) results and clinical findings including fever, cough, dyspnea, anosmia, diarrhea, headache, joint pain, anorexia and sore throat. Tables were made using data. Patients under the age of 18 and those who did not want to participate in the study were not included.

The analysis of the data obtained as a result of the research was carried out in SPSS 23 statistical package program. Descriptive statistical methods (frequency, arithmetic mean, standard deviation, cross tables) were used. The appropriateness of the distribution of the data to the normal distribution was checked by skewness and kurtosis coefficients, and ± 1 interval was taken as reference (12). All of the laboratory data did not show normal distribution. Mann-Whitney U test and Kruskal Wallis tests were used for data which was not suitable for normal distribution. For data which fits a normal distribution, Scheffe test was used in case of homogeneity of variances from post-hoc tests. Chi-square test was used in the analysis of categorical data.

3. Results

Table 1. Demographic characteristics, RT-PCR and Chest CT Results

Demographic Features		$\bar{x}$ **±SS**	**min-max**
Mean Age		57,39± 19,85	19-94
		N	**%**
Age Groups	18-50	105	40,1
	51 and above	157	59,9
Gender	Woman	145	55,3
	Man	117	44,7
RT-PCR Results	Positive (+)	93	35,5
	Negative (-)	169	64,5
Absence or presence of chest CT findings	Present	232	88,5
	Absent	5	1,9
	Didn't undergo	25	9,5
Location of chest CT findings	Right lung	43	16,4
	Left lung	30	11,5
	Bilateral	159	60,7
PCR+ CT+		63	24,0
PCR+ CT-		25	9,5
PCR+ CT (without a CT scan)		5	1,96
PCR- CT+		169	64,5

It was determined that the mean age of the patients participating in the study was 57.39 ± 19.85, the youngest patient was 19 and the oldest was 94 years old. Of the patients, 40.1% was between the ages of 18-50, 59.9% was over 50 years old. 55.3% of the patients were women and 44.7% were men. The result of RT-PCR test was positive in 35.5% of 262 patients. 88.5% of the patients had chest CT findings compatible with Covid-19. Additionally, 24% had both positive RT-PCR results and chest CT findings compatible with Covid-19. Among patients who had CT findings of Covid-19, 60.7% had bilateral findings, 27.9% had unilateral findings. Among those who showed unilateral findings 16.4% were found to be in the right lung and 11.5% in the left (Table 1).

Moreover, among 232 patients who had CT findings compatible with Covid-19, there was a statistically significant relationship between the age groups (p = 0.002 <0.05). Of 232 patients, 84 (36.2%) were between the ages of 18-50 and 148 (63.8%) were 51 years old and above.

Table 2. Clinical features of the patients

Symptoms	Presence of symptoms	Absence of symptoms	p-value
Fever	198 (%75,6)	64 (%24,4)	**0,020***
Cough	188 (%71,8)	74 (%28,2)	**0,005***
Dyspnea	123 (%46,9)	139 (%53,1)	**0,025***
Diarrhea	50 (%19,1)	212 (%80,9)	0,566
Headache	32 (%12,2)	230 (%87,8)	0,298
Joint Pain	27 (%10,3)	235 (%89,7)	0,061
Anorexia	16 (%6,1)	246 (%93,9)	0,365
Sore throat	35 (%13,4)	227 (%86,6)	0,328
Anosmia	12 (%4,6)	250 (%95,4)	0,163

* a value of p<0,05 was taken as significant ** Chi-Square test

To evaluate the relationship between the presence of symptoms in 262 patients; fever, cough and dyspnea were statistically significant (p = <0.05). Among patients with a definitive or probable diagnosis of Covid-19; fever (75,6%), cough (71.8%) and dyspnea (46.9%) were the most frequent symptoms. Diarrhea (19.1%), headache (12.2%), joint pain (10.3%), anorexia (6.1%), sore throat (13,4%) and anosmia (4.6%) were the other symptoms (Table 2).

Table 3. Analysis of laboratory parameters according to the age groups

Analysis of laboratory parameters according to the age groups			
	‘’18-50’’ age group	‘’51 and above’’ age group	p-value
	Median (Min-Max)**		
WBC	7 (2,1-19,8)	7,69 (1,25-26)	0,129
RBC	4,89 (3,47-6,53)	4,44 (1,08-5,78)	**0,000***
LYM	1,78 (0,484-4,75)	1,2 (0,3-4,86)	**0,000***
HGB	14,4 (7,3-18,2)	13 (3,69-17,2)	**0,000***
BASO	0,051 (0-0,6)	0,046 (0-0,9)	0,742
PLT	211 (76-603)	213 (20,5-712)	0,804
PCT	0,178 (0,058-0,396)	0,177 (0,02-0,547)	0,929
NEU	4,4 (0,7-16,5)	5,51 (0-21,7)	**0,005***
MONO	0,567 (0,187-1,89)	0,535 (0,064-2,52)	0,262
D_DİMER	0,39 (0,03-8,36)	1,16 (0,1-19,93)	**0,000***
LDH	221,5 (80-863)	264,5 (54,9-1491)	**0,000***
CRP	8,545 (0-282,7)	36,5 (0-355)	**0,000***

* a value of p<0,05 was taken as significant ** Mann-Whitney U test

Mean RBC, LYM, HGB, D-DIMER, NEU, LDH and CRP values differed significantly between the age groups (p <0.05). Mean RBC, LYM and HGB values in the ‘’18-50 ‘’age group were higher. On the other hand, mean D-DIMER, NEU, LDH and CRP values were higher in the ‘’51 and above’’ age group (Table 3).

Table 4. Analysis of laboratory parameters according to RT-PCR results

Analysis of laboratory parameters according to RT-PCR results			
Parameters	**PCR (+)**	**PCR (-)**	**p-value**
	Median (Min-Max)**		
WBC	5,5 (2,1-15)	9,04 (1,25-26)	**0,000***
RBC	4,72 (1,08-6,24)	4,54 (1,17-6,53)	**0,001***
LYM	1,49 (0,4-4,75)	1,4 (0,3-4,86)	0,386
HGB	13,9 (3,69-17,2)	13,3 (5,5-18,2)	**0,004***
BASO	0,035 (0-0,6)	0,061 (0-0,9)	**0,000***
PLT	199 (96-444)	229 (20,5-712)	**0,001***
PCT	0,165 (0,089-0,33)	0,186 (0,02-0,547)	**0,001***
NEU	3,45 (0,7-12,7)	6,61 (0-21,7)	**0,000***
MONO	0,497 (0,1-1,38)	0,6 (0,064-2,52)	**0,004***
D_DİMER	0,42 (0,03-11,7)	0,97 (0,032-19,93)	**0,000***
LDH	232 (80-644)	261,5 (54,9-1491)	**0,013***
CRP	7,25 (0-162,8)	36,5 (0-355)	**0,000***

* a value of p<0,05 was taken as significant ** Mann-Whitney U test

The relationship between the results of RT-PCR test and laboratory findings were as follows; The mean WBC, BASO, PLT, PCT, NEU, MONO, D-DIMER, LDH and CRP values were found to be higher in patients with negative RT-PCR results (p <0.05). However, it was found that those with positive RT-PCR results had significantly higher mean RBC and HGB values (Table 4).

The relationship between CT findings and laboratory results of patients with positive RT-PCR results was also analyzed; the mean WBC and NEU values were found to be significantly higher in those who had no findings consistent with Covid-19 in chest CT, while the mean LDH and CRP values were significantly higher in those who had findings consistent with Covid-19 in chest CT.

Table 5: Analysis of laboratory parameters according to their reference ranges

	Low	**Normal**	**High**
WBC	39 (% 14,9)	169 (% 64,5)	54 (% 20,6)
RBC	37 (%14,1)	212 (%80,9)	13 (% 5)
HGB	40 (%15,3)	221 (%84,4)	1 (%0,4)
PLT	22 (%8,4)	232 (%88,5)	8 (%3,1)
NEU	9 (%3,4)	177 (%67,6)	76 (%29)
LDH	3 (%1,1)	76 (% 29)	149 (%56,9)
LYM	80 (%30,5)	182 (%64,5)	-
CRP	-	75 (%28,7)	186 (%71,3)
D_DİMER	-	96 (% 43,6)	124 (% 56,4)
MONO	-	224 (%85,5)	38 (%14,5)
PCT	-	262 (%100)	-
BASO	-	229 (%87,4)	33 (%12,6)

Among 262 patients who had a definitive or probable diagnosis of Covid-19; the WBC count was below the normal range in 39 (14.9%) patients and above the normal range in 54 (20.6%) patients; the RBC count was lower than the normal range in 37 (14.1%)

patients and higher than the normal range in 13 (5%) patients; HGB level was below the normal range in 40 (15.3%) patients and above the normal range in 1 (0.4%) patient; 22 (8.4%) patients had the PLT count lower than the normal range in and 8 (3.1%) patients had higher levels than the normal range; the NEU count was lower than the normal range in 9 (3.4%) patients and higher than the normal range in 76 (29%) patients; LDH was found to be decreased in 3 (1.1%) patients and increased in 149 (56.9%)patients; the LYM count was below the normal range in 80 (30.5%) patients; CRP increased in 186 (71.3%) patients; there were 124 (56.4%) patients with an increased level of D-DİMER; the BASO count was higher than the normal range in 33 (%12,6); the MONO count was above the normal range in 38 (%14,5) patients.

4. Discussion

Our study was performed cross-sectionally and retrospectively. It consisted of 262 patients with a definitive or probable diagnosis of Covid-19. Demographic characteristics, clinical features, laboratory abnormalities and chest CT imaging results of the patients were evaluated.

Fever, cough, dyspnea, sore throat, weakness and muscle pain are the most common symptoms of Covid-19. Besides, symptoms such as anorexia, nausea and diarrhea can be seen. (13,14). In a meta-analysis study performed with 656 patients, fever was found in 88.7%, cough in 57.6% and dyspnea in 45.6%. Other common symptoms were recorded as weakness (29.4%), sputum (28.5%), sore throat (11%), headache (8%) and diarrhea (6.1%) (15). In our study, the most common symptoms were fever (75.6%), cough (71.8%) and dyspnea (46.9%). The other symptoms were diarrhea (19.1%), headache (12.2%), joint pain (10.3%), anorexia (6.1%), sore throat (13.4%) and anosmia (4.6%). The percentages of fever, cough and dyspnea were found to be significantly higher ($p = <0.05$).

In a study conducted by Zhou et al, patients' clinical, laboratory and radiological findings were evaluated. The most common symptoms in the study were fever (94%), cough (79%), weakness (23%), myalgia (15%), diarrhea (5%) and nausea (4%). Lymphopenia was found in 40% of the patients, leukopenia in 17%, leukocytosis in 21%, anemia in 15% and thrombocytopenia in 7%. The other findings were elevated ALT (31%), elevated troponin (17%), elevated D-DIMER (42%) and elevated ferritin (80%). The most detected radiological finding in the study was ground glass opacity (71%). Pulmonary infiltration was found to be bilateral in 75% of the patients (16). In our study, radiological findings compatible with Covid-19 were detected in 88.5% of the patients who underwent a chest CT scan. Detected CT findings were bilateral in 60.7% of patients and were unilateral in 27.9% (16.4% in the right lung, 11.5% in the left lung). Among 232 patients possessing radiological findings, 84 (36.2%) were in the''18-50'' age group and 148 (63.8%) were in the ''51 and above '' age group. The older patients were found to have more radiological findings than the younger ones had and the difference was statistically significant.

In a study, laboratory parameters of patients diagnosed with Covid-19 were studied, 63% had lymphopenia, 25% had leukopenia and CK, procalcitonin, HGB and PLT were measured as normal (17). In our study, elevated CRP (71.3%), elevated LDH (56.9%), elevated D-DIMER (56.4%), lymphopenia (30.5), neutrophilia (29%), leukocytosis (20.6%), anemia (15.3%), leukopenia (14.9%), basophilia (12.6%), monocytopenia (14.5%) thrombocytopenia (8.4%) and neutropenia (3,4%) were detected laboratory abnormalities. Laboratory parameters of RT-PCR positive patients were also analyzed according to chest CT findings; the mean LDH and CRP values were significantly higher in patients with compatible CT findings compared to those without any CT findings associated with Covid-19. Additionally, the mean WBC, BASO, PLT, PCT, NEU, MONO, D-DIMER, LDH and CRP values were found to be higher in patients with negative RT-PCR results. On the other hand, patients with positive RT-PCR results had significantly higher mean RBC

and HGB values. The fact that mean WBC, BASO, PLT, PCT, NEU, MONO, D-DIMER, LDH and CRP results were significantly higher in those with negative RT-PCR results can be explained by inadequate sensitivity of PCR method and high sensitivity of CT scan. All the mentioned patients had chest CT findings consistent with Covid-19 in spite of not having positive RT-PCR results.

In a study evaluating the hematological parameters of patients diagnosed with Covid-19, leukopenia was found in 29.2% of the patients, lymphopenia in 36.9% and thrombocytopenia in 20%. In the study, only 1 patient had severe leukopenia and none had severe thrombocytopenia. Severe lymphopenia was observed in 5 patients (18). In a meta-analysis study, it was suggested that thrombocytopenia might be associated with severity of covid-19 (19). As mentioned above, in our study, findings such as lymphopenia, leukopenia and thrombocytopenia were 30.5%, 14.9% and 8.4%, respectively and were found to be similar to previous studies.

In our study, in accordance with our expectation, laboratory abnormalities were mostly seen in elderly patients. The mean D-DIMER, LDH and CRP values were found to be higher in patients aged 51 years and older. The difference was statistically significant. However, the mean LYM value was lower in the older patients.

In a study researching the role of chest CT imaging for early diagnosis of Covid-19, the initial chest CT reports made a correct interpretation in 49 of 51 patients before the diagnosis was confirmed by RT-PCR test and only an error of 3.9% appeared (20). RT-PCR test was positive for 93 patients in our study. Of 93 patients, 63 (67.7%) had radiological findings compatible with Covid-19 on their initial chest CT. Among all 262 patients included in our study, the rate of presence of CT findings was 88.5%, while the rate of positive RT-PCR results was only 35.4%. Because of low sensitivity (45-60%) of some RT-PCR kits (21), and high sensitivity of chest CT imaging compared to RT-PCR test (22), we suggest CT imaging can be considered as a diagnostic tool for Covid-19. Moreover, although RT-PCR is accepted as gold standard for diagnosis of Covid-19, it can't be performed in every health institution. Furthermore, results may be false negative because of various factors like the usage of RT-PCR kits with low sensitivity.

In a retrospective study conducted by Shi et al., radiological findings of 81 patients were evaluated. In the study, ground glass opacity was detected in 65% of the patients (23). In another study, ground glass opacity was the most detected radiological finding, similarly. In that study, a single lesion was detected on the initial CT in some patients. It was revealed that the lesions were mostly seen in the lower and middle zones (24). In our study, chest CT was ordered to 237 patients. CT findings compatible with Covid-19 were found to be in 88.5% of the patients who underwent a chest CT scan. CT findings were bilateral in 60.7% and unilateral in 27.9%. The most common finding was ground glass opacity. Consolidation was also detected in some patients. In our study, similar to previous studies, it was shown that radiological findings were frequent and mostly bilateral in Covid-19. The most common finding was recorded as ground glass opacity. Although some of our patients were detected with filiation method at the asymptomatic stage, the frequency of radiological findings was quite high.

We suggest that an evaluation of clinical and laboratory findings together with radiological findings may help to make a pre-diagnosis. Thus, isolation and treatment of the patients can be provided at an early stage before confirming the definitive diagnosis. Through this method, it would be easier to prevent the spread of the disease and the deterioration of the prognosis of the patients.

5. Conclusion

Covid-19 infection has emerged as an important public health problem affecting our country and our world. Recognizing the disease and starting a treatment at an early stage would help to reduce the destruction caused by the disease. RT-PCR is accepted as

the gold standard for the diagnosis of Covid-19. However, due to the fact that PCR tests could not be carried out in every health center and the results can be affected by various factors such as some PCR kits with low sensitivity, requirement of using other diagnostic tools shows up for early diagnosis. For this purpose, evaluation of clinical and laboratory features together with radiological findings would be an alternative diagnostic method. In this way, it would be possible to provide a treatment for Covid-19 without waiting for RT-PCR results. Our study and some previous studies support that kind of diagnostic approach. Since the patients in our study are limited to a certain region, comprehensive studies with more patients in more than one center will be more informative.

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