DOI: 10.4274/anatoljmed.2022.97947
Anatol J Gen Med Res 2023;33(3):328-33

CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

ANATOLIAN JOURNAL of GENERAL MEDICAL RESEARCH

Evaluation of Differences Between First and Second Waves of the COVID-19 Pandemic in Hospitalized Patients in a Tertiary Health Center

Türkiye'deki COVID-19 Pandemisinin Birinci ve İkinci Dalgaları Arasındaki Farkların Değerlendirilmesi

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Cite as: Ermin S, Polat G, Özdemir Ö, Serçe Unat D, Unat ÖS. Evaluation of Differences Between First and Second Waves of the COVID-19 Pandemic in Hospitalized Patients in a Tertiary Health Center. Anatol J Gen Med Res 2023;33(3):328-33

Abstract

Objective: Coronavirus disease-2019 (COVID-19) pandemic started on March 2020 and is still ongoing with waves of activity. In this study, we aimed to compare the clinical and laboratory characteristics and survival rates of 1st and 2nd waves of COVID-19.

Methods: Patients hospitalized with the diagnosis of COVID-19 pneumonia between 01.03.2020-31.12.2020 were included. Clinical characteristics, laboratory parameters, radiological and treatment properties as well as clinical outcomes of patients were derived from hospital records. Statistical significance level was taken as p=0.05.

Results: A total of 1043 patients, with average age of 55.68±15.72, were included in the study. 57.8% of the study population was male. There were 469 patients (45%) in group 1 (first wave) and 574 patients (55%) in group 2 (second wave). Although the patients in group 2 were older (59.3±14.53 vs. 51.3±16.03, p<0.001), there was no significant difference of sex and smoking history (respectively, 58.8% males vs. 57% males, p=0.57 and 43.4% vs. 48.1%, p=0.24). There was more COVID-19 real time-polymerase chain reaction positivity in group 2 (61.4% vs. 74.7%, p<0.001), and patients had more comorbidity (47.4% vs. 62.3%, p<0.001). Patients in group 2 had significantly higher lactate dehydrogenase, C-reactive protein and D-dimer levels (p<0.001 for all) and lower lymphocyte levels (p=0.02). Corticosteroid treatment and low molecular weight heparin were more commonly used in group 2 patients (p<0.001 for both). But mortality and intensive care unit (ICU) admission were higher in group 1 [respectively, 50 (10.7%) vs. 25 (4.4%), p<0.001 and 57 (12.2%) vs. 47 (8.2%), p=0.04].

Conclusion: Although the patients in second wave of COVID-19 pandemic were older, had more comorbidities, and had worse laboratory parameters, they had less need for ICU and better survival. This difference may represent increasing experience in patient care and construction of better treatment algorithms and guidelines in COVID-19 pneumonia patients.

Keywords: COVID-19, pandemic, waves, survival

Öz

Amaç: Koronavirüs hastalığı-2019 (COVID-19) pandemisi Mart 2020'de başladı ve farklı dalgalarla devam etmektedir. Bu çalışmada, COVID-19'un 1. ve 2. dalgalarının klinik ve laboratuvar özelliklerini ve sağkalım oranlarını karşılaştırmayı amaçladık.

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Received/Geliş tarihi: 19.03.2022
Accepted/Kabul tarihi: 19.09.2022

Öz

Yöntem: 01.03.2020-31.12.2020 tarihleri arasında COVID-19 pnömonisi tanısı ile hastaneye yatırılan hastalar çalışmaya dahil edildi. Klinik özellikler, laboratuvar parametreleri, radyolojik ve tedavi özellikleri ile hastaların klinik sonuçları hastane kayıtlarından elde edildi. İstatistiksel anlamlılık düzeyi p=0,05 olarak alındı.

Bulgular: Çalışmaya yaş ortalaması 55,68±15,72 olan toplam 1043 hasta dahil edildi. Çalışma popülasyonunun %57,8'i erkekti. Grup 1'de (birinci dalga) 469 hasta (%45), grup 2'de (ikinci dalga) 574 hasta (%55) vardı. Grup 2'deki hastalar daha yaşlı olmasına rağmen (59,3±14,53 vs. 51,3±16,03, p<0,001) cinsiyet ve sigara içme öyküsü açısından anlamlı bir fark yoktu (sırasıyla, %58,8 erkek vs. %57 erkek, p=0,57; %43,4 vs. %48,1, p=0,24). Grup 2'de daha fazla COVID-19 gerçek zamanlı-polimeraz zincir reaksiyonu pozitifliği vardı (%61,4 vs. %74,7, p<0,001) ve hastalar daha fazla komorbiditeye sahipti (%47,4 vs. %62,3, p<0,001). Grup 2'deki hastalarda anlamlı olarak daha yüksek laktat dehidrogenaz, C-reaktif protein ve D-dimer seviyeleri (tümü için p<0,001) ve daha düşük lenfosit seviyeleri (p=0,02) vardı. Grup 2 hastalarda kortikosteroid tedavisi ve düşük molekül ağırlıklı heparin daha sık kullanıldı (her ikisi için p<0,001). Ancak mortalite ve yoğun bakım ünitesine (YBÜ) yatış grup 1'de daha yüksekti [sırasıyla, 50 (%10,7) ve 25 (%4,4), p<0,001 ve 57 (%12,2) ve 47 (%8,2), p=0,04].

Sonuç: COVID-19 pandemisinin ikinci dalgasındaki hastalar daha yaşlı olmalarına, daha fazla komorbiditeye sahip olmalarına ve daha kötü laboratuvar parametrelerine sahip olmalarına rağmen, bu hastalarda YBÜ'ye yatışın daha az ve sağkalımın daha iyi olduğu gösterildi. Bu fark, hasta bakımında artan deneyim ve COVID-19 pnömonili hastalarda daha iyi tedavi algoritmaları ve kılavuzlarının oluşturulmasına bağlı olabilir.

Anahtar Kelimeler: COVID-19, salgın, dalgalar, hayatta kalma

Introduction

Coronavirus disease-2019 (COVID-19) started in China[1] in 2019, spread all over the world rapidly, caused a serious pandemic and is still ongoing with waves of activity, with varying degrees of severity[2]. Although most people are asymptomatic or have mild symptoms, there are also patients with rapid progression of diease causing severe acute respiratory failure with thromboembolic complications[3,4]. Therefore, it has profound medical, psychological, and financial implications globally.

COVID-19 shows a very different clinical course both from person to person and in the disease processes of the person who has the disease more than once. In our country, differences in the clinical course of the disease were observed in the time periods of 01.03.2020-30.05.2020 (1st peak) and 01.11.2020-31.12.2020 (2nd peak), which are also called 1st wave and 2nd wave[5,6]. Changing treatment options and variant strains are the main factors in these differences. Many countries have reported studies comparing the two waves[7-13] but the data in our country is limited. In a study about COVID-19 mortality in Italy, fewer deaths were reported in the 2nd wave, and it was interpreted that this may be related with improved health services[14]. Again, it was stated in the same study that the risk of death was higher in the male gender, more prominently in the second wave[14]. With the results to be obtained from such studies, points to be considered in other possible waves will be determined and will help to improve patient management and health services.

The aim of the study is to compare the clinical and laboratory characteristics and survival rates of first and second waves of COVID-19 pandemic in hospitalized patients in a tertiary health center.

Materials and Methods

Patient Selection

For this retrospective, single-center study, we enrolled patients diagnosed as COVID-19 pneumonia who applied between March 01, 2020, and December 31, 2020. The medical data of these patients were obtained from the hospital information management system. All patients underwent a nasopharyngeal swab test for the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) virus using real-time reverse transcriptase-polymerase chain reaction (RT-PCR). Chest X-ray or thorax computed tomography (CT) were were taken in all patients. COVID-19 disease diagnosis was made by either RT-PCR positivity or symptomatologic and radiological findings compatible with COVID-19 pneumonia in the absence of RT-PCR positivity.

Inclusion Criteria

1. Hospitalized with the diagnosis of COVID-19

2. Age ≥18 years

3. Patients diagnosed with typical COVID-19 pneumonia detected in X-ray or thorax CT

4. Having adequate clinical data in the hospital information management system

Exclusion Criteria

1. Age <18 years

2. Patients that RT-PCR was negative and typical COVID-19 pneumonia was not detected in X-ray or thorax CT

3. Lack of adequate clinical data in the hospital information management system

There is no formal definition of pandemic "waves"; but in this study we regarded the pandemic wave as upward and/or downward tendency of number of COVID-19 cases, sustained over a period of time differing from volatility or spikes[15]. In Turkey, COVID-19 first wave was started after reported first case on 11 March 2020, and a downward slope was distinguishable till the end of May 2020[6]. Controlled social life began on mid-June 2020, and second wave started at the end of November 2020, remained active until January 2021[6]. Hospitalized patients with the diagnosis of COVID-19 between March 2020-May 2020 were regarded as "first wave" patients, whereas "second wave" patients were hospitalized between November 2020-December 2020.

Age, gender, smoking history, presence of chronic disease, hemogram parameters, d-dimer, ferritin, albumin, C-reactive protein (CRP) and lactate dehydrogenase (LDH) of the patients included in the study were recorded. The patients were divided into two groups as group 1 (first wave) and group 2 (second wave). In addition, information about patients' radiological involvement, need for oxygen, mechanical ventilator support and intensive care unit (ICU) need, corticosteroid treatment, low molecular weight heparin (LMWH) use, and mortality were obtained for both groups.

Management of COVID-19 cases were achieved according to the guidelines of scientific committee of Ministry of Health, which were revised and updated with emergence of new evidence and data throughout the pandemic period. The updated guideline during second wave of pandemic (9 October 2020) was primarily different from the first wave guideline in regard of corticosteroid treatment indications and usage of effective anticoagulant therapy; as well as introduction of favipiravir treatment in mild and moderate disease[16,17].

This study was approved by both the Scientific Committee of the University of Health Sciences Turkey, Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital Non-Interventional Research Ethics Committee (decision no: 2021/62-66, date: 05.11.2021).

Statistical Analysis

The data were entered into the SPSS (22.0) program. Conformity of continuous variables to normal distribution was investigated. Comparison of independent subgroups of eligible variables was done with Student's t-test and mean and standard deviation data are presented. The median values and interquartile range were presented if the variables did not have normal distribution and comparison of these variables was achieved by using the Mann-Whitney U test. Chi-square test and Fisher's Exact test were used for discrete data. The p-value was taken as 0.05, and results found below this value were considered significant. Sensitivity and specificity calculations of the tests were made, and the results were compared with the literature.

Results

A total of 1043 patients, with average age of 55.68±15.72, were included in the study. 57.8% of the study population was male. Smoking history, either active or former, was present in 45.1% (n=324) of 718 patients whose smoking data were available. SARS-CoV-2 virus RT-PCR was positive in 714 (68.7%) patients. At least one chronic disease was detected in 54.7% of the study population. The most common chronic diseases were hypertension in 301 (28.9%) patients, diabetes mellitus in 210 (20.1%) patients, and cardiovascular disease in 119 (11.4%) patients. Seventy-five (7.2%) patients died due to COVID-19 during the treatment in the hospital. Demographic characteristics of study population and groups according to COVID-19 pandemic waves were presented in Table 1.

There were 469 patients (45%) in group 1 and 574 patients (55%) in group 2. While the mean age in group 1 was 51.3±16.03, it was 59.3±14.53 in group 2 and the difference between the groups was statistically significant (p<0.001). Two hundred and seventy-six (58.8%) of the patients in group 1 and 327 (57%) of the patients in group 2 were male; and there was no significant difference (p=0.57). Also, there was no significant difference of smoking history between groups (p=0.24) (Table 1). Although 286 (61.4%) of the patients had SARS-CoV-2 virus RT-PCR positivity in group 1, it was detected in 428 (74.7%) of the patients in group 2 and the difference between the groups was statistically significant (p<0.001). Patients had more chronic diseases in group 2 and the difference was significant (47.4% vs 62.3%, p<0.001), the difference was prominent in patients with hypertension and diabetes mellitus.

When the laboratory parameters of both groups are compared, patients in group 2 had significantly higher

Table 1. Demographic characteristics of study population and groups according to COVID-19 pandemic waves				
	Total population (n=1043)	**Group 1 (first wave) (n=469)**	**Group 2 (second wave) (n=574)**	**p-value**
Age, years (mean ± SD)	55.68±15.72	51.3±16.03	59.3±14.53	**<0.001**
Sex, male, n	603 (57.8%)	276 (58.8%)	327 (57%)	0.57
Smoking history				
Smoker, n	324 (45.1%)	197 (43.4%)	127 (48.1%)	0.24
Non-smoker, n	394 (54.9%)	257 (56.6%)	137 (51.9%)	
The intensity of smoking, package/year, (median (IQR)	24 (27)	20 (27)	30 (20)	0.06
COVID-19 PCR positivity, n	714 (68.7%)	286 (61.4%)	428 (74.7%)	**<0.001**
Chronic diseases (n=1027)				
Presence of comorbidity, n	570 (54.7%)	222 (47.4%)	348 (62.3%)	**<0.001**
Chronic diseases				
Hypertension, n	301 (28.9%)	107 (22.9%)	194 (34.7%)	**<0.001**
Diabetes mellitus, n	210 (20.1%)	67 (14.4%)	143 (25.6%)	**<0.001**
Cardiovascular disease, n	119 (11.4%)	46 (9.8%)	73 (13.1%)	0.17
Chronic obstructive pulmonary disease, n	98 (9.4%)	46 (9.8%)	52 (9.3%)	0.83
Malignancy, n	78 (7.5%)	42 (53.8%)	36 (6.4%)	0.13
Asthma, n	35 (3.4%)	19 (4.1%)	16 (2.9%)	0.31
Others, n	51 (4.9%)	8 (1.7%)	73 (7.5%)	<0.001
IQR: Interquartile range, SD: Standard deviation, COVID-19: Coronavirus disease-2019, PCR: Polymerase chain reaction				

LDH, CRP and D-dimer levels (p<0.001 for all) and lower lymphocyte levels (p=0.02). Although 53 (11.5%) of the patients had taken corticosteroid treatment in group 1, it was detected in 283 (49.3%) of the patients in group 2 and the difference between the groups was statistically significant (p<0.001). LMWH was used in 215 (46.5%) of the patients in group 1 and 520 (90.6%) of the patients in group 2; and there was significant difference between groups (p<0.001). Contrary to all other findings, 57 (12.2%) of the patients needed ICU in group 1 and 47 (8.2%) of the patients in group 2; the difference was significant in favor of group 1 (p=0.04). Also, mortality was seen 50 (10.7%) of the patients in group 1 and 25 (4.4%) of the patients in group 2; the difference between the groups was statistically significant in favor of group 1 (p<0.001). Laboratory parameters and clinic outcomes of study population and groups according to COVID-19 pandemic waves were presented in Table 2.

Discussion

This study showed the differences between 1st and 2nd waves and this difference may represent increasing experience in patient care and construction of better treatment algorithms and guidelines in COVID-19 pneumonia patients. The patients in the 2nd wave were older and had more comorbidity; but there was no significant difference of sex and smoking history between the 1st and 2nd waves. Patients had significantly higher LDH, CRP and D-dimer levels and lower lymphocyte levels in the 2nd wave. Corticosteroid treatment and LMWH were more commonly used in the 2nd wave; but contrary to all other findings, mortality and ICU admission were higher in the 1st wave.

In a study conducted by Saito et al.[9], a total of 5194 patients were evaluated, 3833 of whom were from the 1st wave and 1361 from the 2nd wave. In the study, it was shown that patients in the 2nd wave were younger and had less comorbidity and had a lower rate of serious disease and lower mortality[9]. In our study, although the patients in the 2nd wave were older and had more comorbidities, the need for ICU and mortality rates were lower; this can be explained by the usage of more corticosteroids and LMWH in management. As the experience on COVID-19 treatment increased, the positive results obtained were also satisfactory.

Table 2. Laboratory parameters and clinic outcomes of study population and groups according to COVID-19 pandemic waves

	Total population (n=1043)	Group 1 (first wave) (n=469)	Group 2 (second wave) (n=574)	p-value
Laboratory parameters				
Hemoglobin, gr/dL, mean ± SD	13.3±4.26	13.1±1.89	13.4±5.4	0.32
Leucocytes, /mm^3	6800 (4125)	6800 (4200)	6800 (4200)	0.84
Leukocytes, /mm^3	1200 (900)	1200 (900)	1100 (800)	0.02
Neutrophils, /mm^3	4600 (3700)	4600 (3700)	4700 (3600)	0.33
Platelets, /mm^3	240000 (124000)	234000 (116000)	243000 (127000)	0.26
LDH, IU/L	251 (137)	222.5 (118)	265 (138)	**<0.001**
CRP, mg/dL	45.6 (95.8)	33.3 (96.7)	53 (91.8)	**<0.001**
D-dimer, mg/L	875 (1157)	722 (980)	962 (1195)	**<0.001**
Ferritin, µg/L	330.5 (578)	290 (592)	349.5 (573)	0.23
Treatment				
Corticosteroid treatment, n	336 (32.4%)	53 (11.5%)	283 (49.3%)	**<0.001**
LMWH treatment, n	735 (70.9%)	215 (46.5%)	520 (90.6%)	**<0.001**
Tocilizumab treatment, n	7 (0.7%)	3 (0.7%)	4 (0.7%)	1.00
ICU admission, n	104 (10%)	57 (12.2%)	47 (8.2%)	**0.04**
Exitus, n	75 (7.2%)	50 (10.7%)	25 (4.4%)	**<0.001**

Data are presented as median (interquartile range) if otherwise is not stated enter. SD: Standard deviation, LDH: Lactate dehydrogenase, CRP: C-reactive protein, LMWH: Low molecular weight heparin, ICU: Intensive care unit

In a study conducted in Madrid, 276 patients who were admitted to the hospital in a one-month period in each wave were examined[13]. While there was a significant age difference between moderate and critical patients in the first wave (64 years & 67.5 years, p=0.038); no difference was detected in the 2nd wave. In terms of respiratory failure, a significant difference was found between moderate and critically ill patients in both waves in favor of critically ill patients (p<0.001)[14]. In our study, the mean age was found to be higher in the second wave, but the fact that the patients were not divided into moderate and critical, was the most important difference between the two studies.

In another study conducted in the USA, a total of 4434 patients were evaluated, of which 1313 (29.6%) were from the 1st wave and 3121 (70.4%) from the 2nd wave[18]. The average age was higher in 2nd wave as it was in our study (66.7±17.1 years vs. 68.0±16.9 years, p=0.021). Contrary to our study, the median ferritin, CRP, LDH and D-dimer were higher in the 1st wave (p<0.05)[18]. But mortality was significantly higher in the 1st wave as compared to the 2nd wave (23.2% vs. 12.3%, p<0.001). This result was a finding that supported the results of our study.

Our study is unique in this field, because although there were studies on this subject from different countries, such a study has not been done before in our hospital and in our region, and it was mostly presented as side data in our country. Although we have to deal with different waves of the COVID-19 disease in these days, the 1st and 2nd waves were very important in understanding the course of the disease. The lower need for ICU and mortality rates during the 2nd wave showed that we had known the disease better and that we got more positive results by starting treatment earlier in the 2nd wave. Beside from treatment options, implementation of social prevention measures and effective application of these measures like social distance, mask wearing, hygiene to whole public should have role in this difference. The first wave started to decline after curfew, travel restrictions and other policy measures with mask and social distance measures[6]. One other parameter influencing the beginning of new waves of pandemic is the emergence of new variants which may have different properties causing change in transmissibility, severity, and resistance of the virus[19].

Study Limitations

Our study had some limitations. It was a retrospective and single-center study. Although the number of our patients was similar to most studies in the literature, studies with a larger number of patients may show more significant

results. Another limitation was that the clinical findings of the patients were not mentioned due to the inadequacy of the database.

Conclusion

The patients in the second wave of COVID-19 pandemic were older, had more comorbidities, and had worse laboratory parameters; but they had less need for ICU and better survival. Comparing the first and second waves will allow us to understand the difference with the second and later waves; and our study is important in this respect.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital Non-Interventional Research Ethics Committee (decision no: 2021/62-66, date: 05.11.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.E., G.P., Ö.Ö., D.S.U., Ö.S.U., Design: S.E., G.P., Ö.Ö., D.S.U., Ö.S.U., Data Collection or Processing: S.E., G.P., D.S.U., Ö.S.U., Analysis or Interpretation: S.E., G.P., Ö.Ö., Literature Search: S.E., G.P., Ö.Ö., D.S.U., Ö.S.U., Writing: S.E., G.P., Ö.Ö., D.S.U., Ö.S.U.

Conflict of Interest: No conflict of interest was declared by the authors.

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

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