ORIGINAL RESEARCH

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A Multicenter Evaluation of the Temporal and Clinical Differences of COVID-19 in Two Different Regions in Turkey: Comparison of İstanbul and Diyarbakır

Türkiye'de İki Farklı Bölgede COVID-19'un Zamansal ve Klinik Farklılıklarının Çok Merkezli Bir Değerlendirmesi: İstanbul ve Diyarbakır'ın Karşılaştırılması

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Abstract

Objective: This study compared the temporal course of virulence and symptomatology of severe coronavirus-19 (COVID-19) infection in two metropolitan cities with different geographic features. The study aimed to shed light on the possible etiology of the differences observed between two regions.

Method: We retrospectively reviewed polymerase chain reaction confirmed COVID-19 cases for the period of March-June 2020 in two different cities (İstanbul and Diyarbakır) located in northern and southern parts of Turkey, respectively. Data on demographic features, presenting symptoms, clinical history, radiological findings, laboratory parameters, and mean hospitalization duration were collected. Additionally, meteorological data including daily temperature, diurnal temperature variation, relative humidity, wind speed, mean rainfall, ultraviolet index, altitude, and latitude were retrieved for the study period.

Results: Total case number was higher in İstanbul during March and April, whereas it was higher in Diyarbakır during May and June (p=0.001). During the study period, daily temperature, diurnal temperature variation, and ultraviolet index were higher in Diyarbakır, whereas relative humidity, wind speed, and mean rainfall was higher in İstanbul (p=0.001). In Diyarbakır, patients presented with a predominance of dyspnea, whereas there was a predominance of fever and cough in İstanbul. Patients in

Öz

Amaç: Bu çalışmada, farklı coğrafi özelliklere sahip iki büyükşehirde şiddetli koronavirüs-19 (COVİD-19) enfeksiyonunun virülansının zamansal seyri ve semptomatolojisi karşılaştırıldı. Çalışmada, iki bölge arasında gözlenen farklılıkların olası etiyolojisine ışık tutulması amaçlandı.

Yöntem: Mart-Haziran 2020 döneminde Türkiye'nin kuzey ve güney kesimlerinde bulunan iki farklı şehirde (İstanbul ve Diyarbakır) polimeraz zincir reaksiyonu ile doğrulanmış COVİD-19 olgularını geriye dönük olarak inceledik. Demografik özellikler, başvuru semptomları, geçmiş klinik öykü, radyolojik bulgular, laboratuvar parametreleri ve ortalama hastanede yatış süresi kaydedildi. Ayrıca çalışma dönemi için günlük sıcaklık, günlük sıcaklık değişimi, bağıl nem, rüzgar hızı, ortalama yağış, ultraviyole indeksi, yükseklik ve enlem gibi meteorolojik veriler de elde edildi.

Bulgular: Toplam olgu sayısı İstanbul'da Mart ve Nisan aylarında daha yüksek iken, Diyarbakır'da Mayıs ve Haziran aylarında daha yüksekti (p=0,001). Çalışma süresi boyunca Diyarbakır'da günlük sıcaklık, günlük sıcaklık değişimi ve ultraviyole indeksi daha yüksek iken, İstanbul'da bağıl nem, rüzgar hızı, ortalama yağış miktarı daha yüksek bulundu (p=0,001). Diyarbakır'da hastalar daha çok nefes darlığı ile başvururken, İstanbul'da ise ateş, öksürük hakimdi. Diyarbakır'daki hastaların nötrofil, nötrofil/lenfosit oranı, D-dimer, laktat dehidrogenaz, ferritin ve C-reaktif protein

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Abstract

Diyarbakır had significantly elevated neutrophil, neutrophil/lymphocyte ratio, D-dimer, lactate dehydrogenase, ferritin and C-reactive protein values compared to patients in İstanbul (p=0.018; p=0.006; p=0.001, p=0.001; p=0.001, p=0.001 respectively). The predominant computed tomography infiltration was multicentric and bilateral crazy-paving pattern in Diyarbakır, whereas unilateral ground-glass opacity was the dominant pattern in İstanbul.

Conclusion: The socio-cultural and genetic factors may affect the epidemiological, clinical and imaging features of COVID-19 more than meteorological variations.

Keywords: COVID-19, etiology, geographic features

Öz

değerleri İstanbul'daki hastalara göre anlamlı olarak yüksekti (p=0,018; p=0,006; p=0,001, p=0,001; p=0,001, p=0,001 sırasıyla). Diyarbakır'da baskın bilgisayarlı tomografi infiltrasyonu multisentrik ve bilateral crazy paving paterni iken, İstanbul'da tek taraflı buzlu cam opasitesi baskın paterndi.

Sonuç: Sosyo-kültürel ve genetik faktörler, COVİD-19'un epidemiyolojik, klinik ve görüntüleme özelliklerini meteorolojik varyasyonlardan daha fazla etkileyebilir.

Anahtar kelimeler: Coğrafi özellikler, COVID-19, etiyoloji

Introduction

Initial detection and peaking of Coronavirus disease-2019 (COVID-19) cases in Turkey were seen relatively later compared to the rest of the European countries. The first COVID-19 case in Turkey was confirmed on March 11, 2020 in İstanbul according to the data published by the Turkish Ministry of Health. In the upcoming weeks, İstanbul, which is a cosmopolitan city with a population of 15 million (constituting 20% of Turkey's population) and a high density national and international city hub, became the epicenter of the disease. The peak period was seen within 2 months with a subsequent plateau phase, similar to other countries. On the other hand, Diyarbakır and other cities located in the Southeastern Turkey did have limited case numbers in the initial phase of infection with a later peak period in 3-4 months. Additionally, hospitalized cases in these southeastern cities had more severe clinical and radiological courses.

Host-related genetic factors may affect infectivity, disease course, and mortality (1). Human genetics have a high similarity ratio; however, *HLA* genes which constitute the pillars of human immune system and immune response to an infectious or allergic factor show considerable variation (2,3). The main entry mechanism of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is via ACE-2 receptors (4,5). Increased ACE-2 expression by host cells may increase viral pathogenicity, replication, and cellular damage (6,7). Several studies have shown a correlation between host ACE-2 receptor numbers and viral load and disease severity (8). On the other hand, mounted immune response is the most important factor in infection control and determines the disease severity, complication, and mortality.

COVID-19 may have variable clinical course ranging from asymptomatic carrier state to a fatal outcome. 18-30% of cases can be asymptomatic or mildly symptomatic, with higher complication and mortality rates seen in elderly males with comorbidities (9-13). In addition to more severe disease course, this susceptible population has higher hospitalization and intensive care unit admission rates. Younger adults usually have milder or even asymptomatic form of the disease; however, even immunocompetent healthy young adults with no risk factors or comorbidities may have severe disease course. There are numerous studies investigating the relationship between the disease course and viral (viral load, pathogenicity, viral genetic subtype/mutation analysis), host (age, sex, ACE-2 receptor status/polymorphism, immune status, comorbidities), environmental (temperature, humidity, rainfall, wind speed), and socio-economic factors (ethnicity, culture, lifestyle, abiding/adapting to isolation and disinfection measures). However, no ground truth could be established to predict transmission dynamics and disease course.

In this study, we assessed the temporal course of clinical and radiological findings of COVID-19 cases in two hospitals from different regions of Turkey. Our aim was to evaluate the relationship between clinical/radiological findings and meteorological, socio-economic, ethnic and genetic variables.

Materials and Methods

Study Population

This study was approved by the Local Ethics Committee (date: 11.06.2020 number: 2020/12). We retrospectively reviewed polymerase chain reaction confirmed COVID-19 cases from two hospitals, Acıbadem Kozyatağı Hospital and Diyarbakir Selahaddin Eyyubi State Hospital, in two different cities in Turkey for the period of March-June 2020. Demographic features, presenting symptoms, clinical history, radiological findings [typical vs atypical lung computed tomography (CT) features, infiltration pattern, and distribution], laboratory parameters [(C-reactive

protein (CRP), leukocyte, neutrophil, lymphocyte counts, hemoglobin, thrombocyte, D-dimer, lactate dehydrogenase (LDH) levels], and mean hospitalization duration were collected.

Meteorological Parameters

Monthly meteorological data including daily temperature, diurnal temperature variation, relative humidity, wind speed, mean rainfall, ultraviolet index, altitude, and latitude were retrieved for the study period. Also, air pollution quality index was recorded.

Radiological Assessment

Chest CT scans were acquired with Siemens Somatom Sensation-Syngo CT and GE Optima 660 in İstanbul and Diyarbakır, respectively. A single radiologist with 10 years of experience in thorax radiology assessed all CT images from two centers based on the Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19 (14). CT images were reviewed for typical/atypical disease patterns, dominant infiltration patterns (ground-glass, crazy-paving, consolidation), and distribution of parenchymal involvement (unilateral/bilateral involvement, lower/upper lobe predominance, diffuse/peripheral/central/mixed). Additionally, changes at follow-up chest CT scans were assessed.

Statistical Analysis

All statistical analyses were performed with NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA). Descriptive statistics were expressed as number and percentage for categorical variables and as mean, standard deviation, median, minimum, and maximum for numerical variables. The Shapiro-Wilk test was used to determine whether the data showed normal distribution. The Student's t-test and Mann-Whitney U test were used for parametric and non-parametric data, respectively. For categorical variables, the chi-square, Fisher's Exact and Fisher-Freeman-Halton Exact tests were used. The Spearman test was used for correlation. A p-value of <0.05 was considered statistically significant.

Results

A total of 429 cases from two cities (Acıbadem Kozyatağı Hospital in İstanbul, Gaziantep Selahaddin Eyyubi State Hospital in Diyarbakır) with a slight male dominance (209 (48.7%) female, 220 (51.3%) male patients) were included in the study. The mean age of the study population was 50.43±16.72 years (5-93). There was a female predominance with a slightly older population (52.06±17.73 years) in patients recruited from Diyarbakır (p=0.049) (Table 1) (Figure 1).

The total case number was higher in İstanbul during March and April, whereas it was higher in Diyarbakır during May and June (p=0.001) (Figure 1). The interval between symptom onset and presentation to the hospital was significantly higher in Diyarbakır (5.34±3.12/3.27±1.26, p=0.001). There was a significantly higher hospitalization rate among presenting patients in Diyarbakır (99.5%/47.8%, p=0.001) with no significant difference in the duration of hospitalization (5.59±3.43/5.85±3.71, p=0.595) (Table 1).

There was no significant difference in comorbidity rates between the two cities. In Diyarbakır, patients presented with a predominance of dyspnea, and myalgia whereas there was a predominance of fever, cough, headache, sore throat, and loss of appetite in İstanbul (Table 1).

Though patients in Diyarbakır had lower white blood cell values compared to İstanbul cases, this difference did not reach a statistical significance (p=0.057). Patients in Diyarbakır had significantly elevated neutrophil, neutrophil/lymphocyte ratio, D-dimer, LDH, ferritin and CRP values compared to those in İstanbul (p=0.018; p=0.006; p=0.001, p=0.001; p=0.001, p=0.001, respectively) (Table 2).

There were significant differences in abnormal chest CT findings according to the number of lesions between the two cities (p=0.001). There was a significant tendency for multiple and bilateral infiltration patterns in Diyarbakır compared to İstanbul (p=0.001). A total of 19% cases had normal CT findings in İstanbul whereas this rate was 4.3% in Diyarbakır. 50% of cases in İstanbul had a typical COVID-19 infiltration pattern whereas 88% of cases in Diyarbakır had the typical COVID-19 infiltration pattern. The predominant CT infiltration was a crazy-paving pattern in Diyarbakır whereas unilateral, solitary ground-glass opacity was the dominant pattern in Istanbul (Tables 3 and 4).

During the study period, daily temperature, diurnal temperature variation, and the ultraviolet index were significantly higher in Diyarbakır compared to İstanbul (p=0.001) (Figure 1). Similarly, the UV index was significantly higher in Diyarbakır compared to İstanbul whereas relative humidity, wind speed, and mean rainfall were higher in İstanbul (p=0.001) (Tables 5 and 6) (Figure 1). The mean air pollution index was 87 (moderate) in Diyarbakır and 101

Table 1. Evaluation of descriptive characteristics by city

			City		
		Total (n=429)	İstanbul (n=224)	Diyarbakır (n=205)	p
Age	**Min-max (median)**	5-93 (49)	5-93 (47)	17-87 (53)	[a]**0.054**
	Mean ± SD	50.43±16.72	48.94±15.64	52.06±17.73	
Gender	**Female**	209 (48.7)	99 (44.2)	110 (53.7)	[b]**0.049***
	Male	220 (51.3)	125 (55.8)	95 (46.3)	
Hospitalization	**No**	118 (27.5)	117 (52.2)	1 (0.5)	[b]**0.001****
	Yes	331 (72.5)	107 (47.8)	204 (99.5)	
Average hospitalization time	Min-max (median)	1-34 (5)	1-20 (5)	1-34 (5)	[c]**0.595**
	Mean ± SD	5.68±3.53	5.85±3.71	5.59±3.43	
Interval between symptom onset to the hospital	Min-max (median)	1-15 (3)	1-8 (3)	1-15 (4)	[c]**0.001****
	Mean ± SD	4.26±2.55	3.27±1.26	5.34±3.12	
Month	**March**	101 (23.5)	89 (39.7)	12 (5.9)	[b]**0.001****
	April	183 (42.7)	117 (52.2)	66 (32.2)	[b]**0.001****
	May	54 (12.6)	16 (7.2)	38 (18.5)	[b]**0.001****
	June	91 (21.2)	2 (0.9)	89 (43.4)	[b]**0.001****
Comorbidities		76 (17.7)	38 (17.0)	38 (18.5)	[b]**0.670**
Complaints	**Headache**	88 (20.5)	59 (26.3)	29 (14.1)	[b]**0.002****
	Anorexia	84 (19.6)	62 (27.7)	22 (10.7)	[b]**0.001****
	Cough	230 (53.6)	133 (59.4)	97 (47.3)	[b]**0.012***
	Shortness of breath	125 (29.1)	48 (21.4)	77 (37.6)	[b]**0.001****
	Weakness	137 (31.9)	43 (19.2)	94 (45.9)	[b]**0.001****
	Sore throat	54 (12.6)	36 (16.1)	18 (8.8)	[b]**0.023***
	Fever	181 (42.2)	129 (57.6)	52 (25.4)	[b]**0.001****

[a]: Student's t-test, [b]: Pearson's chi-square test, [c]: Mann-Whitney U test, *p<0.05, **p<0.01, SD: Standard deviation

(unhealthy for sensitive groups) in İstanbul between March and June 2020.

Discussion

Some of the most intriguing points about the COVID-19 pandemic are variability in transmission rates, clinical course and mortality rates among different countries and regions. Differences in national healthcare policies, type and amount of testing, isolation and treatment protocols might be some of the underlying factors (15). Additionally, variability in climate conditions might affect the virus pathogenicity (16,17). Ma et al. (16), in a study investigating the effects of temperature, humidity and diurnal temperature variation on COVID-19 mortality, reported a negative correlation with temperature and humidity and a positive correlation with diurnal temperature variation (18,19). Additionally, studies reported the effects of other different meteorological parameters like ultraviolet index and wind speed on virulence and transmission rates (16,20,21). However, the results of our study showed a later peak and more severe disease course in Diyarbakır despite higher temperature and ultraviolet index, suggesting

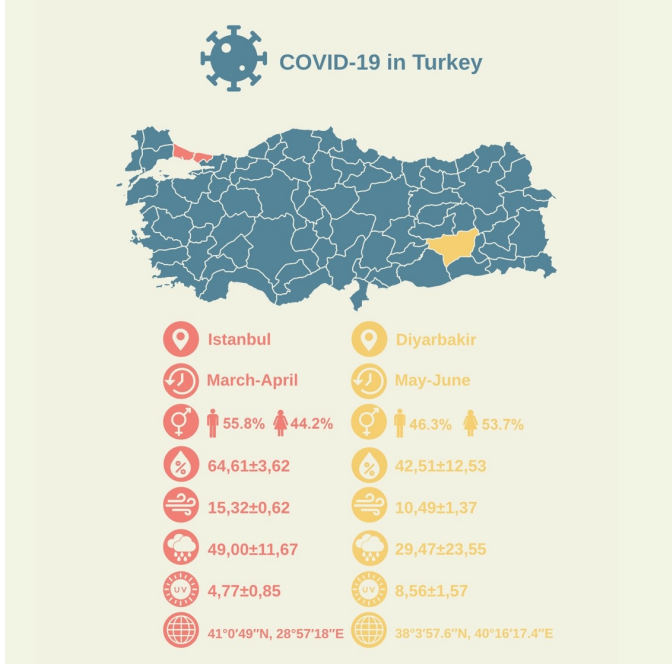

Figure 1. Temporal differences of Diyarbakır and İstanbul according to their geographical locations

COVID-19: Coronavirus disease

Table 2. Evaluation of laboratory findings by city

			City		
		Total (n=429)	İstanbul (n=224)	Diyarbakır (n=205)	p
WBC	Min-max (median)	2.5-23.1 (7)	2.5-20 (7)	2.6-23.1 (6.84)	[c]**0.057**
	Mean ± SD	7.83±3.41	8.01±3.24	7.64±3.58	
NEU (%)	Min-max (median)	0-93.6 (66.1)	0-92.4 (62.7)	35.9-93.6 (70.1)	[a]**0.001****
	Mean ± SD	65.52±13.95	61.93±14.69	69.22±12.12	
LYMP (%)	Min-max (median)	2.5-75.2 (23.4)	2.5-75.2 (24)	3-54.8 (22.1)	[a]**0.031***
	Mean ± SD	24.27±11.31	25.45±11.98	23.06±10.48	
NEU	Min-max (median)	1.1-18.41 (4.43)	1.1-14.3 (4.08)	1.1-18.41 (4.58)	[c]**0.018***
	Mean ± SD	5.09±2.84	4.77±2.65	5.42±3.00	
LYMP	Min-max (median)	0.27-8.56 (1.49)	0.27-8.56 (1.57)	0.3-7.52 (1.44)	[c]**0.236**
	Mean ± SD	1.68±0.97	1.72±0.98	1.63±0.96	
N/L	Min-max (median)	0.2-37.3 (2.85)	0.2-37.3 (2.65)	0.7-30.8 (3.16)	[c]**0.006****
	Mean ± SD	4.14±4.51	3.92±4.83	4.36±4.15	
D-dimer	n	342	150	192	[c]**0.001****
	Min-max (median)	0-1210 (25.3)	0-138 (19)	1.5-1210 (54.5)	
	Mean ± SD	4.9±10.65	1.5±18	8.73±130	
HGB	n	413	210	203	[a]**0.680**
	Min-max (median)	5.4-17.3 (13.7)	9.1-17.3 (13.7)	5.4-17 (13.7)	
	Mean ± SD	13.48±1.83	13.52±1.75	13.45±1.92	
PLT	n	413	209	204	[a]**0.880**
	Min-max (median)	12.2-562 (208)	12.2-562 (209)	80-466 (207.5)	
	Mean ± SD	216.74±74.38	216.19±75.6	217.3±73.3	
LDH	n	262	129	133	[c]**0.001****
	Min-max (median)	81-649 (221.5)	81-489 (181)	132-649 (255)	
	Mean ± SD	246.4±103.78	201.23±72.4	290.21±110.83	
Ferritin	n	138	38	100	[c]**0.001****
	Min-max (median)	0-1588 (107.1)	0-1002 (88)	5.4-1588 (259.55)	
	Mean ± SD	229.13±285.3	21±41	316.12±291.34	
CRP	n	301	97	204	[c]**0.001****
	Min-max (median)	0-350 (8.5)	0-17 (0.71)	1.5-350 (24.5)	
	Mean ± SD	35.95±58.14	2.08±3.18	52.05±64.67	

[a]: Student's t-test, [c]: Mann-Whitney U test, *p<0.05, **p<0.01, SD: Standard deviation, CRP: C-reactive protein, LDH: Lactate dehydrogenase, PLT: Platelet count, HGB: Hemoglobin, WBC: White blood cell, NEU: Neutrophil, LYMP: Lymphocyte

that the effect of meteorological variations on disease virulence and transmission rates might be limited. Patients in İstanbul generally had a milder COVID-19 infection, similar to other viral upper respiratory tract infections. We think that these parameters may be an important factor for the virus to remain as an upper respiratory tract infection without descending to the lower respiratory tract.

Cultural differences affect the social life and behavior. Consequently, this might influence the dynamics of infectious disease like transmission rates and isolation control. Since the main transmission route is respiratory droplets, increased population density and high population mobility may account for higher transmission rates and increased case numbers in crowded cities like İstanbul. Southeastern cities like Diyarbakır have extended family structure with a much higher rate of social interaction. Traditional wedding ceremonies and funeral services with limited social isolation practice might account for high number of cases in relatively less densely populated cities like Diyarbakır. Additionally, lower educational levels in Diyarbakır may have led to lower rates of personal protective equipment utilization. We think that higher rates encountered in Diyarbakır might be related to differences in socio-cultural and educational differences. In support of this hypothesis, a study from Brazil reported varying mortality rates across different regions and ethnicities and suggested that this regional difference might be related to socio-economic factors (22). According to the results of our study, we think that sociocultural characteristics are more effective in the spread of the disease.

Table 3. Evaluation of radiological findings by city

		City			p
		Total	İstanbul	Diyarbakır	
		n (%)	n (%)	n (%)	
CT	**▪Normal**	52	43	9	[b]**0.468**
	Typical	293 (77.7)	113 (62.4)	180 (91.8)	
	Atypical	84 (22.3)	68 (37.6)	16 (8.2)	
	▪Normal	52	43	9	[b]**0.001****
	Single	180 (47.7)	145 (80.1)	35 (17.9)	
	Multiple	197 (52.3)	36 (19.9)	161 (82.1)	
Percentage of parenchyma in the progression phase	**1**	195 (51.7)	60 (33.1)	135 (68.9)	[d]**0.001****
	2	163 (43.2)	121 (66.9)	42 (21.4)	
	3	15 (4.0)	0 (0.0)	15 (7.7)	
	4	4 (1.1)	0 (0.0)	4 (2.0)	
Side	**Unilateral**	79 (21.0)	60 (33.1)	19 (9.7)	[b]**0.001****
	Bilateral	298 (79.0)	121 (66.9)	177 (90.3)	
Dominant infiltration pattern	**Ground glass**	184 (49.3)	102 (57.6)	82 (41.8)	[b]**0.001****
	Crazy-paving	133 (35.7)	43 (24.3)	90 (45.9)	
	Consolidation	56 (15.0)	32 (18.1)	24 (12.2)	
Dominant distribution	**Lower lobe**	224 (59.9)	115 (64.6)	109 (55.6)	[b]**0.083**
	Upper lobe	59 (15.8)	29 (16.3)	30 (15.3)	
	Common	91 (24.3)	34 (19.1)	57 (29.1)	
Distribution	**Basal/peripheral**	238 (63.1)	103 (56.9)	135 (68.9)	[b]**0.001****
	Central	55 (14.6)	41 (22.7)	14 (7.1)	
	Common	84 (22.3)	37 (20.4)	47 (24.0)	
Largest lesion diameter	n	259	131	128	[c]**0.425**
	Min-max (Median)	1-20 (3)	1-20 (3)	1-15 (3)	
	Mean ± SD	4.16±2.84	4.47±3.40	3.84±2.10	
Pleural effusion		42 (11.1)	22 (12.2)	20 (10.2)	[b]**0.548**
Pleural thickening		135 (35.8)	65 (35.9)	70 (35.7)	[b]**0.968**
Fibrotic band		101 (26.8)	73 (40.3)	28 (14.3)	[b]**0.001****
Stage of the disease in the first CT	**Early**	116 (39.6)	59 (52.2)	57 (31.7)	[b]**0.001****
	Consolidation	162 (55.3)	47 (41.6)	115 (63.9)	
	Dissolution	15 (5.1)	7 (6.2)	8 (4.4)	

[b]: Pearson's chi-square test, [c]: Mann-Whitney U test, [d]: Fisher-Freeman-Halton test, **p<0.01, ▪not included in the comparison, CT: Computed tomography, SD: Standard deviation

In addition to regional differences across countries, differences in temporal course, infectivity and pathogenicity have been reported in different districts of the same city. A study evaluating the effect of ethnicity, socio-economic and educational status on hospitalization and mortality rates in different districts of New York reported worse outcomes in Bronx, which have a higher ratio of African American young adult population (23). This supports the hypothesis that lower socio-economic and educational status and ethnicity may affect mortality rate more than patient's age.

Viral and host-related genetic variations have been extensively studied for their effects on infectivity, disease severity and mortality. Variations in viral structure may account for the differences seen in disease severity and mortality across different nations. Karacan et al. (24) isolated 3 different viral strains in a patient population with different clinical course (mild-moderate-severe).

In the present study, hospitalization rates were significantly higher for Diyarbakır. It is possible to explain this situation with the fact that, first, the patients in Diyarbakır had a more severe disease; secondly, those who applied to the hospital in Diyarbakır were most seriously ill; and mild-moderate patients were not admitted to the hospital. On the contrary, in İstanbul, even mild to moderate patients were admitted to the hospital and were hospitalized for different indications.

Table 4. Evaluation of radiological findings of patients with typical CT results by city

CT: Typical		City		p
		İstanbul	Diyarbakır	
		n (%)	n (%)	
	Single	87 (77.0)	30 (16.7)	[b]0.001**
	Multiple	26 (23.0)	150 (83.3)	
Percentage of parenchyma in the progression phase	1	30 (26.5)	124 (68.9)	[d]0.001**
	2	83 (73.5)	39 (21.7)	
	3	0 (0.0)	13 (7.2)	
	4	0 (0.0)	4 (2.2)	
Side	Unilateral	30 (26.5)	17 (9.4)	[b]0.001**
	Bilateral	83 (73.5)	163 (90.6)	
Dominant infiltration pattern	Ground glass	63 (55.8)	73 (40.6)	[b]0.033*
	Crazy-paving	37 (32.7)	84 (46.7)	
	Consolidation	13 (11.5)	23 (12.8)	
Dominant distribution	Lower lobe	68 (60.2)	100 (55.6)	[b]0.738
	Upper lobe	15 (13.3)	27 (15.0)	
	Common	30 (26.5)	53 (29.4)	
Distribution	Basal/peripheral	57 (50.4)	128 (71.1)	[b]0.001**
	Central	25 (22.1)	11 (6.1)	
	Common	31 (27.4)	41 (22.8)	
Largest lesion diameter	n	99	124	[c]0.486
	Min-max (median)	1-20 (3)	1-15 (3)	
	Mean ± SD	4.30±3.19	3.77±2.03	
Pleural effusion		10 (8.8)	20 (11.1)	[b]0.534
Pleural thickening		39 (34.5)	68 (37.8)	[b]0.572
Fibrotic band		47 (41.6)	27 (15.0)	[b]0.001**

[b]: Pearson's chi-square test, [c]:Mann-Whitney U test, [d]: Fisher-Freeman-Halton test, **p<0.01, SD: Standard deviation, CT: Computed tomography

Table 5. Evaluation of climatic conditions by city

			City		
		Total (n=429)	İstanbul (n=224)	Diyarbakır (n=205)	p
Daytime air temperature	Min-max (median)	11.5-31.9 (16)	11.5-25 (16)	13.3-31.9 (24.5)	[c]0.001**
	Mean ± SD	19.71±7.20	14.65±2.88	25.24±6.39	
Night air temperature	Min-max (median)	8.6-29.6 (11.9)	8.6-20.2 (11.9)	9.3-26.9 (18.9)	[c]0.001**
	Mean ± SD	15.48±6.54	10.97±2.31	20.42±6.08	
Temperature difference	Min-max (median)	2.9-5.58 (4.13)	2.9-4.8 (4.13)	4-5.58 (5)	[c]0.001**
	Mean ± SD	4.23±0.80	3.68±0.62	4.82±0.50	
Humidity	Min-max (median)	29-69 (62)	59-69 (62)	29-63 (46)	[c]0.001**
	Mean ± SD	54.05±14.28	64.61±3.62	42.51±12.53	
Wind speed	Min-max (median)	9-16 (14)	14-16 (15)	9-12 (10)	[c]0.001**
	Mean ± SD	13.01±2.63	15.32±0.62	10.49±1.37	
Rainfall	Min-max (median)	4-63 (41)	31-63 (41)	4-56 (35)	[c]0.001**
	Mean ± SD	39.67±20.75	49.00±11.67	29.47±23.55	
UV angle	Min-max (median)	4-10 (5)	4-8 (5)	5-10 (9)	[c]0.001**
	Mean ± SD	6.58±2.27	4.77±0.85	8.56±1.57	

[c]: Mann-Whitney U test, **p<0.01, SD: Standard deviation

Table 6. Evaluation of radiological findings by cities in patients with atypical CT findings

CT: Atypical		City		p
		İstanbul	Diyarbakır	
		n (%)	n (%)	
	Single	58 (85.3)	5 (31.3)	[e]0.001**
	Multiple	10 (14.7)	11 (68.8)	
Percentage of parenchyma in the progression phase	1	30 (44.1)	11 (68.8)	[d]0.003**
	2	38 (55.9)	3 (18.8)	
	3	0 (0.0)	2 (12.5)	
Side	Unilateral	30 (44.1)	2 (12.5)	[b]0.019*
	Bilateral	38 (55.9)	14 (87.5)	
Dominant infiltration pattern	Ground glass	39 (60.9)	9 (56.25)	[d]0.010*
	Crazy-paving	6 (9.4)	6 (37.50)	
	Consolidation	19 (29.7)	1 (6.25)	
Dominant distribution	Lower lobe	50 (73.5)	9 (56.3)	[d]0.74
	Upper lobe	14 (20.6)	3 (18.8)	
	Common	4 (5.9)	4 (25.0)	
Distribution	Basal/peripheral	43 (66.2)	7 (43.8)	[d]0.028*
	Central	16 (24.6)	3 (18.8)	
	Common	6 (9.2)	6 (37.5)	
Largest lesion diameter	n	32	4	[c]0.416
	Min-max (median)	1-20 (5)	2-10 (6)	
	Mean ± SD	5.00±3.98	6.00±3.27	
Pleural effusion		12 (17.6)	0 (0.0)	[e]0.111
Pleural thickening		26 (38.2)	2 (12.5)	[b]0.049*
Fibrotic band		26 (38.2)	1 (6.3)	[b]0.014*

[b]: Pearson's chi-square test, [c]: Mann-Whitney U test, [d]: Fisher-Freeman-Halton test, [e]: Fisher's Exact test, **p<0.01, SD: Standard devaition, CT: Computed tomography

Study Limitations

This study, in which we compared the temporal course of virulence and symptomatology of SARS-CoV-2 infection in two different cities, despite being a multicenter study, is still limited by lack of multiple centers from the same city. Additionally, we did not have access to regional Turkish Ministry of Health data for these two cities, which limited the assessment of actual infectivity and mortality rate for these two cities in total. We could not obtain genetic analysis due to limited funding, which renders the genetic differences between patient populations an assumption at best.

Conclusion

COVID-19 infectivity, pathogenicity, clinical course and mortality rates show variation across nations, cities and individuals. In addition to age, sex and comorbidities, environmental, meteorological, socio-economical, and racial factors might account for some of these variations.

Main points

1. The clinical course of COVID-19 varies according to host-related factors (age, sex, race, ACE-2 receptor status/polymorphism, immune status, comorbidities).

2. Environmental parameters such as temperature, humidity, rainfall, and wind speed can affect COVID-19 virulence.

3. Socio-economic status and cultural characteristics affect the spread of the disease.

Ethics

Ethics Committee Approval: This study was approved by the Local Ethics Committee (date: 11.06.2020 number: 2020/12). We retrospectively reviewed polymerase chain reaction confirmed COVID-19 cases from two hospitals, Acıbadem Kozyatağı Hospital and Diyarbakir Selahaddin Eyyubi State Hospital, in two different cities in Turkey for the period of March-June 2020.

Informed Consent: Written informed consent for publication was not necessary because no identifying patient data have been included in this manuscript.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: Ö.V., D.E.T.Ş., A.A., Design: Ö.V., D.E.T.Ş., A.A., Data Collection or Processing: Ö.V., D.E.T.Ş., Analysis or Interpretation: D.E.T.Ş., A.N.Ş., A.A., Drafting Manuscript: Ö.V., D.E.T.Ş., A.N.Ş., Critical Revisation of Manuscript: D.E.T.Ş., A.N.Ş., A.A., Final Approval and Accountability: Ö.V., D.E.T.Ş., A.N.Ş., A.A.

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