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## Original

# Evaluating the characteristics of patients with SARS-CoV-2 infection admitted during COVID-19 peaks: A single-center study

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### ABSTRACT

**Background:** Nowadays, the world is facing a coronavirus disease (COVID-19) pandemic, elicited by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). At the time of studying, five COVID-19 waves occurred in Iran. We aimed to evaluate the characteristics of patients with SARS-CoV-2 infection admitted to Vasei Hospital of Sabzevar, Iran during COVID-19 peaks.

**Methods:** Clinical manifestations, laboratory findings, radiological findings, and underlying diseases of patients with COVID-19 were obtained from electronic medical records. Then, this information was compared in patients with SARS-CoV-2 infection to the peaks of COVID-19.

**Results:** The highest and lowest respiratory involvements were observed in the third (74.6%) and fourth (38.8%) peaks, respectively. The most common radiological finding in all peaks was ground-glass opacity (28.98%), followed by consolidation, which was the highest (14.6%) in peak three. The lymphocyte count decreased in all peaks. Its highest reduction (16.12) occurred in the third peak. The SpO<sub>2</sub> was lower than normal range in all peaks, except for the second (90.77%) and fifth (91.06%) peaks. Dyspnea (52.36%) was the most and dizziness (1.26%) and sore throat (0.6%) were the least frequent symptoms. The mortality rates were 14.4%, 18.2%, 23%, 9.02%, and 9.4% in the first to fifth peaks, respectively.

**Conclusion:** As different variants of the SARS-CoV-2 virus were predominant in each wave, COVID-19 patients had different features in various peaks. The fifth wave of COVID-19 had the highest number of hospitalized patients, while the first peak had the lowest number. Perhaps, the significant increase in testing capacity in the fifth wave and its long time period are the reasons for this growth. Most of the clinical symptoms were similar in all peaks, but the incidence was different. As patients hospitalized in the third peak had the

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highest rate of underlying disease, it can be a reason for the increase in the death rate of patients. We did not observe any significant differences in laboratory tests among the patients during different peaks. Thus, we should be vigilant in continuously studying the characteristics of the disease, and be able to modify treatments rapidly if necessary.

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## Evaluación de las características de los pacientes con infección por SARS-CoV-2 ingresados durante los Picos de COVID-19: Un estudio de un solo centro

### R E S U M E N

#### Palabras clave:

SARS-CoV-2

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**Antecedentes:** Hoy en día, el mundo se enfrenta a una pandemia de enfermedad por coronavirus (COVID-19), provocada por el síndrome respiratorio agudo severo coronavirus 2 (SARS-CoV-2). En el momento del estudio, se produjeron cinco olas de COVID-19 en Irán. Nuestro objetivo fue evaluar las características de los pacientes con infección por SARS-CoV-2 ingresados en el Hospital Vasei de Sabzevar, Irán, durante los picos de COVID-19.

**Métodos:** Las manifestaciones clínicas, los hallazgos de laboratorio, los hallazgos radiológicos y las enfermedades subyacentes de los pacientes con COVID-19 se obtuvieron de los registros médicos electrónicos. Luego, esta información se comparó en pacientes con infección por SARS-CoV-2 a los picos de COVID-19.

**Resultados:** Las afectaciones respiratorias más altas y más bajas se observaron en el tercer (74,6%) y cuarto (38,8%) picos, respectivamente. El hallazgo radiológico más frecuente en todos los picos fue la opacidad en vidrio esmerilado (28,98%), seguida de la consolidación, que fue la más alta (14,6%) en el pico tres. El recuento de linfocitos disminuyó en todos los picos. Su mayor reducción (16,12) se produjo en el tercer pico. La SpO2 estuvo por debajo del rango normal en todos los picos, excepto en el segundo (90,77%) y quinto (91,06%) picos. La disnea (52,36%) fue el síntoma más frecuente y el mareo (1,26%) y el dolor de garganta (0,6%) los síntomas menos frecuentes. Las tasas de mortalidad fueron 14,4%, 18,2%, 23%, 9,02% y 9,4% en los picos primero a quinto, respectivamente.

**Conclusión:** Como en cada oleada predominaban diferentes variantes del virus SARS-CoV-2, los pacientes con COVID-19 tenían características diferentes en varios picos. La quinta ola de COVID-19 tuvo el mayor número de pacientes hospitalizados, mientras que el primer pico tuvo el número más bajo. Quizás, el aumento significativo en la capacidad de prueba en la quinta ola y su largo período de tiempo sean las razones de este crecimiento. La mayoría de los síntomas clínicos fueron similares en todos los picos, pero la incidencia fue diferente. Dado que los pacientes hospitalizados en el tercer pico tenían la tasa más alta de enfermedad subyacente, puede ser una de las razones del aumento de la tasa de mortalidad de los pacientes. No observamos diferencias significativas en las pruebas de laboratorio entre los pacientes durante los diferentes picos. Por tanto, debemos estar atentos al estudio continuo de las características de la enfermedad, y ser capaces de modificar los tratamientos rápidamente si es necesario.

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## Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes a severe acute respiratory syndrome, commonly known as coronavirus disease 2019 (COVID-19).<sup>1,2</sup> The disease was first reported in January 2020 in Wuhan, China, and officially announced as a pandemic by the World Health Organization (WHO) in March 2020.<sup>3,4</sup> The first two confirmed cases of COVID-19 in Iran were officially reported on 2020-02-19 in the city of Qom, by the Iran's Ministry of Health and

Medical Education.<sup>5</sup> The most widely used current diagnostic method, real-time polymerase chain reaction (RT-PCR) testing, is the gold standard and the most accessible diagnostic tool for SARS-CoV-2 identification.<sup>6,7</sup> People are generally susceptible to SARS-CoV-2 infection at all ages, even children.<sup>8,9</sup> The infection is transmitted by droplet (direct inhalation of droplets from the sneeze, cough, or talking of an infected person) or contact (contacting the virus deposited on an object surface, which then enters the body via the mouth, nose, eyes, or other mucous membrane.<sup>10,11</sup> The clinical characteristics for COVID-19 appear 1–14 days after infection,

and most patients develop symptoms within 3–7 days.<sup>12,13</sup> Fever, cough, and dyspnea were the most common symptoms in patients with COVID-19 pneumonia,<sup>14,15</sup> followed by the manifestation of lower respiratory tract infections.<sup>16</sup> By contrast, upper respiratory tract symptoms were less common in these patients, indicating that the cells targeted by the virus might be located in the lower airway.<sup>17</sup> The most common laboratory findings in patients with COVID-19 are decreased eosinophil count (EOS) and albumin, as well as increased C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), interleukin 6 (IL-6), lymphopenia, and lactate dehydrogenase (LDH).<sup>18,19</sup> Due to the elevated blood coagulation in COVID-19 hospitalized patients, the D-Dimer level should be checked regularly. Other coagulation abnormalities include prolonged prothrombin time (PT) and partial thromboplastin time (PTT), increased fibrin degradation products, and severe thrombocytopenia.<sup>20</sup> The most frequent radiological findings in patients with COVID-19 entail ground-glass opacity (GGO), consolidation, interlobular septal thickening, adjacent pleura thickening, and air bronchogram. Infection often occurs bilaterally, especially in the lower lobe of the lung.<sup>21,22</sup>

SARS-CoV-2 mutations are important for various reasons such as increase in transmissibility or detrimental change in COVID-19 epidemiology, elevation in virulence or alteration in clinical disease presentation, decrease in the effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics. Currently designated variants of concern include Alpha, Beta, Gamma, Delta, and Omicron.<sup>23</sup> The alpha strain was first recorded in the UK in September 2020. While it was initially thought that this variant was around 70% more transmissible than the original SARS-CoV-2 coronavirus, evidence suggests that it is 30–40% more transmissible than the original.<sup>24</sup> Research has shown vaccine efficacy (two doses) against the alpha variant to be 74.5% with the Oxford-AstraZeneca vaccine, 93.7% with the Pfizer-BioNTech vaccine,<sup>25</sup> 85.6% with the Novavax vaccine,<sup>26</sup> and 100% with the Moderna vaccine.<sup>27</sup> The beta strain was recorded for the first time in South Africa in May 2020; this type was associated with increased hospitalization and mortality during the second wave of that country.<sup>28</sup> The US Centers for Disease Control and Prevention (CDC) has linked beta with a 50% increase in transmission, but the big worry is the emerging evidence of its ability to evade some of the existing vaccines.<sup>29</sup> The Gamma variant was first documented in Brazil in November 2020.<sup>30</sup> Data reveals that this variant is 1.7–2.4 times more transmissible than wild-type SARS-CoV-2.<sup>31</sup> The delta strain was first recorded in India in October 2020. Studies have shown that the delta strain is up to 60% more transmissible than the alpha strain.<sup>28</sup> The Delta strain has seen a sharp rise in cases in Asian countries, including Bangladesh, Iran, Iraq, Japan, Kazakhstan, Malaysia, Myanmar, Pakistan, South Korea, Thailand and Vietnam, as well as India.<sup>32</sup> Some investigations have pointed out the clinical differences of the patients in varied peaks of the COVID-19 in Iran.<sup>33</sup>

Assessing the characteristics and features of patients with COVID-19 will help to form an accurate picture of the patients' condition and make the necessary arrangements to provide better medical services. Therefore, the present study was performed by comparing demographic information, clinical

signs, laboratory findings, and radiological characteristics of patients with COVID-19 in peaks in Sabzevar city of Iran.

## Material and methods

### Study design

The present survey is a cross-sectional descriptive study, in which the first peak was in February–May 2020, the second peak in May–June 2020, the third peak in October–November 2020, the fourth peak in March–April 2021, and the fifth peak in June–September 2021. The statistical population consisted of all patients admitted with a diagnosis of COVID-19 in the Vasei Hospital of Sabzevar University of Medical Sciences.

### Inclusion/exclusion criteria

Inclusion criteria included all available files of patients admitted with definitive diagnosis of COVID-19 in special corona wards in Vasei Hospital, and exclusion criteria included patients whose files lacked sufficient information.

### Ethical considerations

This study was approved in Sabzevar University of Medical Sciences (Ethics code: IR.MEDSAB.REC.1400.100). The confidentiality of personal information was observed.

### Research methods

The instruments used in this study encompassed a demographic information questionnaire and a researcher-made checklist, including gender, age, marital status, underlying disease, clinical signs on arrival, and a checklist of laboratory findings, and radiological information. This information was completed using patient records. The method was that the researcher, after obtaining permission to start work from the research vice chancellor of Sabzevar University of Medical Sciences, started the necessary coordination and initiated sampling. Data were collected in such a way that the researcher was present in a large hospital. After introducing himself and stating the goals and necessity of the research, the researcher completed a questionnaire of demographic information, contextual factors, and clinical signs. He then extracted information about vital signs, laboratory findings, and radiological findings by reading patient records and entered them into a checklist.

### Statistical analysis

The analysis of the data was conducted by the aid of descriptive statistics (e.g. mean, frequency tables, standard deviation, and variance) and Mann–Whitney, Kruskal–Wallis, independent t-test, ANOVA, chi-square, and Fisher exact tests for comparisons using SPSS version 28. Data were stratified based on the different waves of COVID-19. The probability level of less than 0.5 was considered to be statistically significant ( $p < .05$ ).

## Results

### Study population

This study evaluated 3753 COVID-19 patients who were hospitalized in Vasei Hospital during five peaks of the disease. The first peak occurred from January to May 2020, the second, third, and fourth peak in June, November, and April 2020, respectively, and the fifth peak happened from July to September 2021. The fifth peak had the highest number of hospitalized patients (2017; 53.7%), while the first peak had the lowest number (203; 7.7%). In addition, the number of cases included 203 (5.4%) in the second peak, 203,897 (23.9%) in the third peak, and 348,203 (9.3%) in the fourth peak (Table 1).

### Demographic data

Demographic data of the patients are depicted in Table 1. Analysis of the patients' age (with a mean age of 61.37 years for both males and females) at different peaks demonstrated

that cases who were hospitalized during the third and fourth peaks were older than those hospitalized during other peaks. The fifth peak, however, involved younger individuals with a mean age of 52.5 years. Gender-based evaluation showed that men were more involved in the first (53.8%) and second (50.2%) peaks, whereas in other peaks, women were more involved, with the percentages of 50.4% (452), 55.7% (194), and 52.3% (1054) in the third, fourth, and fifth peaks, respectively.

### Radiology findings

The radiological findings of the studied patients are represented in Table 2. The highest and lowest respiratory involvements were observed in the third (74.6%) and fourth (38.8%) peaks, respectively. The most common radiological finding in all peaks was ground-glass opacity (28.98%), followed by consolidation, which was the highest (14.6%) in peak three.

### Laboratory findings

The results showed an increased rate of ESR, CRP, and neutrophils in the patients with COVID-19. Neutrophils

**Table 1 – Demographic data and clinical characteristics of patients with COVID-19.**

Waves features	Wave 1 N(%)	Wave 2 N(%)	Wave 3 N(%)	Wave 4 N(%)	Wave 5 N(%)	P-value
<i>Demographic data</i>						
Age (year)	57.5 ± 17	59.42 ± 18	61.37 ± 17	58.6 ± 17	52.5 ± 16	p<.001
Sex (Male)	155(53.8)	102(50.2)	445(49.6)	154(44.3)	963(47.7)	P = .140
Discharge from the hospital	243(85.3)	162(79.8)	618(69.7)	308(88.8)	1765(88.1)	p<.001
<i>Symptoms</i>						
Dyspnea	118(41)	99(48.8)	599(66.8)	171(49.1)	1131(56.1)	p<.001
Cough	81(28.1)	46(22.7)	158(17.6)	128(36.8)	808(40.1)	p<.001
Fever	66(22.9)	49(24.1)	135(15.1)	64(18.4)	347(17.2)	P = .003
Myalgia	9(3.1)	26(12.8)	59(6.6)	53(15.2)	178(8.8)	p<.001
Sore Throat	2(0.7)	0(0)	2(0.2)	4(1.1)	20(1)	P = .123
Tremor	23(8)	14(6.9)	60(6.7)	34(9.8)	85(4.2)	p<.001
Anorexia	11(3.8)	19(9.4)	27(3)	26(7.5)	99(4.9)	p<.001
Weakness	35(12.2)	53(26.1)	145(16.2)	96(27.6)	559(27.7)	p<.001
Nausea	18(6.3)	20(9.9)	51(5.7)	34(9.8)	181(9)	P = .014
Headache	6(2.1)	5(2.5)	9(1)	16(4.6)	103(5.1)	p<.001
Chest Pain	1(0.3)	1(0.5)	16(1.8)	11(3.2)	41(2)	P = .055
Diarrhea	7(2.4)	9(4.4)	15(1.7)	6(1.7)	31(1.5)	P = .051
Vomiting	8(2.8)	2(1)	19(2.1)	12(3.4)	71(3.5)	p<.115
Vertigo	0(0)	6(3)	8(0.9)	1(0.3)	42(2.1)	p<.001
Decreased Consciousness	11(3.8)	5(2.5)	45(5)	7(2)	41(2)	p<.001

Abbreviations: N: number.

**Table 2 – Radiological features of patients with COVID-19.**

Waves Radiological features	Wave 1 N(%)	Wave 2 N(%)	Wave 3 N(%)	Wave 4 N(%)	Wave 5 N(%)	P-value
Grand Glass opacity	85(29.5)	60(29.6)	285(31.8)	115(23)	625(31)	P = .850
Crazy Paving	15(5.2)	14(6.9)	132(14.7)	13(3.7)	172(8.5)	p<.001
HALO	0(0)	0(0)	0(0)	0(0)	2(0.1)	P = .647
Reticular_infiltrates	4(1.4)	4(2)	121(13.5)	14(4)	28(1.4)	p<.001
Multifocal Pachy Consolidation	31(10.8)	15(7.4)	131(14.6)	26(7.5)	136(6.7)	p<.001
Interstitial Changes With Peripheral Distribution	1(0.3)	0(0)	0(0)	2(0.6)	4(0.2)	P = .182

Abbreviations: N: number; HALO: high-acuity, low-occurrence.



**Table 3 – Laboratory finding of patients with COVID-19.**

Waves findings	Wave 1	Wave 2	Wave 3	Wave 4	Wave 5	P-value
WBC	6.71 ± 4.30	6.65 ± 3.61	8.52 ± 7.68	7.07 ± 5.75	7.22 ± 3.90	P<.001
Neu	72.55 ± 14.38	76.84 ± 10.43	81.64 ± 10.20	80.44 ± 10.88	79.74 ± 10.60	P = .000
Lymph	24.01 ± 13.18	20.91 ± 11.82	16.12 ± 10.42	17.42 ± 10.14	18.10 ± 10.15	P = .000
Hb	12.91 ± 2.68	12.74 ± 1.74	12.71 ± 2.59	13 ± 1.8	13.90 ± 2.87	P = .000
PLT	206.64 ± 124.27	196.88 ± 84.99	198.5 ± 83.15	189.02 ± 80.49	202.02 ± 83.75	P = .019
Urea	42.57 ± 48.69	47.58 ± 36.06	55.09 ± 40.17	42.84 ± 31.33	43.08 ± 30.18	P = .000
Cr	1.27 ± 1.05	1.43 ± 1.09	1.363 ± 1.02	1.02 ± 0.6	1.19 ± 0.73	P = .000
Na	136.88 ± 4.37	136.99 ± 5.39	137.45 ± 8.74	135.91 ± 11.14	138.03 ± 7.58	p<.001
K	4.25 ± 1.91	4.34 ± 0.697	4.58 ± 2.52	4.3 ± 1	4.39 ± 1.28	p<.001
LBP	73.90 ± 10.68	75.88 ± 11.05	–	–	–	P = .149
HBP	120.11 ± 20.12	124.55 ± 20.45	121.24 ± 19.83	124.44 ± 18.54	126.77 ± 24.069	P = .043
PR	96.23 ± 16.73	95.74 ± 14.65	94.42 ± 15.4	94.11 ± 13.90	96.78 ± 26.66	P = .049
RR	20.36 ± 3.67	20.315 ± 3.47	21.4 ± 4.34	21.60 ± 3.74	21.55 ± 3.82	P = .115
SpO2	89.47 ± 11.07	90.77 ± 8.11	84.61 ± 11.96	88.05 ± 11.93	91.06 ± 7.60	p < .001
Temperature	37.09 ± 2.37	37.32 ± 2.34	37.42 ± 1.68	37.3 ± 1.17	37.14 ± 1.06	p < .001
ESR	44.09 ± 31.0	50.25 ± 28.10	49.14 ± 29.09	47.94 ± 29.09	44.53 ± 24.61	P = .027
CRP	1.98 ± 0.91	0.00 ± 0.00	2.14 ± 0.84	2.2 ± 0.9	1.76 ± 0.82	P = .670

**Abbreviations:** WBC: White blood cell count; Neu: neutrophils; Lymph: lymphocytes; Hb: Hemoglobin; Plt: platelets; Cr: creatinine; Na: Sodium; K: Potassium; LBP: low blood pressure; HBP: high blood pressure; PR: pulse rate; RR: Respiratory Rate; SPO2: oxygen saturation; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; N: number.

count had the most abnormality. The lymphocyte count decreased in all peaks. Its highest reduction (16.12) occurred in the third peak (Table 3). The results also exhibited no significant elevation in WBC, HB, PLT, Na, and K. The highest amount of urea (55.09) was detected in the third peak. Also, the highest (1.43) and the lowest (1.02) levels of creatinine were found in the second and fourth peaks, respectively.

### Vital signs

Both respiratory and heart rates were associated with a slight increase. The SpO2 was lower than normal range in all peaks, except for the second (90.77%) and fifth (91.06%) peaks. Furthermore, temperature and blood pressure of the patients were normal in different peaks (Table 3).

### Clinical findings

Shortness of breath (dyspnea), cough, fever, body aches, chills, and weakness were common clinical symptoms in all peaks. Dyspnea (52.36%) was the most and dizziness (1.26%) and sore throat (0.6%) were the least frequent complications. Gastrointestinal symptoms, including nausea, diarrhea, vomiting, and anorexia, were the highest symptoms in the second peak (14%) and lowest in the third peak (8.3%). Nausea was the most common gastrointestinal complication in all peaks (Table 1).

### Underlying medical conditions

The most common underlying medical disease was hypertension (HTN), which its highest frequency was detected in 111 (9.31%) cases in the fourth peak. Diabetes mellitus (DM), hyperlipidemia (HLP), and ischemic heart disease (IHD) were the major risk factors in all peaks. These four risk factors (HTN: 9.31%, DM: 2.15%, HLP: 13.6%, and IHD: 3.10%) were the most common among patients in the fourth peak, as compared to the remaining peaks. Kidney failure had the

most prevalence in the third and fifth peaks. In this regard, 14 (56%) cases had kidney stones, and 12 (50%) cases undergone dialysis in the third peak. The occurrence of nervous system-related diseases was higher in the fifth peak. Overall, 55 (9.52%) cases had neurological disorders in the fifth peak, and 13 (50%) had seizures in the third peak (Table 4).

### Mortality

Based on Table 1, the average mortality rate among the patients was 13.4%. The mortality rates were 41 (14.4%), 37 (18.2%), 204 (23%), 32 (9.02%), and 189 (9.4%) in the first to fifth peaks, respectively. The highest mortality rate was observed in 204 (23%) patients in the third peak, but the lowest rate (32 [9.02%]) was found in the fourth peak.

## Discussion

This retrospective study reports demographic information, clinical signs, radiological findings, and laboratory results from 3753 COVID-19-infected patients who were hospitalized in Vasei Hospital following positive SARS-CoV-2 PCR test results.

According to the estimates of Iran's Ministry of Health and Medical Education and considering the peak time periods of COVID-19, the predominant SARS-CoV-2 strains identified in Iran were wild strains in the first peak and also Beta strains, B.1.36 and B.1.1.413, in the second and third peaks. However, Alpha and Delta were dominant strains in the fourth and fifth peaks, respectively.<sup>34</sup>

Our results demonstrated that patients (with the median age of 61.37 years) involved with COVID-19 during the third and fourth peaks were mostly older people (with the median age of 52.5 years), but during the fifth peak, the young individuals were chiefly involved. By comparing the peak

**Table 4 – Comorbidities of patients with COVID-19.**

Waves Comorbidities	Wave 1 N(%)	Wave 2 N(%)	Wave 3 N(%)	Wave 4 N(%)	Wave 5 N(%)	P-value
Diabetes mellitus	38(13.2)	43(21.2)	182(20.3)	53(15.2)	346 (17.2)	P = .020
Hypertension	59(20.5)	57(28.1)	263(29.3)	111(31.9)	482(23.9)	p<.001
Hyperlipidemia	23(8)	20(9.9)	92(10.3)	47(13.5)	255(12.6)	P = .056
ischemic heart disease	30(10.4)	10(4.9)	82(9.1)	36(10.3)	219(10.9)	P = .082
Lung Disease	22(7.6)	19(9.4)	63(7)	17(4.9)	104(5.2)	P = .034
Surgery	21(7.3)	33(16.3)	88(9.8)	32(9.2)	288(14.3)	p<.001
Cancer	5(1.7)	2(1)	13(1.5)	5(1.4)	24(1.2)	P = .916
Pregnant	4(5.3)	0(0.0)	17(22.4)	5(6.6)	50(65.8)	=0.009
Kidney stone	3(12.0)	2(8.0)	2(8.0)	4(16.0)	14(56.0)	=0.009
Anemia	3(16.7)	0(0.0)	3(16.7)	1(5.6)	11(61.1)	=0.009
Sinusitis	1(50.0)	0(0.0)	1(50.0)	0(0.0)	0(0.0)	=0.009
Tuberculosis	1(100.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	=0.009
Hypothyroidism	4(6.3)	2(3.2)	17(27.0)	5(7.9)	35(55.6)	=0.009
Gall stone	2(50.0)	1(25.0)	0(0.0)	0(0.0)	1(25.0)	=0.009
Seizure	2(7.7)	0(0.0)	13(50.0)	4(15.4)	7(26.9)	=0.009
Prostate gland enlargement	2(4.2)	2(4.2)	10(20.8)	6(12.5)	28(58.3)	=0.009
Arthritis	1(33.3)	0(0.0)	0(0.0)	0(0.0)	2(66.7)	=0.009
Alzheimer	1(5.3)	2(10.5)	5(26.3)	1(5.3)	10(52.6)	=0.009
Cerebrovascular accident	5(10.2)	2(4.1)	21(42.9)	3(6.1)	18(36.7)	=0.009
Dialysis	0(0.0)	1(4.2)	12(50.0)	2(8.3)	9(37.5)	=0.009
Migraine	1(10.0)	0(0.0)	1(10.0)	0(0.0)	8(80.0)	=0.009
Kidney	1(3.2)	1(3.2)	13(41.9)	2(6.5)	14(45.2)	=0.009
Gout	1(25.0)	0(0.0)	1(25.0)	0(0.0)	2(50.0)	=0.009
Parkinson	0(0.0)	1(11.1)	4(44.4)	0(0.0)	4(44.4)	=0.009
Hemorrhoids	0(0.0)	1(33.3)	0(0.0)	1(33.3)	1(33.3)	=0.009
Thalassemia	0(0.0)	1(33.3)	0(0.0)	0(0.0)	2(66.7)	=0.009
Malta fever	0(0.0)	0(0.0)	1(25.0)	1(25.0)	2(50.0)	=0.009
Hepatitis	0(0.0)	0(0.0)	2(50.0)	0(0.0)	2(50.0)	=0.009
Epilepsy	0(0.0)	0(0.0)	1(25.0)	0(0.0)	3(75.0)	=0.009
Addiction	10(3.5)	7(3.4)	36(4)	37(10.6)	144(7.1)	p<.001

Abbreviations: N: number.

COVID-19 time periods, it can be concluded that with increasing the vaccination coverage for the older people, they become less infected with the disease, and the infection was shifted to the young individuals. This phenomenon can be related to the nature of the Delta virus as it inherently affects young people more than the elderly.

In this study, men were more involved than women in the first and second peaks, but in other peaks, women were more likely to infect with coronavirus. However, this difference was not statistically significant. Peckham stated no difference between men and women with COVID-19.<sup>35</sup> Bwire et al., on the other hand, reported that biological differences and lifestyle are factors that cause men to be more infected with the disease than women,<sup>36</sup> which is not consistent with our findings. In the studies of Chen et al.<sup>37</sup> and Rodriguez-Morales et al.,<sup>38</sup> the incidence of the disease was slightly higher in men, which is in agreement with the results achieved in the first, second, and third peaks in our study. Stirrup and colleagues denoted that women infected with the Alpha strain were at higher risk of severe disease than men, which supports the obtained data in the fourth peak of the disease in the current study.<sup>39</sup> Differences in the immune system, sex hormones, physiological factors, and lifestyle are the most significant risk factors between men and women that lead to COVID-19.<sup>40-42</sup>

In the present study, the highest number of patients in the fifth peak was infected with the Indian strain (Delta variant).

Based on evidence, the replication rate of the Delta strain is very substantial; it spreads 50% faster than Alpha strain and is 50% more contagious than the wild-type SARS-CoV-2 strain.<sup>43</sup> Baisheng Li and colleagues at the Centers for Disease Control and Prevention in China identified 62 Chinese residents who were quarantined after exposure to COVID-19. They observed that these patients were infected with the Delta strain and proved that this strain can spread twice as much as other strains. Another study found that people with Delta infection are detectable four days after exposure, but in cases with the original strain of coronavirus, it takes an average of six days. This observation indicates that the Delta strain multiplies much faster. Delta-infected people had a viral load of up to 1260 times higher than those infected with the coronavirus's original strain.<sup>44</sup>

Studies on Alpha strain (English variant) have exhibited that the clinical symptoms of this strain are very similar to those of other strains. In this regard, 35% of cases who were positive for this variant and 27% of cases who tested positive for other strains reported cough. Fatigue (32%), muscle pain (25%), fever (21%), or sore throats (21%) were the most common clinical symptoms of the aforesaid variant. These manifestations are comparable with those reported by our patients in the fourth peak and also with those of the predominant strains in other peaks. The clinical signs of the Delta variant, including cough, fever, or headache, and the significant loss of smell, were detected to be the same as the

original version of COVID-19, as well as similar to the symptoms experienced by our patients in the fifth peak. In the present study, the most frequent complication of the patients in all COVID-19 peaks was dyspnea, followed by cough and fever, which were observed in less than 40% of people in each peak. The highest amount of cough epochs was observed in the fifth peak of the disease. Although cough was one of the main symptoms in our study, its prevalence in each peak was much lower than similar studies.<sup>45-47</sup> In the third peak, a high number of patients perceived dyspnea, may be due to the coincidence of the third peak of the disease with the autumn season. Actually, the influenza spreads in the autumn, and dyspnea may have been a symptom of the influenza. However, in the study of Chen et al.,<sup>48</sup> dyspnea was not the most widespread symptom, which contradicts the results of our study.<sup>37,45,46,49-51</sup> In the studies of Wu et al.<sup>49</sup> and Zhong et al.,<sup>48</sup> fever and cough were two main clinical symptoms in most patients. Other frequent clinical complications reported by Zhong<sup>48</sup> included dyspnea, fatigue, and muscle aches.<sup>48</sup> In Cordova et al.'s study,<sup>52</sup> fever, cough, and dyspnea and in Bernheim et al.'s study,<sup>53</sup> fever, cough, muscle pain, and fatigue were the most prevalent symptoms. Dizziness and sore throat were among the uncommon symptoms of COVID-19 in all peaks, which corroborates the study of Sharifi-Razavi et al.<sup>54</sup> Weakness and fatigue were relatively common in each peak, which is in conformity with other investigations.<sup>45-47</sup> In the second peak, gastrointestinal manifestations, including nausea, diarrhea, vomiting, and anorexia, were the most prevalent clinical signs, of which nausea was the most common in all peaks. In other investigations, anorexia, followed by diarrhea and nausea, were the most frequent complications.<sup>38,45-47</sup> In Ghayda et al.'s study, vomiting and diarrhea were reported to be 5% and 6%, respectively, which were significantly less than respiratory symptoms.<sup>45</sup>

Laboratory tests in this study indicated that ESR, CRP, and neutrophil counts increased, but lymphocytes decreased in all COVID-19 peaks. Zhong et al. observed that most of the patients had high levels of CRP, D-dimer, and lymphopenia, followed by abnormal levels of liver enzymes and thrombocytopenia.<sup>48</sup> Decreased lymph nodes may be associated with an increase in the severity of COVID-19 disease. Probably, its mechanism is that the virus attacks the host cells and directly damages the cells. As a result, the viral infection causes nonspecific damage, and the immune cells participate in the antiviral process, thereby leading to apoptosis. Thus, it can be deduced that using lymphocyte supplements can be a key to the improvement of patients with COVID-19.<sup>55,56</sup> In this study, we observed a significant elevation in urea levels in all peaks; however, this increase was the highest in the third peak. Also, in the same peak, the renal involvement was reported to be the highest. This finding is in line with the study of Yang et al.<sup>50</sup> who stated that 22% of patients with COVID-19 were associated with acute renal failure. In the current study, the most frequent underlying disease was hypertension, which was the highest among 111 (9.31%) cases in the fourth peak. The prevalence of DM, HLP, HTN, and IHD in the fourth peak was 2.15%, 9.31%, 6.13%, and 10.3%, respectively. Renal failure was the most prevalent complication in patients in the third and fifth peaks. In the third peak,

12 (50%) cases had dialysis, and in the fifth peak, 14 (56%) cases had kidney stones. Khamis and colleagues reported blood pressure (15%), diabetes (13.8%), and COPD (3.9%) in their systematic review.<sup>57</sup> In a meta-analysis study conducted by Zarifkar et al.,<sup>58</sup> the prevalence of cancer as a comorbid disease among hospitalized COVID-19 patients was estimated to be 2-4%. This finding is in harmony with the prevalence (1-2%) of cancer in the current study.

Based on the radiological findings in our study, the highest and lowest respiratory involvement was observed in the third and the fourth peaks, respectively. The most common radiological finding in all peaks was grand glass, as similarly reported by Cordova et al. and Borges al.<sup>52,59</sup> After GGO, consolidation had the highest prevalence (14.6%) in the third peak. Other researchers reported that the prevalence of consolidation varied from 7% to 19%,<sup>60-63</sup> which is consistent with our finding. However, a number of other researchers have stated a higher prevalence, ranging from 59% to 64%.<sup>64-66</sup> According to Table 1, the mortality rates in the first to fifth peaks were 41 (14.4%), 37 (18.2%), 204 (23%), 32 (9.02), and 189 (9.4%), respectively. The highest 204 (23%) mortality rate of the patients was detected in the third peak, whereas the lowest 32 (9.02%) rate was detected in the fourth peak. As patients hospitalized during the third peak had the highest rate of underlying disease, it could be a reason for the increased mortality rate of the patients. This rate in the second and third peaks was higher than the first peak, suggesting that the Beta strain was more lethal than the wild strain. Lin's meta-analysis showed that the risk of mortality in Alpha-infected patients was significantly higher than those with wild-type virus, which contradicts the data in our study.<sup>67</sup> Lin et al.<sup>67</sup> have also emphasized that the Alpha variant has a higher risk of disease severity than the wild-type virus, but Frampton et al.,<sup>68</sup> Funk et al.,<sup>69</sup> Martínez-García et al.,<sup>70</sup> and Stirrup et al.<sup>39</sup> have expressed different views. In the Chishinga's study, people with chronic renal and cardiovascular diseases at all peaks were more likely to die than those without such disease,<sup>71</sup> which confirms the results of our study.

## Conclusion

This study investigates the characteristics of patients with COVID-19 in different peaks of the disease in Eastern Iran. The fifth wave of COVID-19 had the highest number of hospitalized patients, while the first peak had the lowest number. Perhaps, the significant increase in testing capacity in the fifth wave and its long time period are the reasons for this growth. The results of the present study showed that the patients hospitalized in the fifth wave were younger, and those hospitalized in the third and fourth waves were older. There was a significant difference between the genders of the patients in the first to fifth waves. In the first and second waves, the prevalence of hospitalization in men was higher than in women, and in the third, fourth and fifth waves, it was the opposite. Most of the symptoms, including shortness of breath, cough, fever, body pain, chills, and weakness, were similar in all peaks, but the incidence was different. Gastrointestinal symptoms in the second wave stood out as a



difference. Comorbidities were similar, and hypertension (HTN), diabetes mellitus (DM), hyperlipidemia (HLP), and ischemic heart disease (IHD) were the main risk factors in all peaks. As patients hospitalized in the third peak had the highest rate of underlying disease, it can be a reason for the increase in the death rate of patients. Paying attention to the vital signs of patients upon arrival is helpful in identifying the prognosis of patients. A decrease in Spo<sub>2</sub> was observed in three peaks and a slight increase in respiratory rate and heart rate. We did not observe any significant differences in laboratory tests among the patients admitted to the Vasei Hospital. An increase in ESR, CRP, and neutrophils and a decrease in the number of lymphocytes indicate the involvement of the immune system of these patients. The most common radiological finding in all the peaks was ground glass opacity and then stabilization, which was the highest in the third peak. The highest mortality rate was detected in the third peak, but the lowest rate in the fourth peak. Altogether, we should be vigilant in continuously studying the characteristics of the disease, and be able to modify treatments rapidly if necessary.

### Authors' contribution

S.F.M, M.E, S.A.A.M, N.M, M.J, and M.H contributed in revising and final approval of the version to be published. All authors agreed and confirmed the manuscript for publication.

### Conflict of interests

Authors declare that they have no competing interests.

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