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Original Article

Clinical Manifestations and Associated Mortality Factors of COVID-19: A Large Population-Based Study in the Northeast of Iran During 2020-2021

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Abstract

Background and aims: The emergence of the coronavirus disease 2019 (COVID-19) has become one of the greatest health problems of the 21st century. The current study was conducted to investigate COVID-19's clinical manifestation, mortality factors, and their association with each other during the three devastating waves of the pandemic in Razavi-Khorasan province, Iran.

Methods: This cross-sectional epidemiological population-based study was performed in Razavi-Khorasan province, Iran from January 21, 2020, to March 20, 2021. The data, including demographic characteristics and clinical presentations of the patients, were extracted from the Medical Care Monitoring System (MCMS), disease management portal in the Deputy of Health and hospital information system (HIS) of the medical universities/faculties of the province.

Results: Overall, 80 499 patients were admitted to all hospitals of Khorasan-Razavi with the laboratory/clinical COVID-19 confirmed disease. The male-to-female ratio and the mean age of our COVID-19 individuals were 1.10:1 and 55.67 ± 23.27, respectively. The most frequently reported presenting symptoms in histories provided at the admission time were respiratory distress (58.2%), fever (36.7%), and cough (34.9%), while the less common ones were abdominal pain (2.7%) and alternation in smell/taste (0.9%). Male gender (odds ratio [OR] = 1.32, $P < 0.001$), age over 60 (OR = 2.59, $P < 0.001$), and presence of at least one comorbidity (OR = 1.32, $P < 0.001$) were significantly associated with higher mortality rates.

Conclusion: Healthcare providers and public health managers can benefit from the findings of this study to detect and emphasize patients with poor prognoses.

Keywords: COVID-19, Coronavirus, Clinical manifestations, Iran

Introduction

The coronavirus disease 2019 (COVID-19) has become one of the greatest health crises in the current century.[1] Following the emergence of COVID-19 in Wuhan, Hubei province, China in December 2019, the virus spread all over the world, and in a blink, the World Health Organization (WHO) called it a global pandemic.[2] According to the official reports of the WHO, more than 200 million individuals were infected with the severe acute respiratory syndrome coronavirus type two (SARS-CoV-2), which has led to more than 4 million deaths in the world.[3]

In detail, SARS-CoV-2 is a single-stranded positive-sense RNA virus of the Coronaviridae family.[4] This beta-coronavirus is commonly transmitted by respiratory droplets from an infected individual to others, and each person can transmit the virus to an average of 4 people.[5,6] Although many studies indicated that there is no one completely immune from the virus infection, its clinical manifestations are various from asymptomatic infection to severe multisystemic organ failure and death [7]. However, male gender, old age, smoking, and underlying diseases such as diabetes mellitus, hypertension, cardiovascular disease (CVD), chronic obstructive pulmonary disease, cerebrovascular disease, chronic kidney disease, and liver dysfunctions are reported as factors associated with higher disease severity and its mortality rate.[8,9] The most common clinical manifestations of COVID-19 include fever, dyspnea, fatigue, non-productive cough, nausea and vomiting, diarrhea, and heart failure, but the disease is not limited to these signs and symptoms; moreover, different variants of the virus can be demonstrated with

different manifestations.[7,9,10]

Based on our current knowledge about the clinical manifestations of COVID-19, anorexia, diarrhea, and nausea are the most common gastrointestinal (GI) manifestations of this infectious disease, respectively.[11] However, recent research indicated various GI signs and symptoms of the infected patients due to the mutant variants that infected them.[12] Not only the GI presentations of COVID-19 are going to be changed through the virus genetic changes in new variants, but also some studies demonstrated that the other clinical manifestations and presentations of COVID-19 were changed due to virus mutant variants.[13] On the other hand, there is some contradictory evidence of the relationships between patients' clinical manifestation, disease severity, and mortality.[14] As there are many gray areas regarding COVID-19's clinical manifestations and their associations with mortality, the current study was designed to evaluate COVID-19's clinical manifestation, mortality factors, and their association during the three devastating waves of the COVID-19 pandemic in Razavi-Khorasan province, Iran.

Materials and Methods

Study Design

The current cross-sectional epidemiological population-based study was conducted from January 21, 2020 (first wave) to March 20, 2021 (third wave) to determine the characteristics of COVID-19 patients, clinical presentations of COVID-19, and COVID-19-associated factors with mortality during the first, second, and third wave in COVID-19 patients who were admitted to the hospitals affiliated to the Mashhad University of Medical Sciences in Razavi-Khorasan province, Iran.

Data Source and Study Population

The data were extracted from the Medical Care Monitoring System (MCMC) of Mashhad University of Medical Sciences. This system was created from the beginning of the COVID-19 pandemic in Iran to monitor COVID-19 patients in the country. The data of the MCMC in Razavi-Khorasan province are collected from six medical universities/faculties of the province and are continuously updated 24 hours a day. Moreover, the recorded information in the MCMC is going to be matched with the patient's information in the disease management portal in the Deputy of Health and hospital information system (HIS) of the medical universities/faculties.

Hospitalized patients with a definitive diagnosis of coronavirus infection by the reverse transcriptase-polymerase chain reaction (RT-PCR) method or through clinical evaluations and admission to public hospitals affiliated with Mashhad University of Medical Sciences in Razavi-Khorasan province were included in this study. Their information was recorded through MCMC from January 21, 2020, to March 20, 2021. After the extraction of the patients' reports from the MCMC system and before the statistical analysis of the demographics and clinical presentations of patients, data quality control was performed by researchers, and all duplicate reports were excluded from further analysis.

Outcomes

The information and outcomes gathered from the MCMC archive and assessed in this study were demographic data and clinical presentations of COVID-19 at admission. Demographic data included gender, age, hospitalization date and duration, comorbidities (e.g., hypertension, diabetes, CVD, pulmonary diseases, kidney disease, cancer, neurologic disease, liver disease, and hematologic disease), and patients' status (expired or not). In addition, clinical presentations of COVID-19 at admission were respiratory distress, fever, cough, myalgia, neurologic symptoms (e.g., headache, loss of consciousness, seizure, paresis, plegia), anorexia, nausea, vomiting, diarrhea, chest pain, abdominal pain, and anosmia/ageusia.

Statistical Analysis

The analyses were performed based on non-missing data, and missing data were not imputed in the final logistic regression. The Kolmogorov-Smirnov test was applied to check the normality of variables. The age, gender, and disease presentations were analyzed over all of the three waves of COVID-19 epidemics. The total frequency of the above-mentioned variables was also taken into consideration. The male-to-female ratio (gender ratio) and the case fatality rate (CFR) were calculated as well. Continuous and categorical data were presented as mean ± standard deviation (SD), median (interquartile range), and absolute number (percentage) as appropriate. The chi-square and Fisher's exact tests were employed to compare proportions.

A multiple binary logistic regression model evaluated the effect of multiple variables comprised of age, gender, disease presentations, and comorbidities on COVID-19 mortality. The primary outcome was mortality in COVID-19 subjects. The backward selection method was used for variable selection. Different variables were entered in binary logistic regression one by one, and those with a significance value of < 0.2 were imputed in the final logistic regression to identify independent predictors of mortality in both the total population and the stratified random sample. All data were interpreted using IBM SPSS Statistics (version 26), and statistical significance was set at $P < 0.05$.

Results

Characteristics of COVID-19 Patients

Overall, 80 499 patients were admitted to all hospitals of Khorasan-Razavi University of Medical Sciences with laboratory/clinical COVID-19 confirmed disease between January 21, 2020, and March 20, 2021. Of the subjects, 52.4% were males (male-to-female ratio = 1.10:1). The mean age of our COVID-19 individuals was 55.67 ± 23.27

with a median of 60 years [IQR: 40-74]. The majority (N = 50 708, 63.0%) of the population had > 50 years of age. The patients were hospitalized with a median of 3 days [IQR: 1-7]. In total, 43.6% of subjects had at least one co-existing underlying medical condition (19.7%, 15.1%, and 13.3% had hypertension, diabetes, and CVDs, respectively). Different comorbidities that patients presented before contracting COVID-19 and the demographic data are summarized in Table 1.

Clinical Presentations of COVID-19

In terms of the pattern of COVID-19 presentation, the most frequently reported presenting symptoms in histories provided at the admission time were respiratory distress (58.2%), fever (36.7%), and cough (34.9%), whereas the less common ones included abdominal pain (2.7%) and alternation in smell/taste (0.9%). Table 2 presents the remaining presentation data.

As shown in Figure 1, respiratory distress, fever, cough, myalgia, neurologic, anorexia, and diarrhea were significantly more prevalent in males than females. However, chest pain and dermatitis were slightly more reported in males. Females had higher rates of nausea, vomiting, alternations in smell/taste, and abdominal pain rather than males, and the difference between the presence of stated presentations in males and females was significant ($P < 0.001$).

Factors Associated With COVID-19 Mortality

As of April 21, 2021, 12119 (15.1%) had deceased in our study, following a median of 4 days [IQR: 1-10] of hospitalization. The mean ± SD and the median [IQR] of age were 67.40 ± 18.27 and 70 (59-81) years versus 53.58 ± 23.44 and 57 (37-72), in expired vs. alive subjects, respectively.

The gender-based CFR specified that males had a significantly higher rate of mortality (16.6% vs. 13.4%). Based on the results, 72% of deaths occurred in subjects over the age of 60. The highest age-based CFR was observed in patients aged over 90 with a rate of 31.3%

Table 1. Demographic Characteristics of COVID-19 In-patients*

Variable	Wave			
	First Wave (n = 17231)	Second Wave (n = 25286)	Third Wave (n = 37982)	Total (n = 80499)
Gender, Male	9333 (54.2)	13031 (51.5)	19845 (52.2)	42209 (52.4)
Age	55.46 ± 21.32 58 [39-72]	56.90 ± 22.25 61 [42-75]	54.95 ± 24.69 60 [40-74]	55.67 ± 23.27 60 [40-74]
Hospitalization duration	5.76 ± 10.00 3 [1-7]	5.80 ± 7.68 4 [1-7]	5.20 ± 5.91 4 [1-7]	5.50 ± 7.42 3 [1-7]
Age group				
< 10	434 (2.5)	1129 (4.5)	3385 (8.9)	4948 (6.1)
11-20	486 (2.8)	647 (2.6)	929 (2.4)	2062 (2.6)
21-30	1460 (8.5)	1572 (6.2)	2007 (5.3)	5039 (6.3)
31-40	2274 (13.2)	2612 (10.3)	3558 (9.4)	8444 (10.5)
41-50	2043 (11.9)	2792 (11.0)	3910 (10.3)	8745 (10.9)
51-60	2691 (15.6)	3636 (14.4)	5271 (13.9)	11598 (14.4)
61-70	2984 (17.3)	4803 (19.0)	7285 (19.2)	15072 (18.7)
71-80	2446 (14.2)	4128 (16.3)	6396 (16.8)	12970 (16.1)
81-90	1909 (11.1)	3091 (12.2)	4549 (12.0)	9549 (11.9)
> 91	315 (1.8)	512 (2.0)	692 (1.8)	1519 (1.9)
Comorbidity				
At least one	6431 (37.3)	11412 (45.1)	17287 (45.5)	35130 (43.6)
Hypertension	1962 (11.4)	5368 (21.2)	8550 (22.5)	15880 (19.7)
Diabetes	2099 (12.2)	4106 (16.2)	5972 (15.7)	12177 (15.1)
Cardiovascular disease	2112 (12.3)	3314 (13.1)	5301 (14.0)	10727 (13.3)
Pulmonary diseases	1311 (7.6)	1603 (6.3)	2288 (6.0)	5202 (6.5)
Kidney disease	517 (3.0)	792 (3.1)	852 (2.2)	2161 (2.7)
Cancer	464 (2.7)	648 (2.6)	923 (2.4)	2035 (2.5)
Neurologic disease	365 (2.1)	579 (2.3)	651 (1.7)	1595 (2.0)
Liver disease	138 (0.8)	236 (0.9)	269 (0.7)	643 (0.8)
Hematologic disease	135 (0.8)	193 (0.8)	239 (0.6)	567 (0.7)
Expired	2154 (12.5)	4192 (16.6)	5773 (15.2)	12119 (15.1)

Note. COVID-19: Coronavirus disease 19; SD: Standard deviation; IQR: Interquartile range. *Data expressed as N (% within the wave), Mean ± SD and Median [IQR] as appropriate.

Table 2. Initial Clinical Presentations of COVID-19 at Admission*

Presentation	Frequency (%)			
	First Wave (n = 17231)	Second Wave (n = 25286)	Third Wave (n = 37982)	Total (n = 80499)
Respiratory distress	9340 (54.2)	15199 (60.1)	22340 (58.8)	46879 (58.2)
Fever	6449 (37.4)	10356 (41.0)	12717 (33.5)	29522 (36.7)
Cough	7398 (42.9)	8604 (34.0)	12124 (31.9)	28126 (34.9)
Myalgia	2260 (13.1)	4354 (17.2)	6528 (17.2)	13142 (16.3)
Neurologic[a]	1956 (11.3)	4895 (19.4)	5290 (13.9)	12141 (15.1)
Anorexia	245 (1.4)	2403 (9.5)	3861 (10.2)	6509 (8.1)
Nausea	229 (1.3)	1942 (7.7)	2747 (7.2)	4918 (6.1)
Vomiting	185 (1.1)	1381 (5.5)	2060 (5.4)	3626 (4.5)
Diarrhea	121 (0.7)	1131 (4.5)	1515 (4.0)	2767 (3.4)
Chest pain	120 (0.7)	895 (3.5)	1593 (4.2)	2608 (3.2)
Abdominal pain	174 (1.0)	830 (3.3)	1149 (3.0)	2153 (2.7)
Anosmia/Ageusia	61 (0.3)	228 (0.9)	422 (1.1)	711 (0.9)

Note. COVID-19: Coronavirus disease 19. *Data expressed as N (% within the wave). [a] Neurologic symptoms comprised of headache, loss of consciousness, seizure, paresis, and plegia.

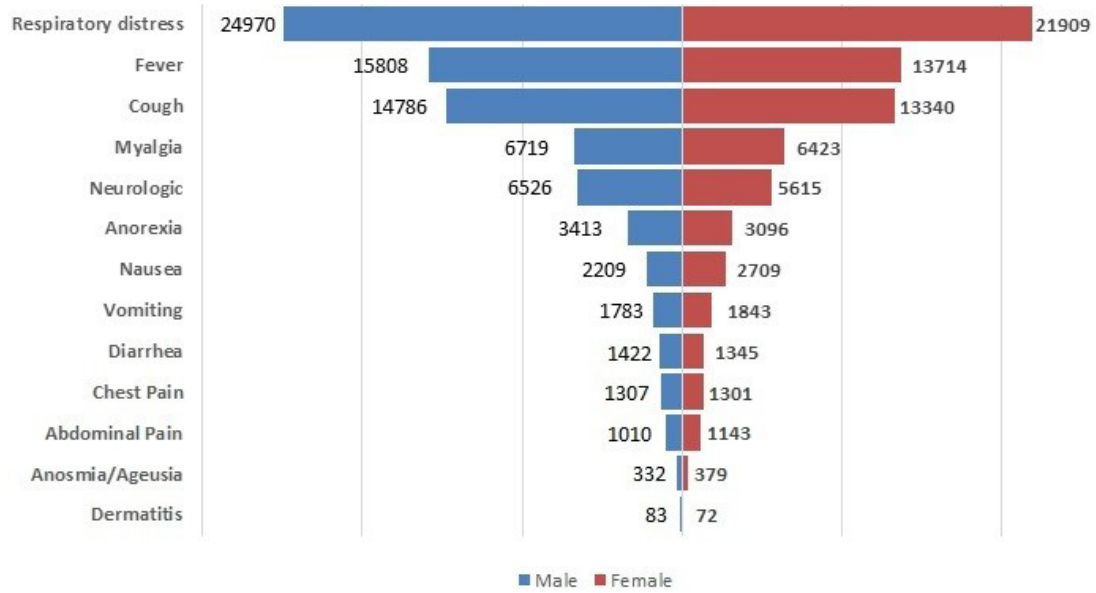

Figure 1. Distribution of COVID-19 Presentations in Males and Females. Note. COVID-19: Coronavirus disease 19

(30.7% vs. 32.1%: Males vs. females). Instead, patients in the age group of 21-30 years had the lowest rate of mortality (3.4%). Patients with at least one comorbidity expired more frequently (19.8%), whereas patients with no mentioned comorbidity had a CFR of 13.9%.

Age, male gender, and the wave of COVID-19 epidemics, as well as cough, myalgia, respiratory distress, alternations in smell/taste, neurologic symptoms, chest pain, the appearance of at least one GI symptom, abdominal pain, anorexia, presence of at least one comorbidity, hypertension, diabetes, and CVD, were independently associated with the mortality of COVID-19, based on the multiple binary logistic regression model (Table 3).

Age > 60 was a strong predictor of disease mortality. Males had a higher probability of death, compared to females. Among the initially reported presentations of COVID-19, having neurologic symptoms, and reported respiratory distress were prominent predictors of death. Smoking, the presence of cough, myalgia, alterations of smell/taste, chest pain, and abdominal pain were associated, on the other hand, with a lower risk of mortality. However, fever, nausea, and vomiting were accompanied by a lower risk of death, but not significantly (Table 3).

Of 12119 deceased subjects, 57.1% had at least one comorbidity, 26.0% hypertension, 21.1% diabetes, and 18.5% CVDs. In addition, having at least one comorbidity increases the odds of mortality (OR = 1.43 [1.35-1.52], $P < 0.001$). Diabetes was more prevalent among the COVID-19 deceased cases than alive ones. However, based on the regression analysis, diabetes was interestingly associated with a decrease in mortality (OR = 0.90 [0.84-

Table 3. Independent Predictors Associated With Mortality: Multivariable Binary Logistic Regression Analysis*

Subject Characteristics	Alive (n = 68380)	Deceased (n = 12119)	Comparison	OR (95% CI)	*P* Value
Age > 60 years	30368 (44.4)	8729 (72.0)	> 60 vs. ≤ 60	2.59 (2.47-2.72)	< 0.001
Gender, Male	35191 (51.5)	6998 (57.7)	M vs. F	1.32 (1.27-1.38)	< 0.001
Waves of epidemics					
1st wave	15077 (22.1)	2154 (17.8)	-	-	< 0.001
2nd wave	21091 (30.9)	4192 (34.6)	W2 vs. W1	1.13 (1.07-1.19)	
3rd wave	32179 (47.1)	5773 (47.6)	W3 vs. W1	0.90 (0.86-0.93)	
Disease presentations					
Fever	25577 (37.4)	3943 (32.5)	Y vs. N	0.99 (0.94-1.03)	0.525
Cough	24683 (36.1)	3441 (28.4)	Y vs. N	0.88 (0.84-0.93)	< 0.001
Myalgia	11706 (17.1)	1436 (11.8)	Y vs. N	0.81 (0.76-0.87)	< 0.001
Respiratory distress	37915 (55.5)	8943 (73.8)	Y vs. N	2.05 (1.96-2.16)	< 0.001
Anosmia/ageusia	648 (1.0)	63 (0.5)	Y vs. N	0.72 (0.55-0.94)	0.018
Neurologic[a]	8587 (12.6)	3537 (29.2)	Y vs. N	2.63 (2.50-2.77)	< 0.001
Chest pain	2352 (3.9)	256 (2.3)	Y vs. N	0.55 (0.48-0.63)	< 0.001
Appearance of GI symptoms	11927 (17.4)	1568 (12.9)		0.68 (0.58-0.78)	< 0.001
Abdominal pain	1987 (3.2)	166 (1.5)	Y vs. N	0.79 (0.66-0.95)	0.013
Nausea	4408 (7.1)	509 (4.5)	Y vs. N	0.92 (0.80-1.04)	0.189
Vomiting	3294 (5.3)	332 (2.9)	Y vs. N	0.95 (0.82-1.10)	0.460
Diarrhea	2532 (4.1)	235 (2.1)	Y vs. N	0.99 (0.84-1.17)	0.935
Anorexia	5528 (8.9)	980 (8.6)	Y vs. N	1.36 (1.19-1.56)	< 0.001
Comorbidities					
Having comorbidity	28178 (41.2)	6919 (57.1)	Y vs. N	1.43 (1.35-1.52)	< 0.001
Diabetes	9617 (14.1)	2559 (21.1)	Y vs. N	0.90 (0.84-0.95)	< 0.001
Hypertension	12731 (18.6)	3149 (26.0)	Y vs. N	1.18 (1.11-1.25)	0.026
Cardiovascular disease	8489 (12.4)	2237 (18.5)	Y vs. N	1.00 (0.94-1.07)	0.895

Note. SD: Standard deviation; GI: Gastrointestinal; IQR: Interquartile range. *Data are expressed as N (% within alive/deceased group, as applicable), mean ± SD, and median [IQR]; as appropriate. [a] Neurologic symptoms comprised of headache, loss of consciousness, seizure, paresis, and plegia. Model: Age, gender, the wave of epidemics, fever, cough, myalgia, respiratory distress, anosmia/ageusia, neurologic symptoms (comprised of headache, loss of consciousness, seizure, paresis, plegia), chest pain, the appearance of at least one GI symptom, abdominal pain, nausea, vomiting, diarrhea, anorexia, presence of at least one comorbidity, diabetes, hypertension, and cardiovascular disease.

0.95], $P < 0.001$). Mortality of COVID-19 in patients with co-existing CVD was elevated than the healthy ones (20.9% vs. 12.4%), but the odds were not significantly different based on the regression (OR = 1.00 [0.94-1.07], $P = 0.895$). Further, hypertension was much more frequent in the deceased patients than in alive subjects (26% vs. 18.6%, OR = 1.18 [1.11-1.25], $P = 0.026$, Table 3).

Discussion

The COVID-19 pandemic is a serious public health problem that has so far challenged humankind for about two years.[5] According to the weekly report of the WHO, as of 31 August 2021, the cumulative number of COVID-19 cases exceeded 200 million.[9] The complete mechanism of pathogenesis and the other aspects of this novel disease are still under study. Although less than half of the infected patients are asymptomatic,[15,16] multiple organ involvement and dysfunction due to the COVID-19 infection have been explained in various studies.[17-19] Cases from distinct locations and cultures are present with relatively different rates of clinical manifestations and co-morbidities.[20] Therefore, population-specific studies are required for prompt management approach, prevention, and treatment in public health policy.

The current study investigated the clinical presentations, including GI symptoms, comorbidities, and demographic features of COVID-19 patients, in Khorasan-Razavi province, Iran. In this retrospective study, the prevalence of these characteristics and their association with mortality were evaluated in 80 499 hospital-admitted COVID-19 cases from January 21, 2020, to March 20, 2021. To the best of our knowledge, our epidemiological study demonstrated the largest number of confirmed COVID-19 cases in Khorasan-Razavi province.

The data of 80 499 cases showed that the majority of hospital-admitted patients (63.0%) were above 50 years old, and only 15% of them were younger than 30 years. Epidemiological evaluations in many countries demonstrated approximately similar age distribution of cases.[21-24] Some reports from Ecuador and Kazakhstan had a meaningful younger mean age of patients in comparison to our data.[25,26] During the three periods of disease surge,

the number of admitted children (< 10 years) surprisingly increased from 2.5% in 1st wave to 8.9% in 3rd wave. Based on the early report as of February 11 from China, only 0.9% of 44 672 cases were < 10 years old[23] compared to 6.1% (4948) in our study. However, rising patterns in the number of younger patients (0-18) were observed in other countries such as Italy.[27] The mean length of hospital stay was 5.50 ± 7.42; the length of stay appears to be related to underlying disease, age, and admission criteria of different territories.[28]

The main clinical COVID-19 signs and symptoms were respiratory distress, fever, and cough which were observed in 58.2%, 36.7%, and 34.9% of patients, respectively. Respiratory distress was strongly associated with a higher rate of mortality (OR = 2.05, $P < 0.001$). On the other hand, patients with a cough had a better prognosis (OR = 0.88, $P < 0.001$). The most common presentation in the younger group (0-20) was fever due to their potent innate immune response.[29] Nonetheless, there was a slightly lower risk of death in patients with fever (OR = 0.99, $P = 0.525$). According to Li et al, not fever per se, but a higher temperature of fever can be associated with COVID-19 severity.[30] Consistent with our study, the information of 1083 patients in Tehran revealed that fever, shortness of breath, and cough were the prominent symptoms; cough and fever were associated with lower mortality, while shortness of breath indicated worse outcomes.[31] Similarly, a study of 20 133 UK patients reported the mentioned symptoms as the most common presentations and represented a high level of overlap between them.[32]

The UK cohort study defined another cluster of symptoms called enteric symptoms (abdominal pain, vomiting, and diarrhea). In general, 29% of their patients had GI manifestations on admission.[32] Our study evaluated the frequencies of GI symptoms, including anorexia (8.1%), nausea (6.1%), vomiting (4.5%), diarrhea (3.4%), and abdominal pain (2.7%), and the overall prevalence was lower (16.76%). There was significant heterogeneity in the prevalence of GI manifestations among various studies; for instance, ~8.7%[33] or 16%[34] in China, 21.7% (diarrhea) and 13.4% (nausea/vomiting) in Spain,[35] 14.6% (diarrhea) and 16.6% (nausea/vomiting),[31] and 25.4%[36] in Tehran. One explanation for this heterogeneity is the different frequencies of enteric symptoms in age groups. Considering that the age distribution of patients was probably not quite similar in various studies, the reports were not similar. Not applying a universal scale for the diagnosis of each GI symptom and small sample sizes of the studies could also cause this diversification.

Comparing the frequency of GI presentations in each age group, it was found that for patients older than 90, anorexia was the prominent symptom, whereas other GI symptoms such as abdominal pain and nausea were more prevalent for the adolescent group [11-20]. Vomiting and diarrhea were mostly observed in children [0-10] compared to other ages ($P < 0.001$). These results match the meta-analysis by Dara et al, reporting the prevalence of diarrhea (12%) and nausea/vomiting (11%) as the most common GI manifestations in children.[37] In addition, several studies demonstrated a meaningfully higher prevalence of GI symptoms in children than in adults.[38-40]

There are conflicting reports about the association between the presence of GI symptoms and the clinical outcome of COVID-19 infection in literature. Several studies found no significant difference in mortality between cases with GI symptoms and those with no GI presentation.[36,41] However, a meta-analysis by Mao et al showed a higher prevalence of severe COVID-19 disease in patients having GI symptoms.[42] Particularly, the results on diarrhea were also controversial, reporting better[43] or worse prognosis in COVID-19 patients with diarrhea.[44] According to the comparison of the percentage of expired cases in the group "with diarrhea" (8.5%) versus the "no diarrhea" group (15.7%) in our study, diarrhea may be related to a lower mortality rate, but the results were not meaningful ($P = 0.935$). Nevertheless, a significant decrease was found in mortality in COVID-19 patients having GI symptoms compared to those with no GI manifestation, which is in conformity with the results of several studies.[45,46]

Various neurological manifestations related to the central or peripheral nervous system in the COVID-19 infection were discussed in studies.[47] The prevalence of neurological symptoms, specifically headache, loss of consciousness, seizure, paresis, and plegia, was 15.1%, and they generally elevated the risk of death based on our data. Impaired consciousness and a higher mortality rate in some studies[48,49] are in line with our results.

Eventually, the overall mortality rate was 15.1%, which is higher than another descriptive study of over 200 000 patients in Tehran (10.0%).[49] In both studies, male gender, age > 60, and hypertension were related to weak clinical outcomes, although diabetes was associated with a lower mortality ratio (OR = 0.90, $P < 0.001$) in our report and not significantly higher death risk in the above-mentioned descriptive study.

Strengths and Limitations

The large number of patients included in our study was a major strength. However, this research had several limitations. First, our data were restricted to admitted cases in hospitals affiliated to Khorasan-Razavi Universities of Medical Sciences. In addition, blood biochemical tests, including liver function tests in GI manifestations, were not analyzed in this study. Finally, the patients were not followed up for further evaluations of post-COVID-19 symptoms and complications.

Conclusion

In general, this investigation was a multi-hospital study of COVID-19 patients in Khorasan-Razavi province. It analyzed the demographics, clinical manifestations, and comorbidities of 80499 cases reported from January 21, 2020 to March 20, 2021. Age over 60, male gender,

presence of neurologic presentations, respiratory distress, anorexia, presence of at least one comorbidity, and hypertension significantly increased the risk of death. Healthcare providers and public health managers can benefit from these findings to detect and emphasize patients with poor prognoses.

Competing Interests

The authors declare no conflict of interests.

Ethical Approval

All data were extracted from Medical Care Monitoring System (MCMC) under the supervision of Mashhad University of Medical Sciences (Ethics committee code: IR.MUMS.FHMPM.REC.1400.060).

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