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Epidemiological Characteristics of COVID-19 Patients in Mazandaran, Iran, 2021

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Abstract

Background: COVID-19 continues to pose a significant healthcare challenge throughout the world. This study aimed to investigate epidemiological characteristics and associated mortality factors among hospitalized patients with COVID-19 in the Mazandaran province.
Materials & Methods: In this descriptive study, the medical information of patients admitted to 39 hospitals in 17 cities in Mazandaran province between February 20, 2020, and February 20, 2021, were initially assessed and then entered the survey based on the study criteria. For data analysis, statistical approaches such as Chi-square and Fisher's exact test were performed at a significance level of 5%.
Results: Out of the initial 34036 patients total patients, 21007 were included in the study with a mean age of 53.75±18.23 years, and 10219(48.6%) were males. The majority of cases and the highest mortality percent belonged to the age groups of 60 to 70 and 70 to 80. The Mortality proportion was 11.6% (n=2431), with a higher value in males than females. Moreover, the highest mortality rate was seen in ICU (n=2803, 85.7%). Underlying diseases with the highest mortality rate were diabetes (n=2058, 43%) and chronic heart disease (n=166, 6.83%). The most common symptoms of illness were fever (n=9025, 43%), hemoptysis (n=5911, 28.10%), sore throat (n=3771, 18%), and low blood pressure (n=3626, 17.30%).
Conclusion: This study showed a high mortality rate among COVID-19 cases and dissected the related risk factors, including age, gender, underlying diseases, and ICU admission.

Keywords: COVID-19, Epidemiology, SARS-CoV-2, Iran

Introduction

In late December 2019, an unknown pneumonia disease was reported in Wuhan, China, for the first time [1-3]. This newly appeared infection, later called Covid-19, has now led to a global health emergency caused by a new type of coronavirus (SARS-CoV-2) [4]. COVID-19 is the third epidemic caused by coronaviruses in the last two decades, after SARS (Severe Acute Respiratory Syndrome) in 2002-2003 and MERS (Middle East Respiratory Syndrome-related coronavirus) in 2012 [5].

Compared with SARS and MERS, SARS-CoV-2 spreads more rapidly [6] among humans [7-10] and shows subsequent higher mortality and case fatality rates (CFR) different from country to country [11]. In this regard, hospital mortality has been reported in Egypt at 11.2% [12], Algeria at 15%, Netherlands at 11.35%, Qatar at 0.17%, Singapore at 0.2%, and the United Arab Emirates at 0.6%[13]. Moreover, crude CFR in Italy, China, Canada, and the United States were 3.2%, 7.2%, 4.9%, and 5.4%, respectively, while adjusted CFR in Canada and the USA were 5.5% and 6.1% on April 22, 2020 [14, 15], respectively.

In particular, there exist reports of CFR in Middle east countries: Egypt (7.1%), Iran (6.3%), Iraq (4.9%), Lebanon (3.4%), Pakistan (2.1%), Saudi Arabia (0.8%), United Arab Emirates 0.7%, Qatar (0.1%), and Kuwait (0.7%). Moreover, it has been established that Iran (76.3%) and Iraq (69.4 %) had the highest recovery rate in this region, followed by Pakistan (22.5%), the United Arab Emirates (19.2%), and Saudi Arabia (13.6%) [16].

COVID-19 is manifested in fever, dry cough, myalgia, fatigue, dyspnea, headache, and anorexia [17-19], with fever as the most frequent manifestation [20]. Multiple organ failure including renal [21], liver [22], and testicular tissue [21] damages are also seen in patients, and some cases show gastrointestinal symptoms such as [23-26] anorexia, diarrhea, abdominal pain, and nausea/vomiting [27]. Moreover, tinnitus, gingivitis, sudden hearing loss, Bell's palsy, hoarseness [28], loss of smell, taste, hearing loss, and conjunctivitis problems [29, 30] have been barely reported. Hospitalized patients with COVID-19 may end up with stroke [31], cardiac injury [32, 33], thrombotic complications [34], and liver injury [35]. Since the global outbreak of COVID-19, various therapeutic options have been developed for treating COVID-19 [36-38]. Epidemiological studies play an essential role in identifying the factors that contribute to an infection and disease, including risk factors or protective factors related to the health status of the individual or population [39, 40]. Thus, this study was conducted to determine the epidemiological features of COVID-19 patients in the Mazandaran province.

Materials and Methods

The present descriptive study was performed in Mazandaran province, Iran, between February 20, 2020, and February 20, 2021. Data were collected from electronic medical records of 39 hospitals in 17 cities. The inclusion criteria were: 1) positive reverse transcription-polymerase chain reaction (RT-PCR) diagnostic test (of pharyngeal specimens). Infected patients were diagnosed according to national guidelines for the diagnosis and treatment of COVID-19; 2) Complete and available epidemiological, clinical, and outcome information. All patients' data remained confidential.

This study's variables included age, sex, symptoms and signs, underlying diseases, mortality and survival percent, treatments, and radiological findings. This study was approved by the ethics committee of Mazandaran University of Medical Sciences, Mazandaran, Iran, with the ethical code number of IR.MAZUMS..REC.1399.8260.

Descriptive analysis of the collected data was performed as mean (±SD: standard deviation) for continuous variables. Also, frequency, and percent were used for discrete variables. For categorized variables, Chi-square and Fisher's exact test were used. All analyzes were performed at a significance level of 5% using Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 24.0.

Results

Among 34036 patients admitted due to Covid-19, 12977 patients diagnosed by other clinical techniques but PCR tests and 53 patients with insufficient data were excluded from the final samples with the remaining 21007 patients. The epidemiological features of patients with COVID-19 are shown in Table 1. The patients comprised 48.6% of males and 51.4% of females, with a ratio of 0.94. The mean age was 55.79 ± 18.23 years, with 56.41 ± 18.86 years and 55.21 ± 17.59 years for males and females, respectively. Most cases were in the age group 60-70 (19.9%) years, and the lowest of cases were in the age group 10-20 (0.8%) years.

The mean age of death was 68.54± 15.51 years; this quantity was 69.46 ± 15.71 years for males and 67.49 ± 15.22 years for females. The overall mortality was 2431 (11.6%), and the number of male mortality was higher, 1292 (53.1%), compared to females 1139 (46.9%). The frequency of morbidity, however, was higher in women than men (Table 1). Moreover, the highest mortality rate was observed among the age group of 70-80 (26.2%).

Table 1. Epidemiological features of patients with COVID-19 in Mazandaran province, Iran, 2021

	Variable	Total (%) (n=21007)	Death (%) (n=2431)	Live (%) (n=18576)
Age (Year)	0-10	305(1.5)	3(0.1)	302(1.6)
	10-20	168(0.8)	8(0.3)	160(0.9)
	20-30	944(4.5)	34(1.4)	910(4.9)
	30-40	2799(13.3)	94(3.9)	2705(14.6)
	40-50	3432(16.3)	140(5.8)	3292(17.7)
	50-60	4082(19.4)	312(12.8)	3770(20.3)
	60-70	4173(19.9)	579(23.8)	3594(19.3)
	70-80	3036(14.5)	636(26.2)	2400(12.9)
	≥80	2068(9.8)	625(25.7)	1443(7.8)
	p-value*	**<0.001**	**<0.001***	**<0.001**
Sex	Female	10788(51.4)	1139(46.9)	9649(51.9)
	Male	10219(48.6)	1292(53.1)	8927(48.1)
	p-value*	**<0.001**	**0.002**	**<0.001**
Underlying Disease	Without background disease	9639(45.88)	1151(47.35)	8487(45.69)
	Cancer	160(0.76)	24(0.99)	136(0.73)
	Chronic heart disease	1840(8.76)	166(6.83)	1674(9.01)
	Chronic blood	133(0.63)	15(0.62)	118(0.64)
	Chronic kidney	242(1.15)	43(1.77)	199(1.07)
	Chronic pulmonary disease	387(1.84)	68(2.80)	318(1.71)
	immunodeficiency disorders	157(0.75)	12(0.49)	145(0.78)
	Diabetes	1872(8.91)	205(8.43)	1666(8.97)
	Hypertension	1342(6.39)	119(4.90)	1223(6.58)
	Chronic neurological disease	330(1.57)	41(1.69)	289(1.56)
	Chronic Liver	63(0.30)	7(0.29)	56(0.30)
	Severe obesity	51(0.24)	7(0.29)	44(0.24)
	Pregnancy	129(0.61)	19(0.78)	110(0.59)
	Diabetes and Hypertension	1085(5.16)	84(3.46)	1001(5.39)
	Chronic heart disease and Hypertension	543(2.58)	59(2.43)	484(2.61)
	Chronic heart disease and Diabetes	705(3.36)	108(4.44)	597(3.21)
	Diabetes Hypertension, and Chronic heart disease	530(2.52)	49(2.02)	481(2.59)
	Chronic kidney and Diabetes	93(0.44)	14(0.58)	79(0.43)
	Chronic kidney and Hypertension	71(0.34)	10(0.41)	61(0.33)
	Chronic kidney and Chronic heart disease	81(0.39)	15(0.62)	66(0.36)
	Chronic pulmonary disease and Diabetes	66(0.31)	7(0.29)	59(0.32)
	Chronic pulmonary disease and Hypertension	57(0.27)	7(0.29)	50(0.27)
	Chronic pulmonary disease and Chronic heart disease	103(0.49)	21(0.86)	82(0.44)
	Chronic neurological disease and Diabetes	59(0.28)	10(0.41)	49(0.26)
	Chronic neurological disease and Hypertension	57(0.27)	11(0.45)	46(0.25)
	Chronic neurological disease and Chronic heart disease	41(0.20)	7(0.29)	34(0.18)
	Several diseases	1160(5.52)	149(6.13)	1011(5.44)
	Other	14(0.07)	3(0.12)	11(0.06)
Symptoms	Fever	9025(43.00)	961(39.53)	8064(43.41)
	Sore throat	3771((18.00)	327(13.45)	3444(18.54)
	Difficult breathing	2311(11.00)	149(6.13)	2162(11.64)
	Hemoptysis	5911(28.10)	537(22.09)	5374(28.93)
	Chest pain	945(4.50)	96(3.95)	849(4.57)
	Low blood pressure	3626(17.30)	395(16.25)	3231(17.39)
Treatment	Standard of care (SOC)	8381(39.90)	858(35.29)	7523(45.50)
	Antiretroviral Therapy	1005(4.78)	124(5.10)	881(4.74)
	Antibiotic Therapy	6804(32.39)	815(33.53)	5989(32.24)
	Combination therapy	4083(19.44)	546(22.46)	3537(19.04)
	Antimalarial	734(3.49)	88(3.62)	646(3.48)

* Chi-square; ** Fisher`s exact test

The screening process of admitted patients is shown in Fig. 1. The most common symptoms in patients were fever (43%), followed by hemoptysis (28.10%), sore throat (18%), difficulty breathing (11%), and low blood pressure (17.30%). The least common symptom was chest pain (4.50%).

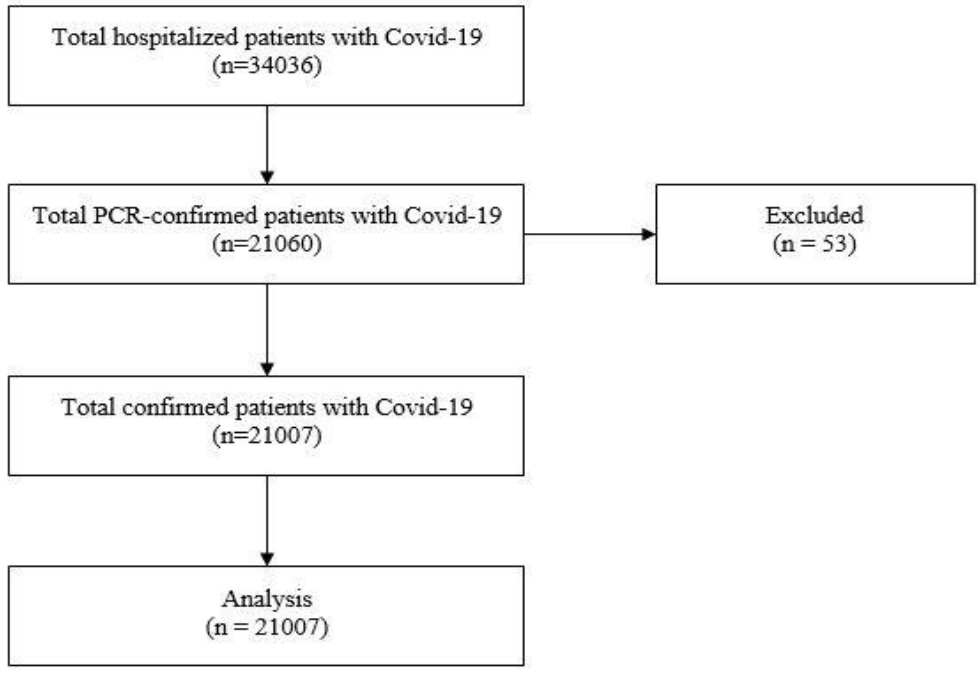

Fig.1. The overall flow chart of the screening process

The result showed that diabetes (8.91%), chronic heart disease (8.76%), hypertension (6.39%), chronic pulmonary disease (1.84%), chronic kidney disease (1.15%), chronic neurological disease (1.57%) were the most frequent underlying diseases. Some patients also had coincident diseases, among which diabetes and hypertension (5.16%), chronic heart disease and hypertension (2.58%), chronic heart disease and diabetes (3.36%), diabetes and hypertension and chronic heart disease (2.52%), and several diseases (5.52%) were the most prevalent ones.

The assessment of clinical records showed that most of the deaths occurred in cases with no clinical background. Among the underlying disease, the highest mortality rate belonged to patients with diabetes (8.43%), while chronic liver (0.29%) and severe obesity (0.29%) conditions caused the lowest mortality. This suggests the probable high and low potentials of diabetes as long as liver and obesity in death rate, respectively. It was also observed that the risk of death in diabetes patients with other underlying diseases like hypertension, hypertension and chronic heart disease, chronic kidney, and chronic pulmonary disease was lower than in diabetes. This matter is true for hypertension and chronic pulmonary disease simultaneously with another condition (Table 1).

The symptom was the next clinical manifestation monitored and recorded to evaluate its probable relationship with the death rate. The results showed that patients with fever (39.53%) had the highest mortality rate, and the least mortality rate was related to Chest pain (3.95%). Regarding the therapeutic approaches, most patients received treatments based on Standard of Care (SOC) guidelines (39.90%) followed by antibiotic therapy (32.39%) and Combination therapy (19.44%), all of which showed the highest mortality values suggesting their ineffective prescription in COVID-19. On the other hand, antiretroviral (4.78%) and antimalarial (hydroxychloroquine) (3.49%) therapies seemed to successfully prevent the death toll as their lower levels of mortality rate indicate.

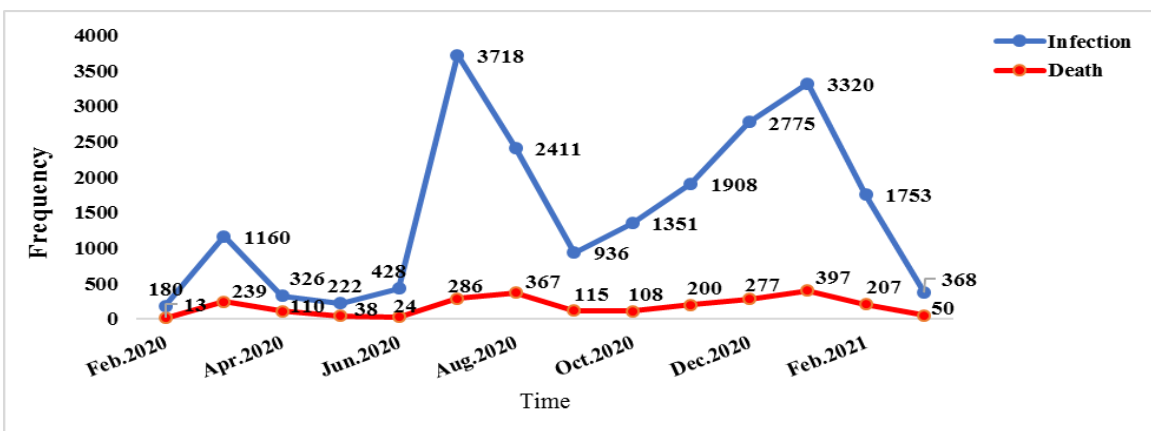

Fig. 2. Monthly morbidity and mortality cases in patients with COVID-19 in Mazandaran, Iran, 2021

Table 2. Mortality of patients with COVID-19 by ward in Mazandaran province, Iran, 2021

Place of death	Number of Cases	Percent
ICU	2803	85.7
CCU	80	3.3
Infectious	85	3.5
Internal	109	4.5
Emergency	35	1.4
Outside the hospital	14	0.6
Other (gastroenterology, NICU, PICU)	25	1.0
Total	2431	100

Our results showed that the highest morbidity of Covid-19 occurred in cold months, July, January, December, and February, during the one year. Also, Monthly mortality was higher in January, August, and July. The assessment of the place of death showed that the highest mortality occurred in the intensive care unit (ICU), with a mortality rate of 85.7% (Table 2). The morbidity and mortality cases were reported for each city and by gender in Table 3. The highest rate of mortality and morbidity was 19 in Sari City.

Table 3. Morbidity and mortality cases by gender in Mazandaran province, Iran, 2021

City	Population			Morbidity			Mortality		
	Total	Male	Female	Total (Per 10000)	Male (Per 10000)	Female (Per 10000)	Total (Per 10000)	Male (Per 10000)	Female (Per 10000)
Amol	411221	208516	202700	4189 (101.87)	1723 (82.63)	2466 (121.66)	366 (8.90)	105 (5.04)	261 (12.88)
Babolsar	145176	73231	71945	187 (12.88)	76 (10.38)	111 (15.43)	22 (1.52)	11 (1.50)	11 (1.53)
Behshahr	168978	84868	84110	1840 (108.89)	973 (114.65)	867 (103.08)	234 (13.85)	159 (18.73)	75 (8.92)
Tonekabon	162155	81548	80605	992 (61.18)	498 (61.07)	494 (61.29)	92 (5.67)	30 (3.68)	62 (7.69)
Juybar	81666	41744	39921	323 (39.55)	137 (32.82)	186 (46.59)	36 (4.41)	29 (6.95)	7 (1.75)
Chalus	103237	51691	51546	973 (34.25)	458 (88.60)	515 (99.91)	148 (14.34)	67 (12.96)	81 (15.71)
Ramsar	75306	37772	37534	846 (112.34)	380 (100.60)	466 (124.15)	129 (17.13)	60 (15.88)	69 (18.38)
Sari	514757	258436	256316	5001(97.15)	2376 (91.94)	2625 (102.41)	612 (11.89)	385 (14.90)	227 (8.86)
Savadkuh	33160	16729	16431	479 (144.45)	241 (114.06)	238 (144.85)	44 (13.27)	3 (1.79)	41 (24.95)
Abbasabad	53957	27806	26151	108 (20.02)	81 (29.13)	27 (10.32)	33 (6.12)	29 (10.43)	4 (1.53)
Fereydunkenar	63838	32574	31263	473 (74.09)	252 (77.36)	221 (70.69)	66 (10.34)	55 (16.88)	11 (3.52)
Qaem Shahr	308165	154289	153872	3291 (106.79)	1699 (110.12)	1592 (103.46)	386 (12.53)	208 (13.48)	178 (11.57)
Galugah	38381	19354	19027	99 (25.79)	51 (26.35)	48 (25.23)	9 (2.34)	6 (3.10)	3 (1.58)
Mahmudabad	102607	52201	50406	344 (33.53)	183 (35.06)	161 (31.94)	60 (5.85)	43 (8.24)	17 (3.37)
Neka	116846	58749	58097	644 (55.12)	353 (60.09)	291 (50.09)	76 (6.50)	44 (7.49)	32 (5.51)
Nur	122956	62270	60686	665 (54.08)	348 (55.89)	317 (52.24)	66 (5.37)	39 (6.26)	27 (4.45)
Nowshahr	131596	66376	65220	553 (42.02)	390 (58.76)	163 (24.99)	52 (3.95)	19 (2.86)	33 (5.06)

Discussion

This study aimed to evaluate the risk of COVID-19 mortality and the involved factors using one-year clinical records of more than 21000 COVID-19 patients from 39 hospitals in 21 cities in the north of Iran.

Based on the results, the estimated case fatality rate in hospitalized cases was approximately 11.6%, consistent with the previously reported range of 4% to 15.4% in Iranian populations and [41-47] and the highest mortality rate of 15.4% in northeast Iran [45]. One reason for the different mortality rates might be the smaller sample size of previous studies. To date, the largest sample size of 8252 was studied by Zali et al. [46] in Tehran, with a mortality rate of 13.52% which is also in line with our findings.

In our study, a significant association was observed between greater age and increased mortality risk in COVID-19 patients. The highest

mortality rate was observed in the age group of 70-80. Similar to our findings, a large cohort study showed that patients ≥75 years old were at higher mortality risk than those <65 years [48]. The results of some meta-analyses [49, 50] revealed that older age is associated with higher death among hospitalized COVID-19 patients. More particularly, there was a positive correlation between Hypertension, weak immunity, poor lung function, and comorbidities that were suggested as the reasons for the increased risk of death in older COVID-19 cases [48, 49].

According to the present findings, the mortality rate in males was significantly higher than in females, consistent with some studies [51-53] in which higher death in male patients was reported. Moreover, a large-scale meta-analysis [50, 54] revealed that the male gender is a risk factor for death. This difference can be attributed to gender discrepancies in immune response [55-57] as long as biological, psychosocial, and behavioral factors [58, 59].

In the present study, the most common symptoms among hospitalized cases were fever, hemoptysis, sore throat, and difficulty breathing. The highest death was observed in patients who had a fever. In complete agreement with our results, fever has been proposed as a predictive factor of COVID-19 mortality [60], and Tharakan et al. [61] showed that there is a significant increase in the mortality rate for every 0.5 °C increase in body temperature in COVID-19 patients.

The present results showed that diabetes, hypertension, and chronic heart disease were significantly associated with more deaths in COVID-19 patients. These findings are supported by other studies conducted on primary and secondary data [49, 62-66] and the meta-analysis by Corona et al. [67], in which diabetes was the most prevalent comorbidity associated with COVID-19 deaths. In these patients, an increased death rate seems to be connected with decreased lymphocyte count, lactate dehydrogenase, hsCRP, and interleukin levels [68]. Although some studies proved that diabetic patients receiving insulin are at higher risk of exacerbation of the disease and death [69, 70], other studies showed that controlling blood glucose reduces the mortality rate of Covid-19 diabetic cases [71]. Anti-diabetic drugs such as metformin, iDPP4, and pioglitazone are beneficial for COVID-19 treatment [72].

Our results showed that ICU witnessed the highest mortality rate, the quantity of which hinges on disease severity, gender, ethnicity, age, comorbidity, blood type, respiratory support, and availability of trained staff [73]. Moreover, bacterial and fungal nosocomial infections, which are common complications in ICU, are shown to be associated with high mortality and longer ICU stays [74]. Moreover, It is undeniable that higher ICU capacity strain causes an increase in mortality rate of Covid-19 [75].

The potential influence of the temperature was another factor that was evaluated. The results showed that both infection and mortality rate increased in the cold seasons. On one hand, there are several studies consistent with our data highlighting the reducing effect of tempresture on COVID-19 infection and death rates. Haklai et al. showed that the incidence of COVID-19 decreases as the temperature increases [76] as the same results were obtained in European countries where the spread of COVID-19 decreased between March and May [77]. Comparing various countries with different climates, it has been found that the average number of COVID-cases was lower in countries with hot weather [78]. This is corroborated by another study indicating that cold countries, despite of having improved economic and social parameters, experienced higher prevalence of COVID-19 and rapid outbreak of the disease is associated with moderate high and low tempreatures [79]. on the other hand, several studies showed that there is no evidence that the number of COVID-19 cases decreases in warm seasons [80, 81] particularly in Iran [82]. Therefore, the temperature-based results should be interpreted with caution.

Our study is the largest multicenter study conducted in Iran on the mortality rate and its risk factors. There are several limitations to our study. Due to insufficient laboratory data, we could not estimate the mortality rate according to the severity of COVID-19 disease. Generalizability can be the next limitation since our study was conducted in the north of Iran and therefore our finding may fail to be generalized to the whole population in Iran.

Conclusion

Our study showed that the case fatality rate of COVID-19 was higher in northern Iran than in other regions. Therefore, greater healthcare resources and facilities would help reduce the mortality rate in this area. Older age, male gender, comorbidities such as diabetes, chronic heart disease, hypertension, and admission to ICU are significant death risk factors in hospitalized COVID-19 patients. The findings of this study would assist health policymakers in developing appropriate management strategies and stratifying the patients according to risk for giving proper treatments and nursing services.

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