DOI: 10.7860/JCDR/2022/49881.16335

Original Article

Epidemiology Section

Clinical Characteristics and Risk Factors for Mortality in COVID-19 Patients: A Retrospective Cohort Study

RAHIMEH KHAJOEI[1], NABIOLLAH HEYDARPOUR[2], REZA SADEGHI[3], MOHADESEH BALVARDI[4], HAMID JAFARI[5], SAJAD SHOKOHIAN[6], FARZAD RAHMANI[7]

ABSTRACT

Introduction: Coronavirus Disease in 2019 (COVID-19) is globally a major factor in the mortality of patients. Hence, there is an immediate requirement to recognise the mortality predictors in the COVID-19 patients.

Aim: To identify the clinical features and risk factors for the mortality of adult patients suffering from COVID-19 in Sirjan, Iran.

Materials and Methods: In this retrospective cohort study, all demographic, clinical, laboratory data of COVID-19 patients who were admitted to hospitals of Sirjan city was collected from July to October 2020 and data was analysed in November 2020. In this period, 269 patients with COVID-19 were admitted. The findings based on the considered parameters of patients in the hospital was recorded; Univariable and multivariable logistic regression methods were applied to find the risk factors due to in hospital death.

Results: Out of 269 patients, 39 patients (14.5%) died in the hospital and the rest were discharged. A total of 152 (56.5%) patients had co-morbidities. Hypertension (HTN) was the most common underlying disease 71 (26.4%), followed by Diabetes Mellitus (DM) 55 (20.4%), cardiac disease, and Chronic Obstructive Pulmonary Disorder (COPD). The most common symptom was dyspnoea 207 (77%), followed by cough, 192 (71.4%) and fever, 127 (47.2%). The most common findings in the chest Computed Tomography (CT) scan of patients was ground-glass opacity with a frequency of 150 among 188 patients (79.8%) in patients with the abnormal CT scan. Multivariable regression indicated the increased odds of in-hospital death associated with COPD (OR=3.20, 95% CI 1.02-10.04; p=0.046), arterial saturation of oxygen ≤93% (OR=5.70, 95% CL 2.42-13.40; p<0.001), and leukocytosis (OR=7.26, 95% CL, 3.02-17.49, p<0.001).

Conclusion: Based on the results of the present study, COPD, arterial saturation of oxygen (≤93%), and leukocytosis were risk factors for the hospital mortality of COVID-19. It might be proper for the initial determination of patients, who may need life saving interventions.

Keywords: Coronavirus disease 2019, Hospital mortality, Infectious diseases, Outcome

INTRODUCTION

It has been more than a year since the beginning of COVID-19. This form of viral pneumonia caused by Severe Acute Respiratory Syndrome (SARS-CoV-2) was identified as a pandemic in March 2020 [1]. It led to many infections and deaths around the world [2-5]. Globally, since 27th December 2020, 79,232,555 confirmed cases of COVID-19 were observed involving 1,754,493 deaths which were reported to World Health Organisation (WHO); also, 54,693 deaths have occurred to that date because of coronavirus in Iran [5]. The outbreak and mortality of COVID-19 in Iran, become a considerable public health concern.

Since COVID-19 outbreak, many studies were performed on the clinical and epidemiological characteristics of COVID-19 disease [6,7]. Moreover, many risk factors were determined in terms of severe disease and death from the disease [8,9]. Symptoms of COVID-19 in the patients were different and it might be aymptomatic in nature and/or patients with mild symptoms to patients with bilateral pneumonia and failure in organs, and COVID-19 may result in death at its severe level [10-12]. The symptoms first replicate a respiratory system disorder involving fever, sore throat, dyspnoea, and cough. Over time, other symptoms like vomiting, abdominal pain, headache, diarrhoea, loss of taste and smell were added to the clinical features [13-15].

Moreover, Hypertension (HTN), being the foremost common disease worldwide, was predominant among the hospitalised COVID-19 patients over diverse countries, and a few meta-analysis researches have indicated a positive relationship between HTN and COVID-19 mortality [16-21]. The results of some researches revealed that diabetes increases COVID-19 severity. Furthermore, tabulated descriptive data show that the mortality rate was higher in the patients with previous diagnosis of diabetes [22-24]. In meta-analysis studies, typical Computed Tomography (CT) imaging appearance for COVID-19 patient's revealed ground-glass opacity [25,26]. Moreover, based on laboratory findings, high C-reactive Protein (CRP), declined albumin, and high Lactate Dehydrogenase (LDH), lymphopenia, and high Erythrocyte Sedimentation Rate (ESR), were reported as the most common laboratory results.

Furthermore, based on risk factors in various research, older age, underlying diseases like HTN, diabetes, cancer, cardiovascular disease are known as the risk factors for severe disease and mortality [27-31]. Risk factors in COVID-19 disease were reported in three other similar viral infections like Influenza Type A virus (H1N1), SARS, and Middle East Respiratory Syndrome (MERS) [32-33].

To decrease the mortality in COVID-19 patients, it is vital to distinguish the clinical characteristics and risk factors related to this infection. The present study identified the clinical characteristics and risk factors for the mortality of adult patients with COVID-19 in Sirjan, Iran.

MATERIALS AND METHODS

This retrospective cohort study includes all patients suspected of COVID-19, who were admitted to Imam Reza and Dr. Gharazi hospitals in Sirjan/Iran between July 20, 2020 and October 22, 2020 and data was analysed in November 2020. The sampling method used was full census. In the study period, 380 suspected patients with COVID-19 who died or discharged were involved, but based on the inclusion and exclusion criteria, 269 patients were assessed. The hospitalisation of these patients was based on WHO protocol

[26]. The Ethical Research Committee approved the present study at Sirjan University of Medical Sciences (IR.SIRUMS.REC.1399.005).

Inclusion criteria: The inclusion criteria were all COVID-19 patients with positive results on Real-Time-Polymerase Chain Reaction test (RT-PCR). A laboratory approved COVID-19 case was defined as a positive result on RT-PCR test for SARS-CoV-2 with presence in nasal and pharyngeal swab specimens.

Exclusion criteria: Patients with unapproved diagnosis, incomplete medical information in the medical records and discharges from hospital against medical advise were excluded from the study.

Study Procedure

The checklist was a standardised data collection form, an adjusted adaptation of WHO/International Serious Intense Respiratory and Rising Disease Consortium case record form for extreme intense respiratory contaminations [3]. It incorporates socio-economic and clinical characteristics, research facility discoveries, and imaging highlights. All clinical and research facility information, CT filters, therapeutic history, fundamental co-morbidities, treatment measures (antiviral treatment, corticosteroid treatment, oxygen treatment, mechanical ventilation) and results from the information of patients were enrolled for all patients. Information collection was done by two staff of the medical sciences faculty of Sirjan. Then, it was evaluated by an infectious disease specialist. Patients with incomplete data were excluded from the research. Underlying diseases were recorded based on medical reports and the patient's self-report.

Disease severity was defined based on these criteria as a moderate, severe, and critical illness: Diagnostic criteria for moderate cases involved fever, respiratory symptoms, and pneumonic changes on CT scan. Diagnostic criteria for serious cases were dyspnoea with a Respiratory Rate (RR) ≥30 breaths/min, Oxygen Saturation (O_2Sat) ≤93% at rest, and chest imaging with progression in the lesion of more than 50% within 24-48 hours. Moreover, there were symptomatic criteria for the basic cases of respiratory dyspnoea with the requirement for mechanical ventilation, shock, and modified function of other organs which needed hospitalisation within Intensive Care Unit (ICU) [34]. Fever was characterised as a temperature at the slightest 37.3°C. Furthermore, hypotension was characterised as blood weight less than 90 mmHg [35]. A Confusion, Uraemia, Respiratory rate, Blood pressure (CURB-65) score was calculated for all patients. CURB-65 scores range from 0 to 4. A score from 0 to 1 indicates a low risk of mortality, whereas, a score of 2 or higher is related to higher mortality [36].

STATISTICAL ANALYSIS

Data was entered into SPSS software version 19.0 (IBM statistics, New York, United States of America). Frequency (percentage) was utilised to explain the qualitative data. To analyse the data between two groups Chi-square or Fisher's-Exact test to assess the risk factors related to in hospital mortality of quiet univariate and multivariate calculated test were utilised. Regarding model overfitting, four variables were chosen due to past research and clinical limitations for univariate logistic tests. In all tests, a significant difference level was set as 0.05.

RESULTS

Demographics and clinical features of the sample are indicated in [Table/Fig-1]. Thirty-nine patients (14.5%) died in the hospital, and 230 patients (85.5%) were discharged from the hospital. Near half of the patients were aged more than 50 years. Gender differences were not significant. Among all patients, 152 (56.5%) of patients had an underlying disease. HTN was the most common underlying disease, followed by DM cardiac disease, and COPD. The most common symptoms at the time of admission were dyspnoea, coughing, fever, and then myalgia, fatigue, and headache, respectively. The most common finding in the chest CT scan of patients was ground-glass opacity with a frequency of 150 among 188 (79.8%) patients with abnormal CT scan and 22 from 31 (71%) among the patients who died. Twenty-nine (10.8%) patients had lymphocytopenia, and 72 (28.5%) had White Blood Cells (WBC) greater than 103/L. Out of 269 patients, 175 patients (64.9%) had moderate status, 42 (15.7%) had severe, and 52 patients (19.4%) had critical status. A totol of 170 (63.6%) patients had a CURB-65 score of 0 or 1.97 patients (36.3%) had a CURB-65 score of ≥2. All deaths had a CURB-65 score ≥2.

Variables	Overall n=269	With mortality n=39	Without mortality n=230	p-value
Age (years), N (%)				
<30	44 (16.4)	2 (5.1)	42 (18.2)	<0.001
30-50	100 (37.2)	11 (28.2)	89 (38.7)	
50-70	79 (29.4)	8 (20.5)	71 (30.9)	
>70	46 (17.1)	18 (46.2)	28 (12.2)	
Gender (in years), n (%)				
Male	139 (51.7)	24 (61.5)	115 (50)	0.182
Female	130 (48.3)	15 (38.5)	115 (50)	
Duration of admission (in hours), n (%)				
0-5	140 (52.1)	19 (48.7)	121 (52.6)	0.001
5-10	105 (39)	14 (35.9)	91 (39.1)	
10-20	24 (8·9)	6 (15.4)	18 (8.3)	
Disease severity status				
Moderate	175 (64.9)	0	174 (76)	<0.001
Severe	42 (15.7)	2 (5.1)	40 (17.5)	
Critical	52 (19.4)	37 (94.9)	15 (6.6)	
Imaging features, n/N (%)				
Consolidation	21/188 (11.2)	6/31 (19.3)	15/157 (9.5)	0.221
Ground-glass opacity	150/188 (79.8)	22/31 (71.0)	128/157 (81.5)	
Bilateral pulmonary infiltration	17/188 (9.0)	3/31 (9.7)	14/157 (9.0)	
CURB-65 score, n/N (%)				
0-1	170/267 (63.6)	0	170/229 (74.2)	<0.001
2	47/267 (17.6)	3/38 (7.9)	44/229 (19.1)	
3-5	50/267 (18.7)	35/38 (92.1)	15/229 (6.5)	
ICU admission, n (%)				
Yes	41 (15.2)	37 (94.9)	4 (1.7)	<0.001
No	228 (87.6)	2 (5.1)	226 (98.3)	
Smoking history, n (%)				
Yes	62 (23)	10 (25.6)	52 (22.6)	0.678
No	207 (76.9)	29 (74.4)	178 (77.4)	
Co-morbidity, n (%)	152 (56.5)	25 (64.1)	127 (55.2)	0.301
Hypertension	71 (26.4)	11 (28.2)	60 (26.1)	0.851
Diabetes	55 (20.4)	5 (12.8)	50 (21.7)	0.202
Coronary heart disease	48 (17.8)	8 (20.5)	40 (17.4)	0·638
Chronic obstructive lung disease	26 (9.7)	10 (25.6)	16 (7.0)	0.001
Chronic kidney disease	13 (4.8)	2 (5.1)	11 (4.8)	0.926
Carcinoma	10 (3.7)	4 (10.3)	6 (2.6)	<0.020
Clinical symptoms, n (%)				
Dyspnoea	207 (77.0)	33 (84.6)	174 (75.7)	0.219
Cough	192 (71.4)	22 (56.4)	170 (73.9)	0.025
Myalgia	98 (36.4)	5 (12.8)	93 (40.4)	0.001
Chest pain	41 (15.2)	4 (10.3)	37 (16.1)	0.349
Fatigue	94 (34.9)	5 (12.8)	89 (38.7)	0.002
Headache	70 (26.0)	6 (15.4)	64 (27.8)	0.102
Sputum	54 (20.1)	6 (15.4)	48 (20.9)	0.429
Low of consciousness	40 (14.9)	17 (43.6)	23 (10.0)	<0·001

Diarrhoea	25 (9.3)	3 (7.7)	22 (9.6)	1.000
Vomit	35 (13.1)	2 (5.1)	33 (14.4)	0.112
Vital sign, n (%)				
Systolic Blood Pressure (SBP) (<90 mmHg)	32 (11.9)	14 (35.9)	18 (7.8)	<0.001
Pulse rate (≥125 beats/ minute)	13 (4.9)	8 (20.5)	5 (2.2)	<0.001
Respiratory rate (>24 breaths/minute)	29 (10.8)	13 (34.2)	16 (7.0)	<0.001
SPO_2 (<93%)	78 (29)	26 (66.7)	52 (22.6)	<0.001
Body temperature (>37.3°C)	127 (47.2)	20 (51.3)	107 (46.7)	0.598
Laboratory data, n (%)				
Lymphocyte count <0.8 (×10^9 per L)	29 (10.8)	15 (38.5)	14 (6.1)	0.001
White blood cell count, ×10^9 per L, n/N (%)				
4-10	180/253 (71.1)	11/39 (26.3)	170/214 (79.4)	<0.001
>10	72/253 (28.5)	28/39 (73.7)	44/214 (20.6)	
HB (g/dL) <10	20/255 (7.4)	4/34 (10.3)	16/221 (7.0)	0.513
Platelet <100 (10^9 per L)	14/231 (5.2)	4/33 (10.3)	10/198 (4.3)	0.122
ALT >40 (IU/L)	28/68 (10.4)	6/15 (15.4)	22/53 (9.6)	0.916
ESR >30 (mm/hr)	66/138 (24.5)	9/12 (23.1)	57/126 (24.8)	0.233
LDH >245 (IU/L)	91/105 (33.8)	12/14 (30.8)	79/91 (34.3)	0.858
CTnI >28 (pg/mL)	46/68 (17.1)	8/11 (20.5)	38/57 (16.5)	0.296
CRP, n/N (%)				
Positive	136/214 (63.5)	18/26 (69.2)	118/188 (62.8)	0.676
Negative	78/214 (36.4)	8/26 (30.8)	70/188 (37.2)	
Mechanical ventilation, n (%)				
Non invasive	7 (2.6)	3 (7.9)	4 (1.8)	0.063
Invasive	41 (15.2)	34 (87.2)	7 (3.1)	<0.001

[Table/Fig-1]: Demographic, clinical, laboratory and radiographic findings of patients.
p<0.05 was considered significant; Data representation n (%), n/N (%). p-values were calculated by χ^2 test or Fisher's-exact test; ICU: Intensive care unit; TLC: Total lymphocyte count; HB: Haemoglobin level; ALK: Alanine transferase; LDH: Lactate dehydrogenase; ESR: Erythrocyte sedimentation rate; CTnI: Cardiac Troponin I; CRP: C-reactive-protein; SBP: Systolic blood pressure; SPO_2: Saturation of peripheral oxygen; CURB-65 score: (Confusion, uraemia, respiratory rate, BP, age ≥65 years). All the findings were not available for all patients

Association between demographic and clinical characteristics and in hospital mortality: There was an association between age and mortality in the patients (p<0.001). Moreover, there was an association among the days of hospitalisation in the healing centre and mortality in the patients (p=0.001). There was an association between COPD (p=0.001) and carcinoma (p<0.020) with hospital mortality.

Based on the symptoms, there was an association among the indications of hacking (p=0.025), myalgia (p=0.001), fatigue (p=0.002), loss of consciousness (p<0.001), and hospital mortality. There was an association among the RR more than 24 per minute (p<0.001), heart rate more than 125 per minute (p<0.001), O_2 saturation less than 93% (p<0.001), and blood pressure less than 90 mmHg with hospital mortality (p<0.001). There was an association among laboratory findings of leukocytosis (p<0.001), lymphocytopenia (p=0.001), and death in patients. There was an association between CURB-65 score and mortality in the patients (p <0.001).

Risk factors associated with in hospital mortality: Based on [Table/Fig-2], risk factors are related to in-hospital mortality. In univariable analysis, lymphopenia were associated with hospital mortality. The hospital mortality odds were also higher in the patients with COPD. Moreover, there was an association among the clinical symptom loss of consciousness with hospital mortality. The mortality was higher in the patients with a RR of more than 24 breaths per minute and O_2 saturation was less than 93%. In the multivariable logistic regression model, we found that COPD (OR=3.20, CI:1.02-10.04), O_2 saturation less than 93%, and leukocytosis were associated with the increased odds of mortality.

Variables	Univariable OR* (95% CI)	p-value	Multivariable OR* (95% CI)	p-value
Age (years)				
30-50	2.60 (0.80-3.21)	0.228	-	-
>50-70	2.37 (0.48-11.67)	0.290	-	-
>70	13.50 (2.90-62.79)	0.001	-	-
Smoking	1.18 (0.54-2.58)	0.678	-	-
Past medical history				
Hypertension	1.10 (0.51-2.35)	0.793	-	-
Diabetes mellitus	0.52 (0.19-1.42)	0.208	-	-
Chronic obstructive lung disease	4.61 (1.91-11.12)	0.001	3.20 (1.02-10.04)	0.046
Coronary heart disease	1.22 (0.52-2.86)	0.638	-	-
Cancer	4.26 (1.14-15.88)	0.310	-	-
Symptoms				
Dyspnoea	1.77 (0.70-4.44)	0.224	-	-
Cough	0.45 (0.22-0.91)	0.280	-	-
Loss of consciousness	6.35 (2.95-13.67)	<0·001	-	-
Vital signs				
Respiratory rate >24 (/minute)	0.14 (0.62-0.33)	<0·001	2.35 (0.84-6.51)	0.100
SPO_2 (<93%)	6.84 (3.28-14.26)	<0·001	5.70 (2.42-13.40)	<0·001
Body temperature (°C)	1.20 (0.60-2.36)	0.599	-	-
Laboratory data				
TLC >10 (×10^9 per L)	10.81 (4.88-23.94)	<0·001	7.26 (3.02-17.49)	<0·001
Lymphocyte count (×10^9 per L)	10.98 (4.64-25.97)	<0·001	-	-
CTnI ≤28 (pg/mL)	1.33 (0.31-5.60)	0.695	-	-
CRP, Positive	1.35 (0.55-3.23)	0.522	-	-

[Table/Fig-2]: Demographic, clinical, laboratory and radiographic findings of patients.
*Odds ratio

DISCUSSION

Total 269 patient's data were evaluated in the present retrospective cohort study. Thirty-nine patients died, and the mortality rate was 14.5%. This rate is less than the meta-analysis study by Young L et al., (16.3%) but some studies showed rate more than the present study (4.3%) [8,9,12,15].

The present retrospective cohort study identified several risk factors for death in the hospitalised COVID-19 patients in Sirjan. COPD, O_2 saturation less than 93%, and leukocytosis were associated with the increased odds of the mortality of patients with COVID-19. WHO has determined COPD, as the third leading reason of death in low and middle income countries [27]. A meta-analysis also found that pre-existing COPD is a risk factor in predicting the adverse consequences in COVID-19 patients [28]. Moreover, in a study by Nandy K et al., there was a considerable association between COPD and the occurrence of serious events in COVID-19 patients [29]. In the study by Lippi G et al., the mortality rate of COPD patients with COVID-19 was over 60% [30]. It is a considerable finding, regarding the high prevalence of COPD worldwide. In clinical settings, necessary measures should be taken to advance patient assessment and management with COPD.

An increase in white blood cells was another risk factor that was identified. The results of a meta-analysis study by Yamada T et al., indicated that leukocytosis was associated with severe disease and leukocytosis at admission may predict severe COVID-19 and poor outcomes in these patients [31]. Furthermore, in the study of

Huang C et al., leukocytosis was determined as one of the risk factors for mortality in the patients with COVID-19 [13].

More than half of the patients had an underlying disease. The results were greater than the findings of another study [32]. Based on recent systematic reviews, co-morbidities prevalence in COVID-19 patients was high, and these co-morbidities were associated with increased disease severity [33]. In similar studies, HTN was the most prevalent disease [33-38]. There was no association between HTN and mortality in this study. While some research noted that HTN should be considered an independent risk factor for COVID-19 severity, this tip should be considered the high prevalence of HTN in critical patients with COVID-19 may be due to older individuals vulnerability to the infection of SARS-COV-2 which is affected by HTN. There is no epidemiologic evidence to indicate HTN as an independent risk factor to increase intense disease in the patients with COVID-19. Similar to the present study, the study by Shibata S also reported that HTN does not constitute as a risk factor for COVID-19 [39].

In a similar research, 20% of all patients had DM, and this condition is determined after HTN as the most prevalent underlying disease [13,40]. Another research found that diabetes was associated with mortality, severity, and acute respiratory distress syndrome in COVID-19 [41]. Despite being determined as the second most common underlying disease there was no association between DM and mortality in the patients with COVID-19 in the index research; and it contradicts the results of the meta-analyses that found DM is considerably associated with the mortality in COVID-19 patients [41-43]. Despite this, it is recommended that patients with DM should manage their blood sugar to decrease the risk of infection.

Similar to the present research, cancer was considerably associated with mortality in other studies [27,44]. COVID-19 infected cancer patients encounter with the risk of mechanical ventilation or ICU hospitalisation 3.5 times more than the general population [45].

As in other similar studies, the most prevalent symptoms of disease in the patients were dyspnoea followed by coughing, fever, myalgia, and fatigue [13,33,38,46]. In addition to common respiratory symptoms, the symptoms of chest pain, headache, diarrhoea, nausea, dizziness, and vomiting were also obvious in some patients. In addition to considering respiratory symptoms in patients, non respiratory symptoms should also be regarded. Other studies showed an association among the symptoms of coughing, myalgia, fatigue, loss of consciousness, and hospital mortality [1,47,48]. In the present research, 47.2% of all patients and 51.3% of patients with mortality had fever. Fever isn't a significant clinical symptom to COVID-19 from January 25th, 2020 [49]. Similar to this research, the prevalence of ground-glass opacity in chest CT scan was higher than of the other signs of bilateral pulmonary infiltration and consolidation [33,50]. Moreover, these results were consistent with the results of meta-analysis studies by Bao C et al., and Kim H et al., [16,51].

The mortality rate was greater in the elderly (over 70 years old). Hence, age is determined as a considerable risk factor in COVID-19 patient mortality. In fact, older age is associated with failure in different organs, which exacerbates the risk of being infected [50]. More prevalence of cardiovascular diseases, HTN, and DM in older adults is related to decrease immune defense against infections [35,40,47]. In a meta-analysis study by Starke KR et al., there was a 2.7% increased risk per age year for disease severity. The author also noted that age related diseases are more significant than age itself, and when taking preventive measures, after adjusting for age related factors, the mild impact of age on the severity of disease must be considered [52].

Furthermore, lymphopenia was observed at 38.5% in patients who died, which was significantly higher than patients who were discharged. An important association was observed between lymphocyte counts and mortality. In the research by Zhao Q et al., lymphocyte counts in COVID-19 patients were considerably lower, and in patients with lymphopenia, the risk of developing severe COVID-19 was almost tripled [53].

Inconsistent with the results by Rodriguez-Morales AJ et al., an increase in CRP in the patients was not a considerable finding in laboratory results of COVID-19 patients [33]. An increase in CTnI was seen in 20.5% of patients with mortality in the index study. Cardiovascular complications due to COVID-19 have been related to cardiac failure, arrhythmia, cardiac shock, acute myocardial infarction, and myocarditis [54-56].

In the present study, total 23% of all patients, 25.6% of patients with mortality, and 22.6% of discharged patients had a positive history of smoking. Another study found no considerable association between smoking and mortality [32]. Nepogodiev D et al., concluded that smoking is not a risk factor for protective factor patients with COVID-19 [47]. Smoking is most prevalent among young people and they usually do not have underlying diseases, the lack of an association between smoking and mortality in patients, thus be justified.

Besides, the mortality rate in men was higher than in women; similar to another systemic review [57]. The reason for in the higher mortality in men may be due to behaviours, which are more common in men. Men are more likely than women to engage in risky behaviours and roles, which are more likely to be present in crowded communities and environments, increasing their risk of infection and death [57]. Besides, females have the stronger innate and acquired immunity against viral infections compared to males, which is one reason for less mortality rate in females [58].

Limitation(s)

First, the present research was handled as a single center form, and multicenter studies are proposed. Another limitation of the research is that it was retrospective. Moreover, incomplete laboratory data in the present research must be related to retrospective analysis nature, and also some laboratory tests were not handled for patients due to resource constraints. For a limited number of mortality, patients due to death in the first hours of hospitalisation in the hospital, some considerable data were not exactly recorded.

CONCLUSION(S)

The clinical characteristics of COVID-19 patients were assessed, and also the risk factors associated with its mortality were provided. There was an association between cancer, COPD, cough and shortness of breath with hospital mortality. It was found that COPD, O_2 saturation less than 93%, and leukocytosis were risk factors for in hospital mortality in patients with COVID-19. These results manage the COVID-19 disease and controlling risk factors associated with mortality from the disease.

REFERENCES

[1] Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalised patients with COVID-19 in Wuhan, China. JAMA Cardiology. 2020;5(7):802-10.
[2] Zimorovat A, Mohammadi M, Ramezani-Jolfaie N, Salehi-Abargouei A. The healthy Nordic diet for blood glucose control: A systematic review and meta-analysis of randomized controlled clinical trials. Acta Diabetologica. 2020;57(1):01-12.
[3] Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020;8(5):475-81.
[4] Lièvre A, Turpin A, Ray-Coquard I, Le Malicot K, Thariat J, Ahle G, et al. Risk factors for Coronavirus Disease 2019 (COVID-19) severity and mortality among solid cancer patients and impact of the disease on anticancer treatment: A French nationwide cohort study (GCO-002 CACOVID-19). European Journal of Cancer. 2020;141:62-81.
[5] World Health Organization. WHO Coronavirus Disease (COVID-19) 2020 [Available from: https://COVID-19.who.int/?gclid=CjwKCAjwkdL6BRAREiwA-kiczNtleO9AcXnV_rJVm1e-ksl4pHAE_7ybFuEXh2_zpfoRLDuQeXjK0RoCGA0QAvD_BwE. [Accessed: 30 December 2020].

[6] Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. Journal of medical virology. 2020;92(4):401-02.
[7] Hui DS, Ei Azhar E, Madani TA, Ntoumi F, Kock RA, Dar O, et al. The continuing epidemic threat of novel coronaviruses to global health-The latest novel coronavirus outbreak in Wuhang, China. International Journal of Infectious Diseases. 1920;91:264-66.
[8] Yang L, Jin J, Luo W, Gan Y, Chen B, Li W. Risk factors for predicting mortality of COVID-19 patients: A systematic review and meta-analysis. PloS one. 2020;15(11):e0243124.
[9] Zhang JJ, Lee KS, Ang LW, Leo YS, Young BE. Risk factors for severe disease and efficacy of treatment in patients infected with COVID-19: A systematic review, meta-analysis, and meta-regression analysis. Clinical Infectious Diseases. 2020;71(16):2199-206.
[10] Bonanad C, García-Blas S, Tarazona-Santabalbina F, Sanchis J, Bertomeu-González V, Fácila L, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. Journal of the American Medical Directors Association. 2020;21(7):915-18.
[11] Albitar O, Ballouze R, Ooi JP, Ghadzi SMS. Risk factors for mortality among COVID-19 patients. Diabetes Research and Clinical Practice. 2020;166:108293.
[12] Sun H, Ning R, Tao Y, Yu C, Deng X, Zhao C, et al. Risk factors for mortality in 244 older adults with COVID-19 in Wuhan, China: A retrospective study. Journal of the American Geriatrics Society. 2020;68(6):E19-23.
[13] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395(10223):497-506.
[14] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. The Lancet. 2020;395(10223):507-13.
[15] Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. D-dimer levels on admission to predict in hospital mortality in patients with Covid-19. Journal of Thrombosis and Haemostasis. 2020;18(6):1324-29.
[16] Bao C, Liu X, Zhang H, Li Y, Liu J. Coronavirus disease 2019 (COVID-19) CT findings: A systematic review and meta-analysis. Journal of the American College of Radiology. 2020;17(6):701.
[17] Xu B, Xing Y, Peng J, Zheng Z, Tang W, Sun Y, et al. Chest CT for detecting COVID-19: A systematic review and meta-analysis of diagnostic accuracy. European Radiology. 2020;30:5720-27.
[18] Puig-Domingo M, Marazuela M, Giustina A. COVID-19 and endocrine diseases. A statement from the European Society of Endocrinology. Endocrine. 2020;68(1):02-05.
[19] Yadaw AS, Li YC, Bose S, Iyengar R, Bunyavanich S, Pandey G. Clinical features of COVID-19 mortality: Development and validation of a clinical prediction model. The Lancet Digital Health. 2020;2(10):e516-25.
[20] Xie J, Covassin N, Fan Z, Singh P, Gao W, Li G, et al. Association between hypoxemia and mortality in patients with COVID-19. InMayo Clinic Proceedings. 2020;95(6):1138-47. Elsevier.
[21] Targher G, Mantovani A, Wang XB, Yan HD, Sun QF, Pan KH, et al. Patients with diabetes are at higher risk for severe illness from COVID-19. Diabetes & Metabolism. 2020;46(4):335.
[22] Jain V, Yuan JM. Predictive symptoms and comorbidities for severe COVID-19 and intensive care unit admission: A systematic review and meta-analysis. International Journal of Public Health. 2020;65:533-46.
[23] Singh AK, Gupta R, Misra A. Comorbidities in COVID-19: Outcomes in hypertensive cohort and controversies with renin angiotensin system blockers. Diabetes & metabolic syndrome: Clinical Research & Reviews. 2020;14(4):283-87.
[24] Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiology. 2020;5(7):811-18.
[25] Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): A systematic review and meta-analysis. International Journal of Infectious Diseases. 2016;49:129-33.
[26] World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: Interim guidance. [Available from: https://apps.who.int/iris/bitstream/handle/10665/330893/WHO-nCoV-Clinical-2020.3-eng.pdf?sequence51&isAllowed5y. [Accessed 28 January 2020].].
[27] Alqahtani JS, Oyelade T, Aldhahir AM, Alghamdi SM, Almehmadi M, Alqahtani AS, et al. Prevalence, severity and mortality associated with COPD and smoking in patients with COVID-19: A rapid systematic review and meta-analysis. PloS one. 2020;15(5):e0233147.
[28] Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. The Lancet Infectious Diseases. 2020;20(7):773.
[29] Nandy K, Salunke A, Pathak SK, Pandey A, Doctor C, Puj K, et al. Coronavirus disease (COVID-19): A systematic review and meta-analysis to evaluate the impact of various comorbidities on serious events. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(5):1017-25.
[30] Lippi G, Wong J, Henry BM. Hypertension and its severity or mortality in Coronavirus Disease 2019 (COVID-19): A pooled analysis. Pol Arch Intern Med. 2020;130(4):304-09.
[31] Yamada T, Wakabayashi M, Yamaji T, Chopra N, Mikami T, Miyashita H, et al. Value of leukocytosis and elevated C-reactive protein in predicting severe coronavirus 2019 (COVID-19): A systematic review and meta-analysis. Clinica Chimica Acta. 2020;509:235-43.
[32] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. The Lancet. 2020;395(10229):1054-62.
[33] Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Medicine and Infectious Disease. 2020;2020:101623.
[34] National Health Commission of the People's Republic of China. Chinese management guideline for COVID-19 (version 6.0). Feb 19, 2020. http://www.nhc.gov.cn/yzygj/s7653p/202002/8334a8326dd94d329df351d7da8aefc2/files/b218cfeb1bc54639af227f922bf6b817.pdf. (Accessed Feb 19, 2020; in Chinese).
[35] Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020;323(16):1574-81.
[36] Satici C, Demirkol MA, Altunok ES, Gursoy B, Alkan M, Kamat S, et al. Performance of pneumonia severity index and CURB-65 in predicting 30-day mortality in patients with COVID-19. International Journal of Infectious Diseases. 2020;98:84-89.
[37] Yu C, Lei Q, Li W, Wang X, Li W, Liu W. Epidemiological and clinical characteristics of 1663 hospitalised patients infected with COVID-19 in Wuhan, China: A single-center experience. Journal of Infection and Public Health. 2020;13(9):1202-09.
[38] Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalised with COVID-19 in the New York City area. JAMA. 2020;323(20):2052-59.
[39] Shibata S, Arima H, Asayama K, Hoshide S, Ichihara A, Ishimitsu T, et al. Hypertension and related diseases in the era of COVID-19: A report from the Japanese Society of Hypertension Task Force on COVID-19. Hypertension Research. 2020;43:1028-46.
[40] Tadic M, Saeed S, Grassi G, Taddei S, Mancia G, Cuspidi C. Hypertension and COVID-19: Ongoing controversies. Front Cardiovasc Med. 2021;8:639222.
[41] Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia–a systematic review, meta-analysis, and meta-regression. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(4):395-403.
[42] Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(4):535-45.
[43] Mantovani A, Byrne CD, Zheng M-H, Targher G. Diabetes as a risk factor for greater COVID-19 severity and in-hospital death: A meta-analysis of observational studies. Nutrition, Metabolism and Cardiovascular Diseases. 2020;30(8):1236-48.
[44] Ssentongo P, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM. Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: A systematic review and meta-analysis. PLOS ONE. 2020;15(8):e0238215.
[45] Gosain R, Abdou Y, Singh A, Rana N, Puzanov I, Ernstoff MS. COVID-19 and cancer: A comprehensive review. Curr Oncol Rep. 2020;22(5):53.
[46] Xiong S, Liu L, Lin F, Shi J, Han L, Liu H, et al. Clinical characteristics of 116 hospitalised patients with COVID-19 in Wuhan, China: A single-centered, retrospective, observational study. BMC Infectious Diseases. 2020;20(1):01-11.
[47] Nepogodiev D, Glasbey JC, Li E, Omar OM, Simoes JF, Abbott TE, et al. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: An international cohort study. The Lancet. 2020;396:27-38.
[48] Mesas AE, Cavero-Redondo I, Álvarez-Bueno C, Sarriá Cabrera MA, Maffei de Andrade S, Sequí-Dominguez I, et al. Predictors of in-hospital COVID-19 mortality: A comprehensive systematic review and meta-analysis exploring differences by age, sex and health conditions. PloS one. 2020;15(11):e0241742.
[49] Tsou TP, Chen WC, Huang ASE, Chang SC, Taiwan COVID-19 Outbreak Investigation Team. Epidemiology of the first 100 cases of COVID-19 in Taiwan and its implications on outbreak control. J Formos Med Assoc. 2020;119(11):1601-07.
[50] Tabata S, Imai K, Kawano S, Ikeda M, Kodama T, Miyoshi K, et al. Clinical characteristics of COVID-19 in 104 people with SARS-CoV-2 infection on the Diamond Princess cruise ship: A retrospective analysis. The Lancet Infectious Diseases. 2020;20:1043-50.
[51] Kim H, Hong H, Yoon SH. Diagnostic performance of CT and reverse transcriptase-polymerase chain reaction for coronavirus disease 2019: A meta-analysis. Radiology. 2020;2020:201343.
[52] Romero Starke K, Petereit-Haack G, Schubert M, Kämpf D, Schliebner A, Hegewald J, et al. The age-related risk of severe outcomes Due to COVID-19 infection: A rapid review, meta-analysis, and meta-regression. International Journal of Environmental Research and Public Health. 2020;17(16):5974.
[53] Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Deng Y, et al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis. Int J Infect Dis. 2020;96:131-35.
[54] Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. JAMA. 2020;323(16):1612-14.
[55] Bangalore S, Sharma A, Slotwiner A, Yatskar L, Harari R, Shah B, et al. ST-segment elevation in patients with Covid-19—a case series. N Engl J Med. 2020;382(25):2478-80.
[56] Fried JA, Ramasubbu K, Bhatt R, Topkara VK, Clerkin KJ, Horn E, et al. The variety of cardiovascular presentations of COVID-19. Circulation. 2020;141(23):1930-36.

[57] Abate BB, Kassie AM, Kassaw MW, Aragie TG, Masresha SA. Sex difference in coronavirus disease (COVID-19): A systematic review and meta-analysis. BMJ Open. 2020;10(10):e040129.

[58] Klein SL, Flanagan KL. Sex differences in immune responses. Nature Reviews Immunology. 2016;16(10):626-38.

PARTICULARS OF CONTRIBUTORS:
1. Department of Medical Emergencies, Sirjan School of Medical Sciences, Sirjan, Iran.
2. Emergency Department, Sirjan School of Medical Sciences, Sirjan, Iran.
3. Department of Public Health, Sirjan School of Medical Sciences, Sirjan, Iran.
4. Department of Public Health, Sirjan School of Medical Sciences, Sirjan, Iran.
5. Department of Medical Emergencies, Sirjan School of Medical Sciences, Sirjan, Iran.
6. Emergency Department, Sirjan School of Medical Sciences, Sirjan, Iran.
7. Department of Medicine, Emergency and Trauma Care Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Farzad Rahmani,
Associate Professor, Department of Medicine, Emergency and Trauma Care Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran.
E-mail: rahmanif@tbzmed.ac.ir

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 14, 2021
- Manual Googling: Sep 02, 2021
- iThenticate Software: Mar 09, 2022 (10%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Apr 12, 2021**
Date of Peer Review: **May 13, 2021**
Date of Acceptance: **Dec 23, 2021**
Date of Publishing: **May 01, 2022**