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The Prevalence of Cardiovascular Risk Factors in Fatal Cases of COVID-19 in Fars Province, Iran

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ABSTRACT

Background: Human health has been challenged drastically by the emergence of COVID-19. This pandemic has imposed a serious burden on different aspects of life. Apart from the high rates of morbidity and mortality, reporting of newly formed variants with enhanced contagious capacity has made the future vague. Existence of different comorbidities is a prominent factor towards poor prognosis and fatal outcomes.

Objectives: The present study aimed to identify the most important comorbidities in the COVID-19 patients who passed away during the first wave in Fars province, Iran.

Methods: Trained general physicians obtained data from medical files in the referral hospitals of COVID-19 throughout the province. These included demographic data, past medical history, and existence of comorbidities. The data were analyzed using chi-square test, independent sample t-test, and Mann-Whitney test. P-values less than 0.05 were considered statistically significant.

Results: Out of the 3700 confirmed cases, 87 patients died from February to May 2020. Among these patients, 81.1% had comorbidities, with hypertension, diabetes, and cardiovascular disease being the most prevalent ones. The results revealed no significant differences between the individuals with and without comorbidities regarding age, gender, and duration of ICU hospitalization. Oxygen saturation was also poor in both groups. However, the patients with comorbidities had significantly higher blood urea nitrogen and creatinine levels compared to their comorbidity-free peers.

Conclusions: Cardiovascular disease and the related risk factors contributed greatly to the deadly fate in COVID-19 patients. Hence, early prophylactic and therapeutic interventions should be considered in COVID-19 patients harboring such comorbidities. This can play a pivotal role in reducing the rate of mortality and the consequent financial and social harms.

1. Background

One year ago, it was not believable if someone warned others about the emergence of a highly transmissible infectious disease that could hamper activities all over the world. Not only it became a reality, COVID-19 is going to be a borderless tragedy for the international community, resulting in a growing rate of mortality. The mortality rate has been reported to vary from 0.0% in Singapore to 29% in Yemen (https://coronavirus.jhu.edu/data/mortality, Johns Hopkins University of Medicine, last updated at October 30). Comorbidities have been considered the most weighted factors for prediction of mortality (1). Early findings revealed that the majority of patients with COVID-19 had underlying diseases, including Cardiovascular Disease (CVD), diabetes, hypertension, and Chronic Obstructive Pulmonary Disease (COPD) (2). In addition, the number of comorbidities was higher in the patients who needed intensive care compared to other COVID-19 patients (3). Overall, identification of comorbidities has been found to be a critical step towards management and reduction of the mortality rate during the COVID-19 pandemic.

Iran, with the mortality rate of 5.7%, is among the

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countries that is bearing a huge burden, and Fars province has substantially contributed to this trend from the first days.

2. Objectives

The present investigation aims to identify the comorbidities in the COVID-19 patients who passed away during the first wave in Fars province.

3. Patients and Methods

The data of this multi-center, retrospective, observational study were obtained from the hospitals affiliated to Shiraz University of Medical Sciences throughout Fars province, which were designated as the referral centers for COVID-19. The data were gathered by using medical records and there was no intervention in routine medical treatment of the patients in this study. Fars Province is geographically located in south-west of Iran. Its capital, Shiraz, is a metropolitan city and is known as the medical hub in south of Iran with its extensive infrastructure since old times (4).

Among the confirmed cases of COVID-19 (PCR test), the dead ones were analyzed from 20 February to 1 May 2020. This study was in conformity with the declaration of Helsinki and was approved by the regional institutional ethics board (IR.SUMS.REC.1399.006).

Trained general physicians under the supervision of the principal investigator and other experts in the team retrieved information from the patients' files and filled predefined forms. Patients' information included demographics, medical history, and existence of comorbidities. At the next step, three cardiologists and a qualified statistician reviewed and analyzed the information.

Frequency rates (numbers, percentages) and mean ± SD were used to present categorical and continuous variables, respectively. Chi-square test, independent sample t-test, and Mann-Whitney test were used in order to compare frequencies or means, as appropriated. All statistical analyses were performed by the SPSS 16 software (IBM Corporation), and $P < 0.05$ was considered statistically significant.

4. Results

During the first wave of COVID-19 in Fars province, 87 out of the nearly 3700 confirmed cases died. It should be noted that two cases were omitted from analysis because of data insufficiency. The patients' ages ranged from 21 to 96 years, with a median of 66.08 ± 18.82 years, and male was the dominant gender (63.5%). Duration of hospitalization prior to Intensive Care Unit (ICU) admission and in the ICU was 2.8 ± 3.26 and 4.56 ± 5.84 days, respectively. It should be noted that ICU admission was based on the patients' previous conditions (frailty, age, comorbidities, neurocognitive status, and worsening of their general conditions over the last few months) and current clinical severity (number of organ failures, respiratory status, hemodynamics, neurological status, and worsening of organ dysfunction) (5).

Out of the 85 patients, 69 (81.1%) had at least one comorbidity. The most prevalent comorbidities were hypertension (48.2%), diabetes (41.2%), and CVD (31.8%) (Table 1). Among the patients with comorbidities, 85.5% had hypertension, diabetes, or CVD.

Table 1. Distribution of Comorbidities among the 69 Patients

Comorbidities	No. of Patients
Hypertension	41 (48.2%)
Diabetes	35 (41.2%)
CVD	27 (31.8%)
CKD	15 (17.6%)
Smoking	13 (15.3%)
Cancer	8 (9.4%)
COPD	7 (8.2%)
Hyperlipidemia	7 (8.2%)
Opium use	6 (7.2%)
Autoimmune disease	5 (5.9%)
Asthma	4 (4.7%)

Abbreviations: CVD, cardiovascular disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease.

Table 2. Distribution of the Patients according to the Number of Comorbidities

No. of Comorbidities	No. of Patients
0	16 (18.8%)
1	17 (20.0%)
2	25 (29.4%)
3	13 (15.3%)
4	8 (9.4%)
5	6 (7.1%)

Distribution of the patients according to the number of comorbidities has been presented in Table 2. Among diabetes, CVD, hypertension, cancer, smoking, opium consumption, hyperlipidemia, COPD, asthma, Chronic Kidney Disease (CKD), and autoimmune disease, the majority of the patients (29.4%) had two comorbidities, while the minority (7.1%) had five comorbidities at a time. In addition, 18.8% of the patients did not have any comorbidities.

Some variables were compared between the patients with and without comorbidities (Table 3). Although the two groups were not significantly different with respect to age, the patients with comorbidities were about 9.9 years older compared to those without comorbidities. In addition, the two groups were similar concerning gender distribution. Oxygen saturation was also suboptimal in both groups, with no significant differences between them. However, Blood Urea Nitrogen (BUN) and creatinine levels were significantly higher in the patients with comorbidities. Of course, these two biomarkers were lower than the normal range even in those without comorbidities. Furthermore, duration of hospitalization prior to ICU admission was significantly shorter in the comorbidity-free patients compared to their peers. Nevertheless, no significant difference was observed between the two groups regarding the duration of ICU hospitalization.

5. Discussion

The present study aimed to investigate the distribution of comorbidities in the dead patients during the first wave of COVID-19 in Fars province, Iran. Hypertension, diabetes, and CVD were the most prevalent comorbidities.

Table 3. Comparison of Some Variables between the Dead Patients with and without Comorbidities

	Without Comorbidities	With Comorbidities	P
Age (years)	58.06 ± 20.78	67.94 ± 17.99	0.054
Gender (male)	9 (56.3%)	45 (65.2%)	0.502
Oxygen saturation (%)	81.74 ± 14.80	86.34 ± 10.33	0.162
BUN (mg/dL)	24.78 ± 12.03	38.74 ± 26.43	0.017
Creatinine (mg/dL)	1.54 ± 1.0	2.63 ± 2.15	0.005
Hospitalization prior to ICU admission (days)	1.11 ± 1.16	3.16 ± 3.45	0.003
Hospitalization in ICU (days)	5 ± 5.86	4.46 ± 5.89	0.797

Abbreviations: BUN, blood urea nitrogen; ICU, intensive care unit. Bold values imply statistical significant.

About 19% of the patients died without any comorbidities. Nonetheless, the majority of non-survivors had two comorbidities simultaneously. The results revealed no significant difference between the patients with and without comorbidities with respect to age, gender, and duration of ICU hospitalization. Obviously, oxygen saturation was low in both groups. However, the patients with comorbidities had significantly higher levels of BUN and creatinine. This might be related to the existence of cardiovascular risk factors, including hypertension and diabetes, which could adversely affect renal function.

According to the Center for Disease Control and Prevention, hypertension, coronary artery disease, stroke, and heart failure (totally defined as CVD) as well as diabetes, CKD, and COPD were the frequent comorbidities among the 10647 dead cases of COVID-19 (6). Diabetes was the most important comorbidity in deceased COVID-19 patients in India (7). In the same vein, hypertension, diabetes, and chronic heart disease were the most prevalent comorbidities among the 1138 confirmed cases of COVID-19 in China with 218 deaths. In addition, patients with two coexisting comorbidities were dominant (8).

Comorbidity, irrespective of its type, significantly increased the rate of mortality in COVID-19 patients (9). A report from Mexico indicated that COVID-19 fatality was increased when accompanied by obesity, diabetes, CKD, COPD, and hypertension (10). COPD, CKD, obesity, and liver disease played the same role in the UK (11). Several meta-analyses have also corroborated increased disease severity and mortality in the presence of comorbidities (12-16). In the present study, CVD and the related risk factors increased the risk of fatal outcomes. Another study also demonstrated that death was more likely to happen in the COVID-19 patients with hypertension, diabetes, and coronary heart disease (17). In fact, hypertension, diabetes, CVD, COPD, CKD, and cancer increased the COVID-19 severity by a 1.5-3-fold magnitude. The risk of mortality was also doubled with CVD or hypertension (18).

In comparison of survivors and non-survivors, CVD was a significant player. Considering the population under the current investigation, hypertension itself represents a cardiovascular disorder and diabetes is classically known as a cardiovascular risk factor. In one study on COVID-19 patients with a critical health status, the prevalence of comorbidities, including CVD, chronic cardiac disease, and cerebrovascular disease, was remarkably higher in non-survivors compared to survivors. Organ malfunctions like Acute Respiratory Distress Syndrome (ARDS) and cardiac injury were also seen in most of these patients. It was concluded that older age, existence of comorbidities, and ARDS were the predictors of death (19). Among non-survivors, respiratory failure, myocardial damage, and circulatory failure were diagnosed as the main causes of death (20). Moreover, the prevalence of CVD was higher in hospitalized COVID-19 patients compared to ambulatory, non-hospitalized, and non-severe cases (1). Heart failure and acute cardiac injury were also higher amongst non-survivors in another study (17). Overall, CVD was assumed as a stronger predictor of death compared to hypertension, diabetes, and chronic respiratory disease (21). Shi et al. reported that 57 out of the 416 hospitalized patients with COVID-19 had died due to myocardial injury (coronary heart disease and heart failure) and cerebrovascular disease. Those with myocardial injury were older and had more comorbidities beside elevated levels of high sensitivity troponin I, N-Terminal pro-Brain Natriuretic Peptides (NT-proBNP), and C-reactive protein. Reasonably, cardiac injury significantly smoothed the incidence of ARDS and mortality (22). In the research carried out by Guo et al., 35% of the patients had hypertension, coronary heart disease, or cardiomyopathy and 28% showed acute myocardial injury. Additionally, mortality rate was higher in the patients with acute myocardial injury. They concluded that male gender and existence of hypertension, coronary heart disease, and cardiomyopathy made the patients vulnerable to cardiac injury and the subsequent deadly outcomes (23). On the other hand, the lowest survival rates were detected among the COVID-19 patients with escalation of troponin T (TnT) and underlying CVD. Intriguingly, the subjects with escalated TnT without underlying CVD experienced more unfavorable outcomes compared to those with normal TnT and underlying CVD (24). This implied that direct myocardial injury by SARS-CoV-2 significantly impaired cardiovascular function (25). To substantiate, TnT and NT-proBNP increased among non-survivors during the period of hospitalization, while no such changes were observed in survivors (24). Moreover, in-hospital mortality was closely related to the degree of myocardial injury (22, 24). However, elevated troponin did not necessarily result in poor outcomes since cases with elevated troponin were among the discharged patients (24). Furthermore, mortality was five times higher in the patients with a history of CVD compared to their peers without such a history (9). In other words, CVD, either preexisting or SARS-CoV-2-induced, was a determining factor in disease prognosis (24).

In the present study, patients without comorbidities experienced shorter hospitalization periods prior to ICU and received intensive care sooner. This implies that

such patients referred to the hospitals later due to their comorbidity-free conditions. This carelessness gave time to SARS-CoV-2 to induce more injuries that resulted in admission with severe conditions. On the contrary, those with comorbidities were more conscious about their health status, proceeding to receive clinical care earlier. However, there are divergent reports regarding the duration of hospitalization in COVID-19 patients. A prior study revealed no significant difference between the individuals with and without CVD who experienced fatal outcomes regarding the length of hospital stay (26). Another study showed that although the mortality rate was significantly higher in the COVID-19 patients with cardiac injury compared to those without this condition, time from the onset of symptoms to admission was not different between the two groups (22). Another study indicated that even though death rate was significantly higher in the patients with elevated TnT levels compared to those with normal TnT levels, duration of hospitalization was not different between the two groups. However, time from the onset of symptoms to death or discharge was higher in those with high TnT levels (24).

5.1. Conclusion

Existence of comorbidities, especially CVD and the related risk factors, increased the risk of mortality in COVID-19 patients. In the population under the present investigation, hypertension, diabetes, and CVD were the most prevalent comorbidities in the deceased COVID-19 patients during the first wave.

5.2. Informed Consent

The data were gathered by using medical records and there was no intervention in routine medical treatment of the patients in this study.

5.3. Ethical Approval

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Authors' Contribution

Study concept and design: MJ.Z. and H.B.; data collection and interpretation: Z.D., N. P., N.F., MR.H., M.B., A.E., M.Kh., Z.E., and M.Z.; drafting of the manuscript: I.R-J. and Z.E.; critical revision of the manuscript for important intellectual content: MJ.Z., and I. R-J.; statistical analysis: M.S. and N.P. All authors have read and approved the manuscript.

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The authors have no financial interests related to the material in the manuscript.

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