

**Original research****Potential risk factors for mortality in patients with COVID-19:
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Abstract: Although severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection caused more than five million deaths throughout the world and more than five thousand deaths in Libya, a little is known about the mortality rate and the risk factors for death from this serious infectious disease in Libya. Thus, it is aimed in this study to identify the potential risk factors for mortality from SARS-CoV-2 infections among 176 Libyan COVID-19 patients in Zawia city. This research is a retrospective cohort study that was conducted on 176 randomly selected volunteers who had been infected with SARS-CoV-2 during a period of December 2020 to February 2021 in Zawia city, Libya. Following filling the prepared validated questionnaire by COVID-19 patients, the data was analyzed to determine the previously mentioned risk factors. The mean age (SD) of the total 176 participated COVID-19 patients was 45.06 (17.7) and the mortality rate among these total involved cases (mild to severe cases) was 10.8%. It is found that the mortality among the severe COVID-19 cases was 41.3% and the mean age (SD) of COVID-19 deaths was 69.1 years (13.8) and 73.7% of them were 60 years old or older. In addition, it is found that 63.2% of the SARS-CoV-2 deaths were females and 78.9% of them had a positive history of chronic diseases. Moreover, it was found that the most common chronic diseases among COVID-19 deaths are diabetes mellitus and hypertension (73.3% and 53.3%, respectively). Collectively, it is concluded that COVID-19 elderly female patients aging 60 years or older with a positive history of chronic disease are more likely at high risk for death from SARS-CoV-2 infection among the participated COVID cases.

Keywords: COVID-19, Libya, mortality, risk factors, SARS-CoV-2, Zawia

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease (COVID-19) is still ongoing serious pandemic trouble that frustrating all over the world since December 2019 [1]. It has affected more than 307 million people worldwide with approximately over five million deaths as of January 10, 2022 [1]. Although of presence of several routes for transmission of SARS-CoV-2 infection, the

airborne droplets remain the main route of SARS-CoV-2 transmission. The clinical features of the disease range from mild symptoms to severe or life-threatening that might result in loss of life. Acute respiratory distress syndrome (ARDS) and multi-organ dysfunction were found to be the major causes of mortality and morbidity in COVID-19 patients [2 - 5]. In Libya, the first case of COVID-19 was reported on March 24, 2020 [6].

To date, there have been over 393 000 confirmed cases of COVID-19 with approximately 5 800 deaths in the country [6]. The low national case fatality rate (CFR) in Libya (1.6%) was difficult to interpret as reported by the World Health Organization (WHO), especially in comparison to other countries of eastern Mediterranean region which have a similar or much better health care system and even that, they have reported a much higher CFR as Syria (6.5%), Tunisia (3.2%) and Egypt (5.6%). Actually, WHO explained this difference by weak mortality surveillance system in Libya [7].

Worldwide, several published reports provided an evidence for the association of sex, age and comorbidities with mortality in COVID-19 patients [8 - 11]. Elderly, male gender and chronic diseases such as diabetes mellitus and hypertension were reported as high risk factors for death from SARS-CoV-2 infection [4, 8 - 11]. However, the conducted studies about the mortality from COVID-19 and risk factors for mortality from this serious disease are scarce in Libya, especially in Zawia city, which is located 46 kilometers west of the capital city, Tripoli. Therefore, it is aimed to identify the most potential risk factors for mortality from SARS-CoV-2 infection among the participated Libyan COVID-19 patients in Zawia city.

Materials and methods

This research work is a continuous projects of the retrospective cohort study that was conducted and

published previously about COVID-19 pandemic in Zawia city, Libya [12] and it is involved 176 randomly chosen volunteers who had been infected with SARS-CoV-2 during the period of December, 2020 to February, 2021 in Zawia city (during the second wave of SARS-CoV-2 epidemic in Libya). The participants' consents were obtained prior to the start of this research study as it has been mentioned previously [12]. A validated questionnaire was prepared and tested (see below) consisting of several questions that cover the full history of COVID-19 disease in the participated volunteers. The questionnaire tool was reviewed by two independent scientists (university of Zawia, Faculty of Medicine, Department of Community) to evaluate the relevancy, clarity and adequacy of all the questions asked for the patients. The information was collected either directly from the patient or from his/her close relative through the phone calls or the social media resources. The collected data were categorized and statistically described using excel-software, version 16 (Microsoft Corporation, USA). Data presented by means of descriptive statistics. Categorical variables were presented as number, percentage (n, %) and normally distributed continuous variables were presented as mean and standard deviation (SD).

Results

Mortality among severe COVID-19 cases: Of the total 176 SARS-CoV-2 infected patients, 46 patients were severe COVID-19 cases and the mortality rate in these severe cases was found to be 41.3% (n = 19) (**Table 1**).

Table 1: Percentage of recovered and death cases among severe COVID-19 patients

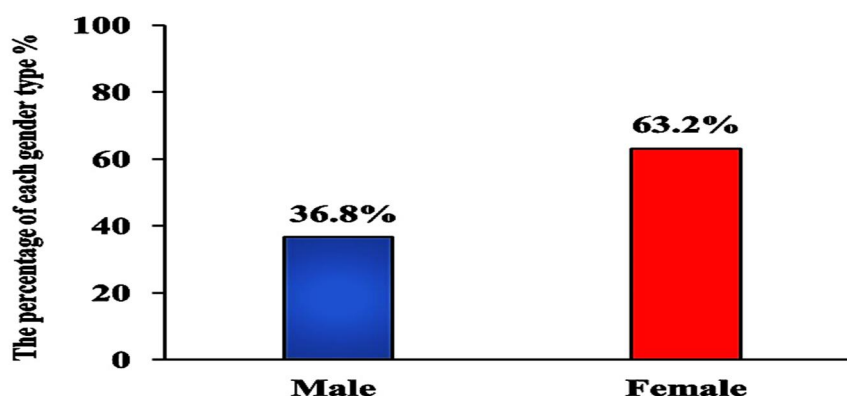
Type of group	COVID-19 patients, n	Percentage
Recovered cases	27	58.7%
Death cases	19	41.3%
Total cases	46	100%

Table 2: Age distribution of COVID-19 death cases with average age of COVID-19 deaths

COVID-19 death case	Age of COVID-19 death, years
1	65
2	56
3	68
4	58
5	83
6	63
7	68
8	92
9	90
10	68
11	42
12	92
13	55
14	60
15	72
16	79
17	80
18	67
19	55
Mean age (\pm SD)	69.1 \pm 13.8

Table 3: COVID-19 death cases who were 60 years old or older among COVID-19 death cases

COVID-19 deaths \geq 60 years n	Total number COVID-19 deaths	COVID-19 deaths \geq 60 years, %
14	19	73.7%

**Figure 1:** Gender distribution among COVID-19 deaths
Data are expressed in percentage (total number of COVID-19 deaths, $n = 19$).

Demographic features of COVID-19 deaths: The findings showed that mean age of COVID-19 deaths was 69.1 years (13.8, SD) and 73.7% ($n = 14$) of them were 60 years old or older (Tables 2

and 3). Moreover, the current findings revealed that 63.2% ($n = 12$) of the COVID-19 deaths were female patients (Figure 1).

History of chronic disease in COVID-19 deaths: Fifteen cases (78.9%) of the COVID-19 deaths had a positive history of chronic disease and the most

common chronic diseases among COVID-19 deaths were diabetes mellitus (73.3%, n = 11) and hypertension (53.3%, n = 8) (Tables 4 and 5).

Table 4: COVID-19 deaths with history of chronic diseases among total COVID-19 deaths

Type of the group	Number of COVID-19 deaths	Percentage of each group
Positive history of chronic disease	15	78.9%
Negative history of chronic disease	04	21.1%
Total COVID-19 deaths	19	100%

Table 5: Chronic diseases among COVID-19 deaths with positive history of chronic diseases

Diseases	Number of deaths	Percentage of deaths
Diabetes mellitus	11	73.3%
Hypertension	08	53.3%
Chronic asthma	02	13.3%
Cardiac diseases	01	06.7%
Renal diseases	01	06.7%
Total number of COVID-19 deaths with positive history of chronic diseases	15	-----

Figure 2 shows an illustrative diagram that summarizing the potential risk factors for mortality from SARS-CoV-2 infection in the participated COVID-19 patients. Age 60 years or older, female

gender and a positive history of chronic diseases are the most prevalent risk factors for mortality in the participants with COVID-19.

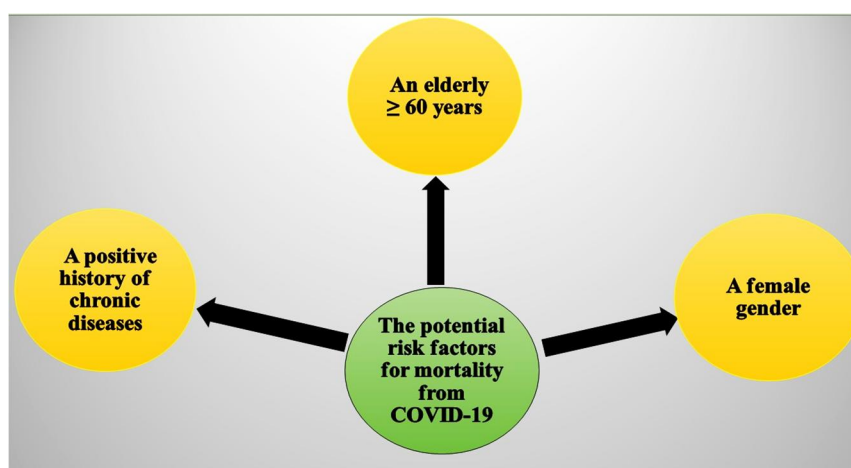


Figure 2: Potential risk factor for mortality from SARS-CoV-2 infection in COVID-19 patients

Discussion

As it has previously been mentioned, this study is a continuous part of our published study about

patients with COVID-19 and its management in Zawia city [12].

In the first report from this study, it was shown that mortality rate among the total involved 176 COVID-19 patients from mild to severe cases was found to be 10.8% and it was 6 - 7 folds higher than that reported by National Center for Disease Control [12]. This discrepancy is related mainly to the weak registration system of COVID-19 cases and deaths in Libya and, on the other hand, to the limited research interest to Zawia city rather than the whole country [12].

Here, in this study, it is demonstrated that the mortality rate among the severe COVID-19 cases is about 40% (i.e. more than one third of severe COVID-19 cases were died). Indeed, the present finding supports the previous published data that showed 40% - 60% of their studied severe COVID-19 patients were died [13 - 15]. WHO has given the term severe COVID-19 disease to patients who have had clinical signs of pneumonia plus one of the following: oxygen saturation < 90% on room air, respiratory rate > 30 breaths per min in adults and children more than five years old, ≥ 60 breaths per min in children less than two months old, ≥ 50 in children of two to eleven months old and ≥ 40 in children of one to five years old or signs of severe respiratory distress [16]. In the current study, the criteria of severe COVID-19 cases were comparable to those defined by WHO for severe COVID-19 disease.

Moreover, it is revealed that the COVID-19 females are more likely at higher risk for death from this disease than male patients because about 60% of COVID-19 deaths were females. This finding was opposing to several international studies that showed the male patients are at greater risk for death from this pandemic than the female subjects [8, 9, 17 - 20]. This difference could be explained by that present finding is a consequent result to the previous finding, of the first report of this study, that showed the female patients are at higher risk for SARS-CoV-2 infection than the males because 58.5% of the total 176 participated COVID-19 patients were females [12]. Therefore, a higher mortality percentage would be

expected in female subjects as a consequential event. Thus, it is explained this variation between the present finding and the other studies throughout the world by Libyan cultural life where the females are more prone to social collections than males who make them at an increased risk for SARS-CoV-2 infection and thereby for death from this pandemic.

Furthermore, it is found that the mean age (SD) of COVID-19 deaths was about 70 years and 73.7% of them were 60 years old or older. This is in a good agreement with the previous several studies from different parts of the globe [8, 9, 17 - 23]. For example, Deng and others [17] demonstrated that the median age of COVID-19 deceased cases was 69 years ranging from 62 to 74 years and Li and others [23] showed that the median age of COVID-19 deaths was 71.8 years ranging from 63.3 to 80.3 years, thereby, COVID-19 patients who are 60 years or older are more likely prone to die. It is stated that the elderly people are at a greater risk of mortality because of reduced natural immunity, decline in organ function and coexisting chronic diseases that all together make them more vulnerable to infection and at an increased risk of mortality [11, 24].

In regard to comorbidities in COVID-19 deaths, the current study found that more than three quarters of COVID-19 deaths were having chronic disease/s and the most common chronic diseases were diabetes mellitus (73.3%) and hypertension (53.3%). Therefore, the present data are similar to the findings of several studies throughout the world [8, 17, 25 - 28]. A study by Espinosa et al. [27] reported that 77% of COVID-19 deceased patients had comorbidities and hypertension was the most common comorbidities while Cao et al. [8] showed that hypertension and diabetes mellitus were the most common comorbidities in COVID-19 deaths. In addition, another study demonstrated that COVID-19 patients suffering from chronic diseases including hypertension, diabetes mellitus, cardiovascular diseases, respiratory diseases and

cancer are at a higher risk of death from SARS-CoV-2 infection [28]. Some studies reported that comorbidities may be involved in reduction of natural immune response. For instance, the dramatic reduction of natural immunity in diabetic patients may reduce body ability for production of specific antibodies against any infectious agent and this consequently might increase the risk of mortality in those patients [11, 29]. COVID-19 patients with comorbidities should follow the necessary precautions to avoid infection with SARS-CoV-2 because they usually have the worst prognosis.

To the best of our knowledge, this is the first report that handles the potential risk factors for mortality of SARS-CoV-2 infection in randomly chosen sample of COVID-19 Libyan patients in Zawia city. However, the current study had certain limitations, including, a short-term retrospective cohort study but a long term prospective or

retrospective study would give a better insight about risk factors for mortality from SARS-CoV-2 infection. It is mostly relied on self-reported data in questionnaire which is subject to bias. Small sample size due to a refusal of several individuals with positive past history of SARS-CoV-2 infection to participate because of what so called the patient stigma from COVID-19.

Conclusion: It can be concluded that female and elderly cases aging 60 years or older with a coexisting comorbidity especially diabetes mellitus and hypertension are at high risk for mortality from SARS-CoV-2 infection. This study could help clinicians to identify COVID-19 patients at greater risk for mortality, so they can strictly follow them to avoid SARS-CoV-2 related complications and significantly reduce the risk for mortality among the COVID-19 patients.

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Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data availability statements: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All the authors substantially contributed to the conception, compilation of data, checking, and approving the final version of the manuscript, and agreed to be accountable for its contents.

Ethical issues: Including plagiarism, informed consent, data fabrication or falsification and double publication or submission have completely been observed by authors.

Author declarations: We confirm all relevant ethical guidelines have been followed and any necessary IRB and/or ethics committee approvals have been obtained.

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