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Case fatality rate of zoonotic SARS.CoV2 and associated risk factors in the Libyan population

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ABSTRACT

Background: Infectious zoonotic viral respiratory diseases have dramatically emerged and reemerged globally, with high socioeconomic and public health impacts. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak was first reported in China as a transmissible disease among animals and humans with great universal public concern. Later, it slipped across the world as a pandemic with a high significant case fatality rate (CFR).

Aim: This study was conducted to estimate the CFR and potentially associated risk factors among animals and the Libyan population.

Methods: This retrospective cohort study assessed the CFR of coronavirus disease 2019 (COVID-19) and investigated the potentially associated risk factors (socio-demographic data, animal reservoir, household characteristics, and health status) among the Libyan population from July 2020 to January 2021. A total of 3,000 respiratory specimens (nasopharyngeal swabs) were screened by real-time reverse transcription polymerase chain reaction to detect SARS-CoV-2. Descriptive analyses, frequency, and percentage were measured for numerical data and numbers, and rate for qualitative data. The level of the association among variables at the significance level ($p < 0.05$) was investigated using SPSS version 22.

Results: The present study reported a variable degree of association with the investigated risk factors included in this study: sociodemographic data, household characteristics, and health status. The overall CFR showed significant differences in vitamin D, Blood group system (ABO), health status, and comorbidity.

Conclusion: The CFR seems to have been underestimated; however, our result reported a relatively high CFR in Libya, at least in the surveyed region (targeted population). The risk factors measured in this study potentially significantly influenced the CFR. Among these potential risk factors were animal welfare, vitamin D levels, the ABO system, lymphocyte count (level), and healthy status. In contrast, the results showed that other risk factors were not significantly associated with the CFR. The results highlighted the potential risk of fatalities in the country. A large set of prospective studies is required to enhance our understanding of the CFR associated with zoonotic COVID-19 in Libya.

Keywords: Animal reservoir, Case fatality rate, Libya, SARS-CoV2, Zoonoses.

Introduction

Coronavirus disease 2019 (COVID-19) is a highly communicable respiratory zoonotic viral disease (Contini *et al*., 2020). The outbreak was first reported in the Chinese territory and then spread rapidly beyond; later, the WHO declared it a public health outbreak of international concern (Chakraborty and Maity, 2020). Contact with respiratory secretions or fomites of asymptomatic and symptomatic carriers is the primary transmission route (Kulkarni *et al*., 2020). Coronaviruses are RNA viruses that are enclosed and found in mammals, birds, and humans. Six coronavirus species are now known to cause human disease. Four common viruses can cause respiratory symptoms: 229E, OC43, NL63, and HKU1. The other two viruses, severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome coronavirus (MERS-CoV) are zoonotic and have the potential to be

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lethal (Li *et al*., 2020). The evolutionary features that enable severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to leap from species to species (animals to people) and spillover across the globe as a pandemic has increased alarms regarding the zoonotic sources of COVID-19. However, coronaviruses are identified as zoonotic in origin, and they rapidly spread, causing high fatalities in humans. The initial infectious sources of COVID-19 are infected animals, especially bats, and rodents, and pangolins may act as intermediate hosts (Animal Reservoir) (Li *et al*., 2020; Shi *et al*., 2020). Interestingly, bats are considered native precursors of COVID-19; correspondingly, horseshoe bats of the genus *Rhinolophus* are considered the reservoir host of SARS-CoV, and masked palm civets (*Paguma larvata*) act as the intermediate host, while dromedary camels (*Camelus dromedarius*) act as the intermediate host that transmitted MERS-CoV to humans (Wang and Eaton 2007; Hemida *et al*., 2017; Zhou *et al*., 2020). Remarkably, the initial COVID-19 Chinese patients were related to Wuhan's live wild and pet animal market. The viral respiratory droplets of infected individuals are an initial means of dissemination between humans and animals, especially pet felines (Cats), that can act as silent intermediate hosts of viral transmission (Kulkarni *et al*., 2020; Sharun *et al*., 2021). Studies have shown that snakes serve as intermediary hosts for the virus, transmitting it from bats to humans via homologous recombination within the S protein (Ji *et al*., 2020). During the COVID-19 pandemic, most citizens were extremely at risk of viral infection, especially those who traveled to Wuhan City and visited the animal market (NCDC, 2019). Genetic association with COVID-19-related mortality is usually measured by the case fatality rate (CFR), which is affected by different risk factors (Kim and Jeong, 2020; Kim *et al*., 2021). The COVID-19 mortality rate is calculated by dividing the number of deaths by the number of confirmed cases of COVID-19, usually ranging from 0% to 31% (Eikenberry *et al*., 2020; Ritchie *et al*., 2020).

CFR varies by region and country and is significantly influenced by various factors, such as age, healthcare infrastructure, population distribution, and government public health capacities (El-Masry *et al*., 2021; Pang *et al*., 2021). Furthermore, certain preexisting medical disorders may enhance an individual's chance of virus-related death (Natesan *et al*., 2024). In Libya in 2020, the CFR was estimated to be 1.40%, and the mortality rate was found to be approximately 16% (Mahmoud *et al*., 2021). Most epidemiological studies have reported high mortality and morbidity rates in COVID-19 cases (Daw *et al*., 2021).

Materials and Methods

Study design and area

The study was conducted at the Libyan Center for Biotechnology Research from June 2020 to February 2021. Study samples (1,004) were randomly collected from men and women aged 18–70 years from different regions of Libya, according to a questionnaire designed specifically for the study. The questionnaire consists of two parts: the first part includes identifying animals, gender, age, weight, weight mass, and function. Part II covers the infection history, blood type, coronavirus-related symptoms, prevention methods, sources of infection, and treatment during infection. Samples were thoroughly examined and evaluated in the Libyan Biotechnology Research Center laboratory in Tripoli, Libya, using real-time reverse transcriptase polymerase chain reaction testing to determine the positivity or negativity of coronavirus.

Statistical analysis

All relevant data were entered into Microsoft Excel spreadsheets and coded for analysis. Descriptive analyses' frequency and percentage were measured for numerical data and number, and percentage for qualitative data using SPSS version 22. The chi-square test was used to measure the level of association among variables at a significance level of $p < 0.05$.

Ethical approval

Ethical considerations were conducted throughout the study to obtain all relevant information by providing informed consent from all tested patients. However, during this study, we followed all the criteria considering basic ethical principles in the research, like, providing anonymity and confidentiality.

Results

The results of this study reported a variable degree of association with the investigated risk factors included in this study, sociodemographic data, household characteristics, and health status. The overall CFR was estimated at 5%. Regarding animal maintenance, results showed a significant difference $p < 0.00001$. Significant at $p < 0.05$ (Fig. 1). The results also showed that vitamin D significantly influences the CFR ($p = 0.032$) (Fig. 2). The ABO system significantly ($p = 0.00001$) influences the CFR at $p < 0.05$ (Fig. 3). Regarding health status, the results reported (6.1%) and (2.2%) CFR among patients with and without comorbidities, respectively (Fig. 4). Health status significantly influenced the CFR ($p = 0.005$). Likewise, occupation level, referring to the risk-based level category (low-based risk group, moderate-based risk group, and high-based risk group), had a significant ($p = 0.003$) influence on the CFR (Fig. 5). The clinical forms of COVID-19 were estimated to be (5.9%) and (0.21%) symptomatic and asymptomatic, respectively (Fig. 6). The clinical form significantly influenced the CFR ($p = 0.006$). Regarding the hematological parameter values (profile), the results showed variability in the significance of the association with CFR. The White Blood Cell (WBC) profile significantly ($p = 0.00001$) influences the CFR. However, there was no statistically significant association between CFR and other risk

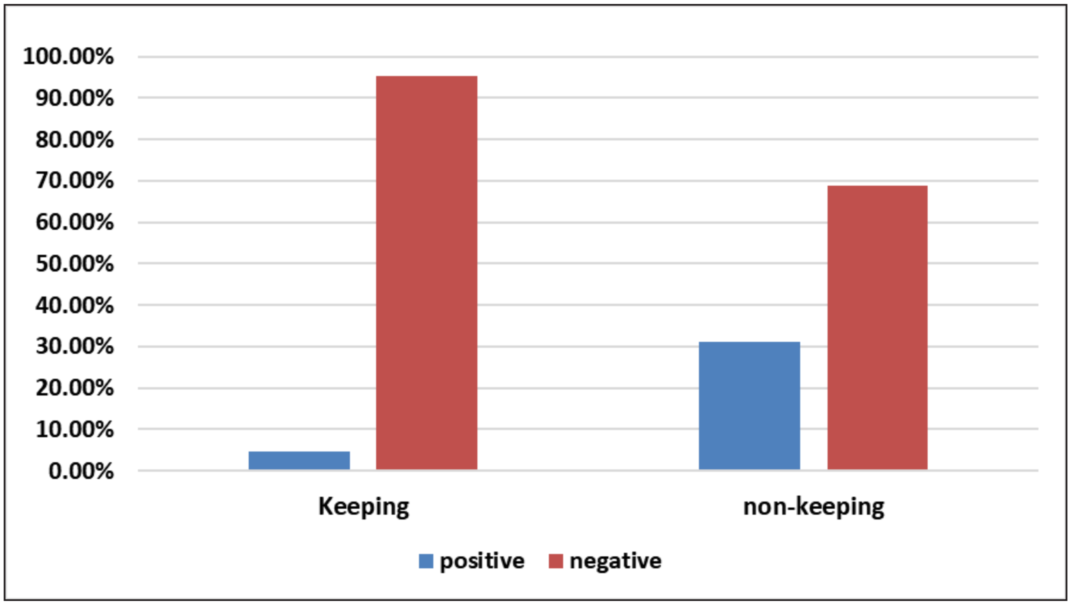

Fig. 1. COVID-19 hypothesis based on keeping and non-keeping animals.

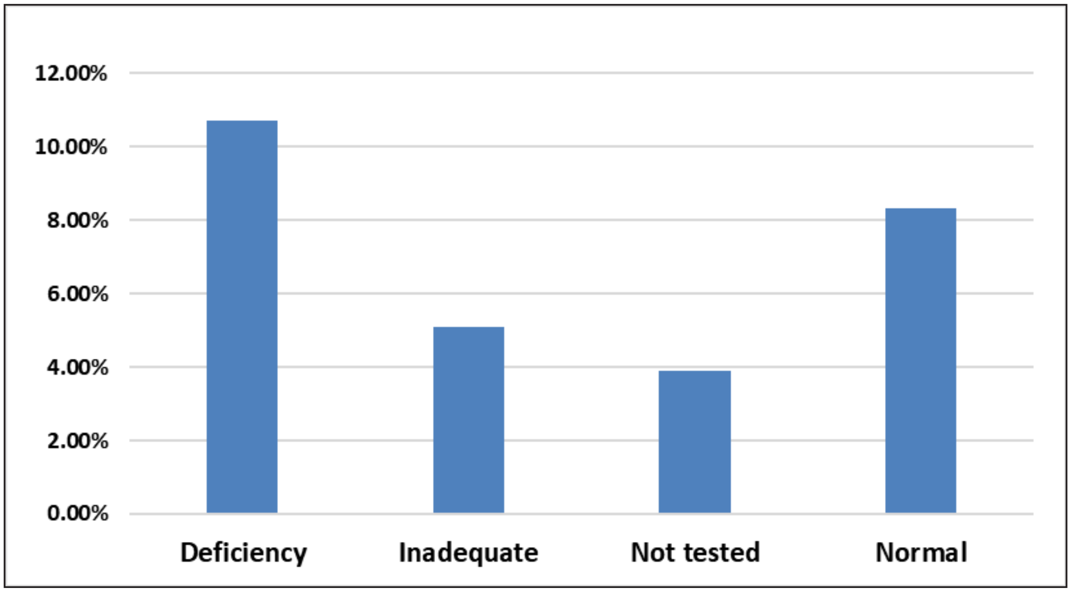

Fig. 2. CFR according to Vitamin D values.

factors, including body mass index, smoking, infection source, Bacillus Calmette-Guérin (BCG) scar, and marital status.

Discussion

The global unpredictable CFR of COVID-19 among different populations was significantly influenced by the variability in potential risk factors associated with the CFR of COVID-19. The present study analyzed the risk factors affecting the CFR of COVID-19 among the Libyan population. In line with various studies, there is a somewhat high CFR of COVID-19 among hospitalized patients (Mahmoud *et al*., 2021). However, there is variability in the frequency transmission rate of SARS-CoV-2 among different geographical regions, which might be attributable to various risk factors that increase the CFR of the COVID-19-infected population. Comparatively, the CFR (5%) reported in this study is less than that reported in other countries at the regional level (Daw, 2021; Mahmoud *et al*., 2023). Regarding the Vitamin D level among the study population, it significantly affects the CFR. In

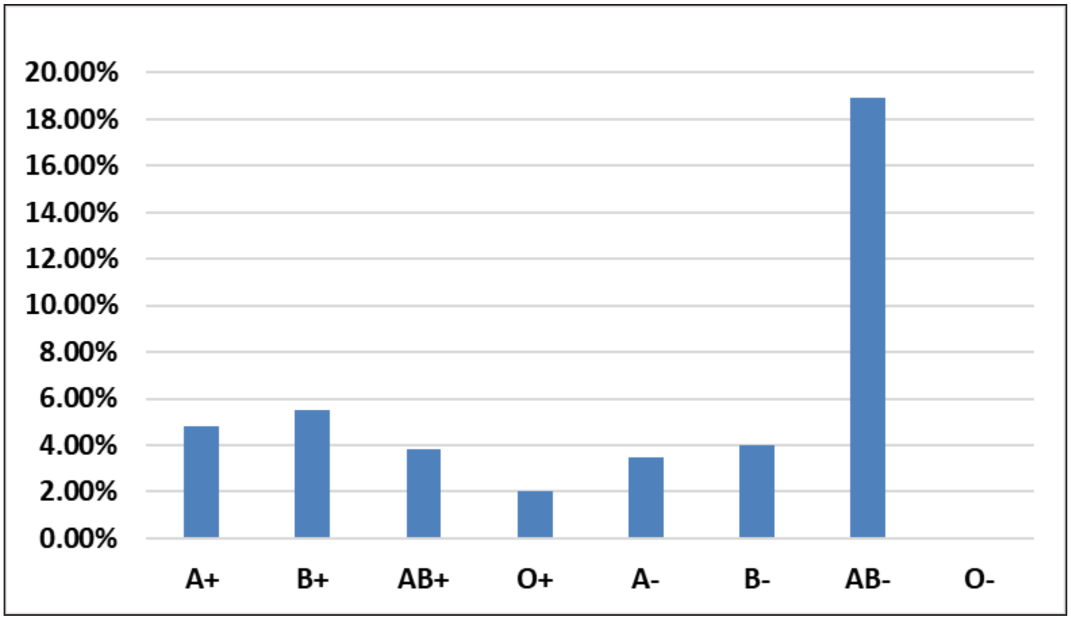

Fig. 3. CFR based on the ABO system.

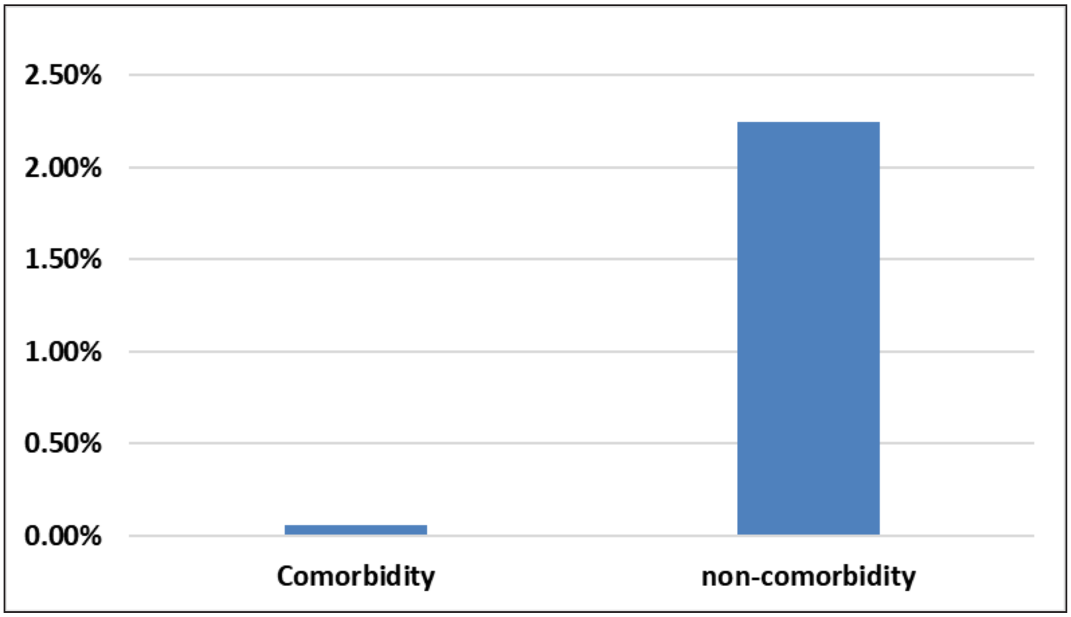

Fig. 4. CFR according to comorbidity.

agreement with a previous study reporting significance associated with vitamin D content (Lau *et al*., 2020; Whittemore, 2020). It is well known that vitamin D in the body plays a vital role in the biological activity of body systems due to the maintenance of healthy status and functional capacities for body systems (Abushhewa *et al*., 2024). Therefore, vitamin D deficiency could be a predisposing factor that increases the risk of developing infectious diseases. Nevertheless, a high CFR among the population with vitamin D deficiency was of significant interest in the study population. The results revealed a significant difference in animal welfare, especially for feline species. However, there is limited evidence of the transmission of SARS-CoV-2 from humans to cats. Several studies reported evidence of SARS-CoV-2 seroprevalence in pet animals in Wuhan during the COVID-19 outbreak (Zhang *et al*., 2020; Michelitsch *et al*., 2021). The transmission of SARS-CoV-2 from species to species (trans-species spreading) suggests an increased unrestricted host

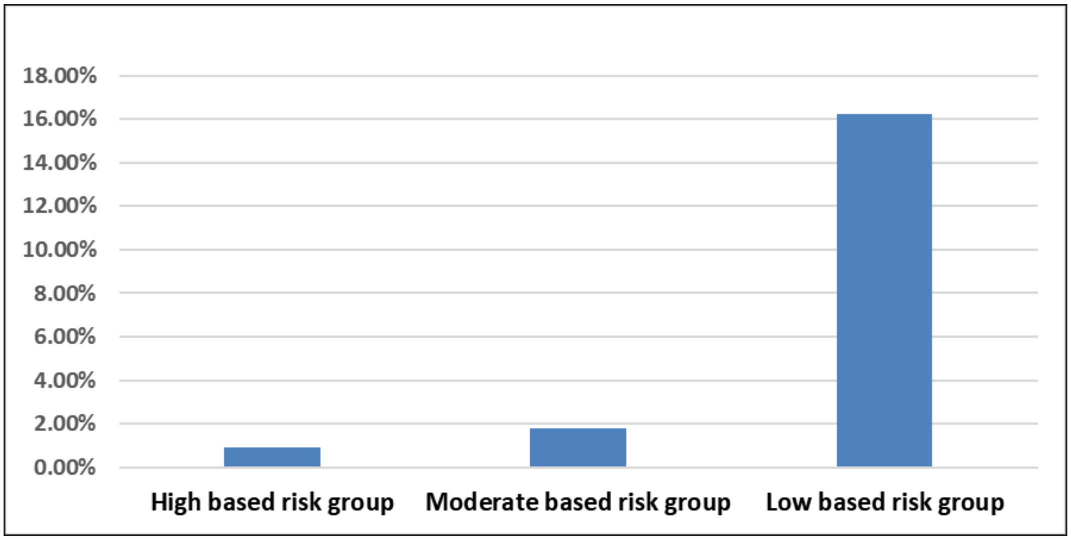

Fig. 5. CFR according to occupation.

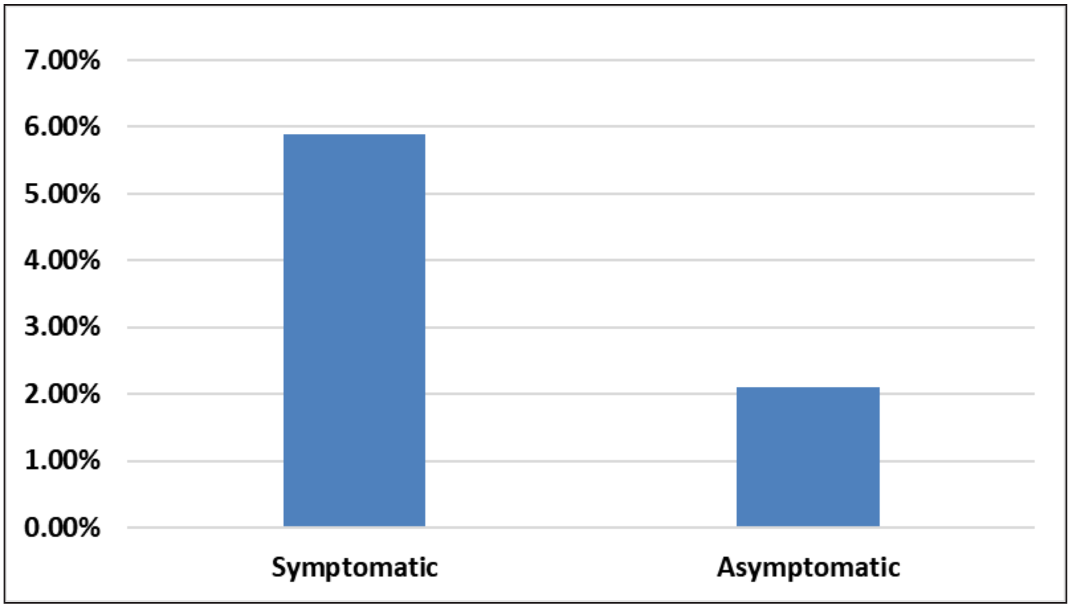

Fig. 6. CFR according to COVID-19 clinical form.

range for SARS-CoV-2 (Michelitsch *et al*., 2023). According to phylogenic analyses, approximately 96.2% of SARS-CoV-2 has a similar genome sequence identity with Bat CoV RaTG13, indicating that SARS-CoV-2 could also originate from bats (Zhang *et al*., 2020). Correspondingly, sequence analysis of viral genomes from domestic cats and humans showed high similarity within the conservation region. The study results revealed variable outcomes of COVID-19 CFR in correlation with the ABO system. The AB- blood group showed a significant association with case fatality of COVID-19, whereas a lower CFR of COVID-19 was reported among the O^+ blood group compared with the other blood groups. On the other hand, 0% CFR was reported among patients with O− blood group. According to published data, the ABO system might be a potential factor influencing COVID-19 clinical outcomes among hospitalized infected patients (Aljanobi *et al*., 2020). As a result, the variable difference in the CFR of COVID-19 in this study was reported as a consequence of the clinical outcome of the infected population. Various studies reported that those with blood group O had a lower incidence of SARS-CoV-2 infection than the non-O as compared to blood groups (Esref *et al*., 2020).

Concerning health status, the study results showed statistical significance in association with the CFR of COVID-19. Patients with comorbidities increase the risk of mortality from COVID-19, and they are considered the most at-risk group due to the increase in the clinical severity of the infection (Deng *et al*., 2020; Mahmoud *et al*., 2023). The results showed a high CFR among patients with comorbidities compared with patients without comorbidities. Similarly, according to various studies, the CFR was higher among patients with comorbidities (Deng *et al*., 2020; Fang *et al*., 2020). Therefore, health status is an important factor affecting the CFR of COVID-19.

The results of this study revealed statistically significant differences among the occupation groups. Compared to previous studies that reported substantial findings regarding CFR among different occupation groups, the high-based risk group showed a higher CFR from COVID-19 than other based-risk groups (Fang *et al*., 2020; Mena *et al*., 2021). High-risk group: health care workers without personal protective equipment are at great risk of infection with COVID-19. The proportion of symptomatic COVID-19 cases was higher than that of asymptomatic cases. The clinical form of COVID-19 has a significant influence on the CFR of COVID-19.

The present study revealed significant differences in the hematological profile of infected patients. The WBC profile significantly impacted the CFR of COVID-19 among the target population. Therefore, differences in the hematological profile could be a marker for the severity and clinical outcomes of COVID-19 (Bairwa *et al*., 2021). Regarding the other risk factors included in this study, there was no statistically significant association between CFR and other risk factors, including body mass index, smoking, infection source, BCG scar, and marital status.

Conclusion

The CFR of COVID-19 could have been underestimated; however, our results showed a relatively high CFR of COVID-19 in Libya, at least in the surveyed region (targeted population). Many risk factors analyzed in this study were significantly influenced by the CFR; among those potential risk factors were vitamin D, keeping animals, the ABO system, lymphocyte count (level), and healthy status. On the contrary, the findings indicated no significant correlation between the CFR and other risk factors, and the present results highlighted a potential risk associated with case fatality in the country. However, more research is needed to understand the role of animals as SARS-CoV-2 reservoirs.

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Conflict of interest

The authors declare no conflict of interest.

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Authors' contributions

The authors confirm their contributions to the paper as follows: Study conception and design: Hafsa A. Alemam and Abdusalam Sharef Mahmoud; data collection: Hafsa A. Alemam; analysis and interpretation of results: Abdusalam Sharef Mahmoud; Ahlam Masaud Ellafi; supervision: Abdusalam Sharef Mahmoud; Draft manuscript preparation: Abdusalam Sharef Mahmoud, Mouna A. Abdunnabi, Ahlam Masaud Ellafi, Hafsa A. Alemam, Abdurrezagh A., Khaled M. Ibrahim, Salah Edin El Meshri, and Adam Elzghied. All authors have reviewed the results and approved the final version of the manuscript.

Data availability

All data are provided in the manuscript.

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