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Sociodemographic predictors of confirmed COVID-19 mortality and hospitalization among patients in Saudi Arabia: Analyzing a national COVID-19 database

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Abstract

Background: Even with the widespread availability of vaccines for the COVID-19 disease, there is no sign of decline in the rate of spread of the disease. Based on findings of different studies across the globe, the disease is characterized by poor outcomes in specific sociodemographic categories such as age, gender and presence of symptoms.

Methods: In this study, we carried out a multivariable logistic regression analysis on a national database (HESN+) of confirmed COVID-19 cases in Saudi Arabia to determine predictors of hospitalization and mortality for these patients.

Results: Data was extracted for 328,301 confirmed COVID-19 patients (mean age (SD) = 37.79 (1.68)) with 34.92% females and 65.08% males. Of these, 59.87% were Saudi Arabian citizens and 40.13% were non-Saudi. 36.81% of cases were confirmed in Riyadh (n = 67,384), Makkah (n = 72,590) and the Eastern Province (n = 79,666). 72.2% of all cases were diagnosed and treated by the Ministry of Health (MOH). Of all confirmed cases, 95.28% showed one or more symptoms associated with COVID-19. 5.48% of these were hospitalized and 1.11% died. Predictors of mortality and hospitalization, respectively, included age (OR: 1.088 and 1.03), being male (OR: 1.443 and 1.138), nationality (OR: 2.11 and 1.993), presence of symptoms (OR: 1.816 and 4.386), and the health care sector in which patients received treatment (MOH OR: 1.352 and 4.731).

Conclusion: We found that COVID-19-related hospitalization or mortality was higher among males, older adults, and patients showing one or more symptoms, and mortality likelihood was more than fourfold for patients treated by the MOH. Immigrants were also more likely to be hospitalized or die from COVID-19 infection compared to Saudi nationals.

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Introduction

The global outbreak of coronavirus disease 2019 (COVID-19), a respiratory disease caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) in early 2020, has resulted in more than 240 million cases globally and almost 5 million deaths as of October 2021. The rate of infection and deaths show no sign of slowing despite the availability of an effective vaccine [1]. This is due to the highly
contagious nature of the SARS-CoV-2 RNA virus, which is closely related to the bat coronavirus (RaTG13) [2]. The first case of COVID-19 in Saudi Arabia was reported on 2nd March 2020 [3]. At 18 months into the pandemic, Saudi Arabia had reported over 500,000 cases and over 8000 deaths as a result of COVID-19 infection [4]. With similar trends globally, the rapid increase in COVID-19 cases has overwhelmed health care services during the surge, leading to a global rise in mortality.

Clinical presentation of COVID-19 in patients range from being asymptomatic or having mild upper respiratory infection with a fever and cough to more severe cases of multi-organ failure and, ultimately, death [5]. For challenging public health issues, such as the COVID-19 pandemic, prediction of the clinical course of the disease often aids better management of the disease to improve patients’ outcomes. Unfortunately, prediction of the clinical course of the disease is difficult given the unique experiences of patients in different risk strata. In general, age has been identified as a strong predictor of mortality and morbidity in COVID-19 [6]. In addition, co-morbidities, such as chronic respiratory disease, cardiovascular risks, kidney injury, and diabetes mellitus are known prognostic factors for poor outcomes in patients infected with COVID-19 [7–9]. However, extrapolation of these data to other geographic locations, such as the Middle East, requires caution due to the different genetic and socio-demographic backgrounds of patients involved in these studies.

A recent study of a cohort of 648 patients in Saudi Arabia with COVID-19 assessed risk factors associated with poor disease outcomes in a logistic regression model [10]. The study showed that age, gender, and the presence of co-morbidities were associated with poor patient outcomes. Another study of 565 Saudi Arabian patients with COVID-19 from a cohort of Saudi patients also used univariable Cox proportional hazards regression analysis to identify cardiovascular, renal and respiratory diseases as predictors of poor outcomes [11]. These co-morbidities have also been identified as predictors of mortality in a cohort of 768 Saudi patients with COVID-19 [12]. While these studies have been carried out on Saudi citizens and provide useful information on risk factors of the disease, the number of patients in these studies is not large enough to permit generalizability. In this study, we used multivariable logistic regression to analyze significant predictors of mortality and hospitalizations in COVID-19 patients in Saudi Arabia using the HESN+, a national database of confirmed COVID-19 cases in Saudi Arabia.

The HESN+ system is an interconnected web-based application developed by the Saudi Public Health Solutions for Diseases Surveillance and Management (PHSDSM). This national electronic surveillance system provides health professionals and decision-makers with accurate information that enables them to provide a high level of health services using several programs and services that maintain public health and primary health care [13]. The HESN+ system currently contains several units, such as investigation of infection, outbreak of epidemic diseases, vaccinations, stock of vaccines and immunization materials, and public health reports.

HESN+ was created in response to the COVID-19 pandemic to deal specifically with COVID-19 testing, surveillance and reporting. This electronic system allows for the nationwide unification of health processes, forms and reports relating to COVID-19 in Saudi Arabia. Health providers from different sectors electronically report key information related to COVID-19 patients, which includes patient identification information, date of birth, gender, nationality, region of residence, hospital sector, symptoms, COVID-19 test status, and if the patient was hospitalized or died due to COVID-19.

Methods

Data Collection and Sample

This study features a cross-sectional research design to examine relationships between sociodemographic characteristics of patients (i.e., age, gender, nationality, region of residence, hospital sector, and if the patient was symptomatic) and confirmed COVID-19 mortality and hospitalization rates. The study’s data were obtained from “HESN+”, which is a national unified COVID-19 surveillance platform in Saudi Arabia, on which all COVID-19 diagnoses, treatments, hospitalizations, and mortalities are reported by all health-related sectors. This national unified COVID-19 surveillance platform uses an online dashboard that allows for open engagement and the sharing of data with researchers.

Following approval from the Institutional Review Board of King Fahad hospital’s Scientific and Research Committee (which is under the administrative umbrella of the Ministry of Health of Saudi Arabia), analysis of the previously collected and disaggregated HESN+ data began. The study examined the responses of all confirmed COVID-19 cases that were reported to HESN+ from March 1st 2020 to January 31st 2021. The inclusion criteria for this study were confirmed COVID-19 cases with complete information about age, gender, nationality, region of residence, hospital sector, mortality, hospitalization, and if the patient was symptomatic. Data from 367,863 confirmed COVID-19 patients were collected from the HESN+ online dashboard. Due to missing data on the measures described below, the final merged analytic sample included 328,301 confirmed COVID-19 patients. Data is available on request.

Measures

The measures used in this study specifically examined data from HESN+ related to age, gender, nationality (i.e., Saudi or non-Saudi), region of residence (i.e., Riyadh, Makkah, Asir, Tabuk, Ha’il, Northern Borders, Jawf, Madinah, Eastern Province, Qassim, Jizan, Najran, and Bahah), hospital sector (i.e., Educational Health Care Facilities, Hajj Health Care Facilities, Ministry of Defense, Ministry of Interior, Mobile Field Hospitals, Ministry of Health, National Guard, Non-Government, Other-Non-MOH Organizations), if the patient was symptomatic, whether the patient was hospitalized, and whether the patient died from COVID-19.

Data analysis

All data analysis was conducted in R Studio version 3.6.1, which included a calculation of descriptive statistics to summarize characteristics of the patients and the use of inferential statistics to test the study’s research questions. This study used multivariable logistic regression analysis to assess the odds of confirmed COVID-19 mortality and hospitalization among patients in Saudi Arabia. The analysis generated two models that were used to test the study’s research questions. Fixed covariates in both models included sociodemographic information for the patients (i.e., age, gender, nationality, region of residence, hospital sector, and if the patient was symptomatic). First, the study used a multivariable logistic regression analysis to examine if sociodemographic variables were predictors of confirmed COVID-19 mortality among patients in Saudi Arabia. For this mode, a dummy variable was created with value “1” if the patient was confirmed to have died due to COVID-19 and “0” if the patient had not died due to COVID-19 and instead recovered. Second, the study used a multivariable logistic regression analysis to examine if sociodemographic variables were predictors of confirmed COVID-19 hospitalization among patients in Saudi Arabia. For this model, a dummy variable was created with value “1” if the patient was confirmed to be hospitalized due to COVID-19 and “0” if the patient was not hospitalized due to COVID-19. To determine statistical significance, the alpha level for model coefficients was set to < 0.05 for all analyses.
Results

Sample Characteristics

Data used for analysis were extracted for 328,301 confirmed COVID-19 patients (mean age = 37.79, SD = 1.68), of whom 34.92% (n = 114,637) were female and 65.08% (n = 213,664) were male. Additionally, the nationality of the study subjects was primarily Saudi Arabian (59.87%, n = 196,559), followed by non-Saudi patients (40.13%, n = 131,742). The majority of the cases (68.91%) were from the regions of Riyadh (n = 67,384), Makkah (n = 72,590), and the Eastern Province (n = 79,666). Moreover, 72.2% (n = 236,939) of the cases were diagnosed and treated by the Ministry of Health (MOH). Of all the confirmed cases, 95.28% (n = 312,794) were symptomatic; that is, having at least one or more symptoms such as fever, cough, sore throat, shortness of breath, or runny nose. 5.48% (n = 18,001) of these were hospitalized, and 1.11% (n = 3636) died (see Table 1).

Sociodemographic predictors of confirmed COVID-19 mortalities among patients in Saudi Arabia

A multivariable logistic regression analysis was used to examine if sociodemographic variables (i.e., age, gender, nationality, region of residence, hospital sector, and if the patient was symptomatic) were predictors of confirmed COVID-19 mortality among patients in Saudi Arabia. According to the Nagelkerke R² statistic, the model explained 6.6% of the variance in the dependent variable (i.e., deceased vs. not deceased due to COVID-19 among patients in Saudi Arabia). Patients’ age, gender, nationality, region of residence, hospital sector, and if the patient was symptomatic emerged as the statistically significant predictors in this model. Patients’ age significantly increased their likelihood of dying due to COVID-19 (aOR = 1.088, 95% CI = 1.086, 1.091). In other words, as patients’ age increased, so too did their likelihood of dying due to COVID-19. Additionally, patients’ gender (aOR = 1.443, 95% CI = 1.330, 1.566) (i.e., specifically males) significantly increased their likelihood of dying due to COVID-19. Patients’ nationality (i.e., Saudi vs. non-Saudi) significantly increased their likelihood of dying due to COVID-19 (aOR = 2.11, 95% CI = 1.945, 2.286). Non-Saudi citizens were more likely to die due to COVID-19 than Saudi citizens. Furthermore, the patients’ region of residence within Saudi Arabia either increased (i.e., for Makkah, Asir, Tabuk, Ha’il, Northern Borders, and Jawf) or decreased (i.e., Madinah, Eastern Province, Qassim, Jizan, Najran, and Bahah) their likelihood of dying due to COVID-19 when compared to the Riyadh region. The patients’ hospital sector (i.e., specifically Mobile Fields Hospitals) in which they were diagnosed and/or treated decreased their likelihood of dying due to COVID-19 when compared to Educational Health Care Facilities (aOR = 0.091, 95% CI = 0.022, 0.374). Finally, being symptomatic significantly increased patients’ likelihood of dying due to COVID-19 (aOR = 1.816, 95% CI = 1.487, 2.218). A complete breakdown of the regression results for the sociodemographic predictors of confirmed COVID-19 mortalities is presented in Table 2.

Sociodemographic predictors of confirmed COVID-19 hospitalizations among patients in Saudi Arabia

A multivariable logistic regression analysis was used to examine if sociodemographic variables (i.e., age, gender, nationality, region of residence, hospital sector, and if the patient was symptomatic) were predictors of confirmed COVID-19 hospitalizations among patients in Saudi Arabia. According to the Nagelkerke R² statistic, the model explained 6.9% of the variance in the dependent variable (i.e., being hospitalized vs. not hospitalized due to COVID-19 among patients in Saudi Arabia). Patients’ age, gender, nationality, region of residence, hospital sector, and if the patient was symptomatic emerged as the statistically significant predictors in this model. Patients’ age significantly increased their likelihood of being hospitalized due to COVID-19 (aOR = 1.030, 95% CI = 1.029, 1.031). In other words, as patients’ age increased, so too did their likelihood of being hospitalized due to COVID-19. Additionally, patients’ gender (i.e., specifically males) significantly increased their likelihood of being hospitalized due to COVID-19 (aOR = 1.138, 95% CI = 1.095, 1.182). Patients’ nationality (i.e., Saudi vs. non-Saudi) significantly increased their likelihood of being hospitalized due to COVID-19 (aOR = 1.993, 95% CI = 1.920, 2.069); non-Saudi citizens were more likely to be hospitalized due to COVID-19 than Saudi citizens. Moreover, the region of the country in which patients lived either increased (i.e., for Makkah, Asir, Tabuk, Ha’il, Najran, and Jawf) or decreased (i.e., Madinah, Eastern Province, Qassim, Jizan, Northern Borders, and Bahah) their likelihood of being hospitalized due to COVID-19 when compared to the Riyadh region. The patients’ hospital sector in which they were diagnosed and/or treated with COVID-19 increased their likelihood of being hospitalized due to COVID-19 when compared to Educational Health Care Facilities. Finally, being symptomatic significantly increased someone’s likelihood of being hospitalized due to COVID-19 (aOR = 4.386, 95% CI = 3.829, 5.0237). A complete breakdown of the regression results for sociodemographic predictors of confirmed COVID-19 hospitalizations are presented in Table 3.

Discussion

Important findings from our analysis showed several risk factors for both mortality and hospitalization of COVID-19 patients.
Generally, similar trends were found for factors associated with both mortality and hospitalizations, which may be because approximately 98% of the mortality occurred in hospitalized patients. Age, gender (male), nationality, region of residence, and presence of one or more symptoms were associated with increased odds of hospitalization and mortality. Although new information on COVID-19 is published daily, the findings of this study are in agreement with most studies across the globe. Age and gender have been reported in multiple studies to be good predictors of COVID-19 outcomes, with older patients (≥55 years) and males reported to have a higher probability of mortality [14–20]. Interestingly, 70% of the reported mortality in our study was in age groups above 55 years. This is in agreement with reports from other studies that have found that patients above 55 years of age are at least three times more likely to die from COVID-19 [16,21]. Generally, the higher mortality rate in older COVID-19 patients might be explained by the higher occurrence of comorbidities in this age group such as obesity, cardiovascular disease and type II diabetes [22]. It should be noted that comorbidities, such as type II diabetes and cardiovascular disease, are also risk factors that are significantly associated with increased mortality in COVID-19 infected patients [8,23,24]. In support of this, a national study carried out using data from the NHS Trust in the UK, which was comprised of 470,034 confirmed COVID-19 cases, showed that older patients were more likely to be frail, have long term health conditions and poor lung function, and still be at increased risk of COVID-19-related mortality even though they were less likely to be smokers [14]. Although in our study, age was a risk factor for hospitalization, it was more significantly related to mortality.

Analysis for gender-based influence on mortality and hospitalization post-COVID-19 infection revealed a strong association between gender and mortality in COVID-19 patients. Our findings showed that 81% and 74% of the recorded mortality and hospitalizations, respectively, were male. This is in agreement with reports in several other studies across the globe that indicate males being more predisposed to a high risk of mortality post-COVID-19 infection [20,25,26]. Few studies have attributed this to the difference in lifestyle between males and females such as higher rates of smoking among males [27,28]. One study, in particular, showed that COVID-19-related mortality was more likely among smokers due to the high expression of the angiotensin-converting enzyme 2 (ACE2) receptor in their lungs [29]. One of the mechanisms of SARS-CoV-2 viral entry into a host cell is via the ACE2 receptor in the airway lining. This process is believed to increase viral infection and load in smokers, who are disproportionately male.

Multivariable logistic regression analysis revealed that the presence of one or more symptoms significantly increased the likelihood of hospitalization and death post-infection. Approximately 98.8% of the hospitalized patients and 97% of deceased patients showed one or more symptoms. Data on the association between post-COVID-19 infection symptoms and mortality or hospitalization are scarce, but a number of studies have reported high fever and severe respiratory distress requiring oxygen supplementation in hospitalized patients [30–32]. Symptoms, such as respiratory

Table 2
Sociodemographic Predictors of Confirmed COVID-19 Mortality.

| Variable          | aOR     | Lower  | Upper  |
|-------------------|---------|--------|--------|
| Age:              | 1.088 * | 1.086  | 1.091  |
| Gender:           |         |        |        |
| Female            | Ref.    | Ref.   | Ref.   |
| Male              | 1.443 * | 1.330  | 1.566  |
| Nationality:      |         |        |        |
| Saudi Arabian     | Ref.    | Ref.   | Ref.   |
| Non-Saudi         | 2.110 * | 1.945  | 2.286  |
| Region of Residence: |       |        |        |
| Riyadh            | Ref.    | Ref.   | Ref.   |
| Makkah            | 3.726 * | 3.368  | 4.123  |
| Madinah           | 0.601 * | 0.521  | 0.698  |
| Eastern Province  | 0.269 * | 0.202  | 0.359  |
| Qassim            | 0.464 * | 0.333  | 0.647  |
| Asir              | 1.097   | 0.919  | 1.309  |
| Tabuk             | 1.723 * | 1.426  | 2.080  |
| Ha’il             | 2.773 * | 2.192  | 3.506  |
| Northern Borders  | 1.518 * | 1.176  | 1.959  |
| Jizan             | 0.020 * | 0.003  | 0.144  |
| Najran            | 0.166   | 0.023  | 1.188  |
| Bahah             | 0.436 * | 0.258  | 0.737  |
| Jawf              | 3.971 * | 3.063  | 5.147  |
| Hospital Sector:  |         |        |        |
| Educational Health Care Facilities | Ref. | Ref.  | Ref.   |
| Ministry of Defense | 0.778 | 0.580  | 1.045  |
| Ministry of Interior | 1.352 | 0.945  | 1.933  |
| Mobile Fields Hospitals | 0.091 * | 0.022  | 0.374  |
| MOH (Ministry of Health) | 1.001 | 0.786  | 1.309  |
| National Guard     | 1.042   | 0.707  | 1.534  |
| Non-Government     | 0.963   | 0.751  | 1.236  |
| Other-Non-MOH      | 1.303   | 0.899  | 1.888  |
| Organizations      |         |        |        |
| Symptomatic:       |         |        |        |
| No                | Ref.    | Ref.   | Ref.   |
| Yes               | 1.816 * | 1.487  | 2.218  |

Table 3
Sociodemographic Predictors of Confirmed COVID-19 Hospitalizations.

| Variable          | aOR     | Lower  | Upper  |
|-------------------|---------|--------|--------|
| Age:              | 1.030 * | 1.029  | 1.031  |
| Gender:           |         |        |        |
| Female            | Ref.    | Ref.   | Ref.   |
| Male              | 1.138 * | 1.095  | 1.182  |
| Nationality:      |         |        |        |
| Saudi Arabian     | Ref.    | Ref.   | Ref.   |
| Non-Saudi         | 1.993 * | 1.920  | 2.069  |
| Region of Residence: |       |        |        |
| Riyadh            | Ref.    | Ref.   | Ref.   |
| Makkah            | 2.895 * | 2.765  | 3.031  |
| Madinah           | 0.620 * | 0.584  | 0.658  |
| Eastern Province  | 0.607 * | 0.552  | 0.666  |
| Qassim            | 0.800 * | 0.702  | 0.912  |
| Asir              | 1.490 * | 1.3856 | 1.601  |
| Tabuk             | 1.408 * | 1.285  | 1.544  |
| Ha’il             | 2.220 * | 1.961  | 2.512  |
| Northern Borders  | 0.489 * | 0.410  | 0.584  |
| Jizan             | 0.471 * | 0.382  | 0.580  |
| Najran            | 1.694 * | 1.247  | 2.301  |
| Bahah             | 0.387 * | 0.292  | 0.513  |
| Jawf              | 6.398 * | 5.710  | 7.169  |
| Hospital Sector:  |         |        |        |
| Educational Health Care Facilities | Ref. | Ref.  | Ref.   |
| Ministry of Defense | 3.475 * | 2.637  | 4.581  |
| Ministry of Interior | 4.459 * | 3.280  | 6.063  |
| Mobile Fields Hospitals | 32.779 * | 23.121 | 46.472 |
| MOH (Ministry of Health) | 4.731 * | 3.645  | 6.141  |
| National Guard     | 6.180 * | 4.579  | 8.340  |
| Non-Government     | 9.694 * | 7.463  | 12.502 |
| Other-Non-MOH      | 8.623 * | 6.460  | 11.510 |
| Organizations      |         |        |        |
| Symptomatic:       |         |        |        |
| No                | Ref.    | Ref.   | Ref.   |
| Yes               | 4.386 * | 3.829  | 5.0237 |

Note: * p < 0.05; aOR = adjusted odds ratio; CI = confidence intervals.
distress and high fever, will more likely result in complications if such patients are not monitored closely or placed on respiratory support.

Global travel is usually one of the factors that contributes to the spread of COVID-19 disease over a short period. This is supported by studies from different countries, showing that immigrants are more prone to COVID-19 infection compared to native citizens [33–35]. These studies agree with the finding of our study that immigrants were at greater risk of mortality or hospitalization due to COVID-19 compared with non-immigrants. This finding may be because immigrants in Saudi Arabia are more likely to be employed in blue-collar jobs, where there is an increased chance of physical contact (i.e., cleaners, meat factory workers and farmers). In addition, employees in these occupations may be less likely to have health insurance or access to adequate and timely healthcare [34,35]. That said, Saudi Arabia implements universal health care whereby health care is free for all. However, even when access to healthcare was controlled for, disparity in the likelihood of hospitalization and mortality of patients with COVID-19 still existed between immigrants and native citizens. These findings show that immigration status is an important predictor of this pandemic that needs to be considered by national and public health officials.

Findings from our study show that mortality was significantly associated with the health care sector in which the patient was treated. This may be attributed to specific factors that are particular to the hospital in which care was received, such as the availability of specialized equipment required to manage disease progression and convalescence, availability of medical experts, and accessibility of timely testing. Our findings showed that 68.5% of mortality cases were reported in the MOH, which houses a disproportionate number of medical experts and care facilities. This is in agreement with the findings in a study by Sandoval and Nguyen [36], which showed that the flagship hospital in the region documented the highest COVID-19-related death rates compared to rural hospitals. This death rate was attributed to the fact that the flagship hospital is present in a major city within a large medical center; thus, more patients have access to this hospital [36]. This also agrees with the data from our study showing that 72% of all patient cases were handled in the MOH. If this factor is considered, mortality in the MOH is 1.05% of the total patient pool in the hospital sector and 1.254% of the mortality for all other sectors combined. These data would indicate slightly lower rates of mortality among patients treated in the MOH sector when compared with the other health care sectors combined. Thus, further research is needed to better understand how to reduce mortality rates among the other health care sectors to be parallel to those of the MOH sector.

Limitations

This study used a national database of COVID-19 patients (i.e., HESN+) to extract sociodemographic data such as age, gender, and nationality, among other variables. The following limitations to this study need to be addressed. Mortality records were extracted from the HESN+ database, and it may be possible that some individuals died due to reasons other than complications from COVID-19. In addition, a small number of individuals recorded as deceased may have been misreported or miscoded. Another limitation in this study is the lack of complete and detailed information on the types of symptoms patients presented. This prevented us from carrying out subgroup analysis on stratified data for the number of symptoms that may have resulted in death or hospitalization.

Multivariable analysis of the association between region of residence and hospitalization or mortality also depicted interesting results. COVID-19 patients were at greater risk of mortality or hospitalization if they were from the regions of Makkah, Ha’il and Jafw. While our results for Makkah are likely to be highly accurate due to the sample size for this region, results for Jafw may be less accurate due to the smaller number of patients (i.e., n = 904). A similar statistical phenomenon occurred with the nationality data. Non-Saudi nationals were more likely to be hospitalized or die, but this might be due to the number of nationalities that make up the 100,000 non-Saudis. Different genetic predispositions, socioeconomic status levels, and travel history may all confound this finding. Nonetheless, this data provides an opportunity to consider national-level outcomes amid the COVID-19 pandemic for the purpose of improving health care.

Conclusion

The current study’s findings show that the risk of COVID-19-related hospitalization or mortality is higher among males and older adults. In addition, a significant proportion of patients showing one or more symptoms were also either hospitalized or deceased due to complications of COVID-19 infection. Immigrants were also more likely to be hospitalized or die from COVID-19 infection compared to Saudi nationals. This study is based on data extracted from a national database (i.e., HESN+), and the findings from this study can be extrapolated to the general population. However, care should be taken to consider the highlighted limitations when doing so. Thus, the surveillance and monitoring of age, gender, and patient symptoms may aid policymakers in making swift decisions regarding hospitalization to prevent mortality.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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