Risk Factors of COVID-19 Critical Outcomes in the Eastern Mediterranean Region: A Multicountry Retrospective Study .

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Abstract

Background: The establishment of empirical evidence in the Eastern Mediterranean Region (EMR) necessitates the implementation of wide-scale studies to describe the demographic, clinical features, and severity profile ofCOVID-19 patients.

Objective: Hence, this study aimed to to assess the patterns of COVID-19 severity and mortality in seven countries and to determine the risk factors of COVID-19 severity and mortality.

Methods: This multi-country study was based on a retrospective review of medical records of hospitalized patients confirmed to have COVID-19. This study included data from Iraq, Pakistan, Sudan, Somalia, Morocco, Egypt, and Yemen. All demographic and clinical data were extracted from hospital records (paper files) by trained data collectors.

Results: A total of 4141 patients were included in this study from seven countries. Comorbidities were reported by nearly half of the patients, with hypertension (HT)(24.7%)and diabetes (22.7%) being the most common. Older age, diabetes mellitus,

hypertension, and heart diseases were significantly associated with COVID-19 severity and mortality. Ever smoking and renal diseases were significantly associated with severity but not mortality, while male gender, respiratory diseases, and malignancy were significantly associated with mortality but not severity.

Conclusions: The study confirmed the role of comorbidities and demographic features on the severity and mortality of COVID-19. Understanding the contributing factors ensures attentive care and informs clinical management of patients with poorer prognosis in early stages of

(JMIR Preprints 18/08/2021:32831)
DOI: https://doi.org/10.2196/preprints.32831

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Keywords: Critical outcomes; COVID-19; severity; mortality

Introduction

On 31st December 2019, cases of pneumonia of unknown etiology were reported from Wuhan City, Hubei Province of China [1]. Later, the Severe Acute Respiratory Syndrome Corona Virus2 (SARS-CoV-2) was identified as a causative agent and the disease was named COVID-19. The World Health Organization (WHO) declared SARS-CoV-2 to be a global pandemic on March 11, 2020 [1,2]. Globally, 200,840,180 cases of COVID-19 were confirmed and 4,265,903 deaths were reported as of August 6, 2021. In the Eastern Mediterranean Region (EMR), a total of 12,949,856 cases and

240,395 deaths were reported as of August 6, 2021 [3]. The recent forecasting by Institute for Health Metrics and Evaluation (IHME) has projected COVID-19 related deaths in North Africa and the Middle East to reach up to 327,956 deaths by December 2021 [4].

As many of the countries in the region are suffering from war and political instability, cases and deaths are underreported because of inadequate testing facilities, weak health system response, and inadequate vital registration and documentation [5]. The high hospital admissions and poor surge capacity of critical care were experienced as one of the key health facility challenges that would undermine the response to the COVID-19 pandemic [5]. Difficulties in the estimation of COVID-19 hospital admission rates were highlighted early during the pandemic as it depends on community testing and admission criteria which varies between countries. Studies from China, Europe, and the United States, have indicated rates of admission to intensive care ranging from 5% to 32%, respectively [6–9].

A recent report showed that Iran has scored the highest number of cumulative deaths (85 694; case-fatality rate (CFR) 2.6%) followed by Pakistan (22 582; CFR 2.3%) and Iraq (17 515; CFR 1.2%) [10]. Whereas, Yemen reported the highest CFR (19.7%) followed by Sudan (7.5%). The lowest CFR was reported from Qatar (0.2%) [10]. The difference in the population profile and health system capacity between countries might result in variation in epidemiological characteristics and clinical outcomes. It is worthy to note that the Middle East region has a high prevalence of diabetes (DM) and cardiovascular diseases (CVD) that may contribute to heighten the severity of the disease resulting in high mortality and life-long disability [11–13].

Severe cases of COVID-19 are more likely to deteriorate to conditions that necessitate vital and timely care [6,7]. Epidemiological studies in China, Canada, the US, and the UK have identified risk factors associated with severe cases of COVID-19 that require hospital admission [6–9]. Old age, chronic co-morbidities, and male sex have consistently been cited as risk factors associated with COVID-19 severity and increased mortality [14–16]. Other risk factors including chronic obstructive pulmonary disease (COPD) and smoking were reported in other studies [17].

Despite the fact that there is limited evidence on the severity of COVID-19 across EMR, yet recent studies from Iraq were consistent with global evidence that old age, male gender, and pre-existing comorbidities were associated with increased mortality among hospitalized COVID-19 patients [18,19].

The establishment of empirical evidence in the EMR necessitates the implementation of wide-scale studies to describe the demographic, clinical features, and severity profile of COVID-19 patients. Assessing the risk factors of the severe form of COVID-19 is essential to develop appropriate risk

reduction strategies and to plan resources for healthcare as the pandemic unfolds. Furthermore, it will inform clinical management by predicting clinical outcomes and prognostic markers to facilitate the development of a care pathway for COVID-19 critical care. Thus, this study aimed to assess the patterns of COVID-19 severity and mortality in seven countries and to determine the risk factors of COVID-19 severity and mortality.

Methods

Study Design and Data Sources

This multi-country study was based on a retrospective review of medical records of hospitalized patients confirmed to have COVID-19. This study included data from Iraq, Pakistan, Sudan, Somalia, Morocco, Egypt, and Yemen. All data were extracted from hospital records (paper files) by trained data collectors who used a standardized Kobo collect form for data entry. In all participating countries, the data collected were for patients admitted to hospitals by October 2020.

In Iraq, data were collected for patients with COVID-19 who were admitted during the period between the 1st to the 30th of June 2020 to any one of the six selected hospitals in Baghdad and one hospital in Babylon. The seven hospitals were selected out of the 10 hospitals that received COVID-19 patients in Baghdad and Babylon because of the presence of Field Epidemiology Training Program (FETP) residents who collected the data. In Sudan, the study was limited to Khartoum and Gazira states as they were the high spots for COVID-19 in the country. The data were collected from the two main secondary isolation centers and two primary isolation centers (All hospital records of patients with a confirmed diagnosis between March 2020 and October 2020 were included). In Morocco, data were collected from The Cheikh Zaid International University Hospital of Rabat city which was dedicated to the hospitalization of COVID-19 patients. In Egypt, data from El-Agoza Hospital in Giza governorate (a high-risk governorate) was collected between May - June 2020. El-Agoza Hospital was designated for screening and isolation of COVID-19 patients. In Yemen, data were collected on patients with COVID-19 who were admitted to three main isolation hospitals in Sana'a City. In Pakistan, data were collected from two hospitals in Rawalpindi [Benazir Bhutto Hospital (BBH) and Holy Family Hospital] and two other hospitals in Islamabad [Pakistan Institute of Medical Sciences (PIMS) and Pakistan Air force Hospital] of cases admitted between February and August. All four hospitals were COVID-19 treatment centers. In Somalia, data of patients admitted between March and August to De-Martino Hospital (the only COVID-19 treatment center in Mogadishu) were collected.

Data Abstraction Form

A standardized data collection tool for all countries was developed and converted to Kobo Toolbox

form. The form consisted of four sections. The first section included patients' baseline and demographic characteristics (age, gender, smoking history, profession as being healthcare worker (HCW) or not, travel history, and history of contact with confirmed COVID-19 patient). The second section included variables related to clinical history and presentation severity, signs and symptoms, and comorbidities. The third section included severity classification. Section four included outcomes (fully recovered, discharged improved, palliative discharge/ disable, and death).

Variable Definitions

WHO guidelines were used to define the history of contact (Exposure during the 2 days before and the 14 days after the onset of symptoms)and travel history (History of travel 14 days before symptom onset) [20]. The severity of the disease was classified into mild (upper respiratory disease), moderate (Pneumonia but no need for oxygen), severe (pneumonia and need oxygen), and critical (needs ICU admission) [21]. Clinical outcomes were defined as follows: fully recovered (negative PCR test before discharge or full resolution of symptoms as noted by the attending physician), discharged improved (no PCR was done before discharge but the patient was discharged based on improvement in the clinical picture), palliative discharge/ disable (discharged with long term disability due to COVID-19), and death. During the analysis, we grouped the first three categories under "survivors" and compared them to the fourth category "death". Critical outcomes included death, palliative discharge, or disability.

Ethical considerations

Ethical approval was obtained from the Institutional Review Boards in selected countries and hospital permissions were sought to access patients' records. Data were coded to maintain confidentiality. All data files were encrypted and saved in a secure database with limited access to the study team.

Data management and analysis

Data were entered and managed using the kobo toolbox (a tool developed by the Harvard Humanitarian Initiative to be used for field data collection in challenging environments) and then exported to IBM SPSS version 23 for analysis. Data were described using percentages and counts. The differences between percentages were tested using the Chi-square test. Two separate multiple logistic regression analyses were conducted to determine factors associated with COVID-19 severity and mortality. The final logistic regression models included significant variables only. A p-value of less than 0.05 was considered statistically significant.

Results

Demographic and Relevant Characteristics

A total of 4141 patients were included in this study from seven countries, of which Iraq and Pakistan composed almost 60% of the sample followed by Sudan (24.4%). Almost 38% (n = 1571) of patients aged 40-59 years and males constituted 64% of the sample. About 14.6% of patients were ever smokers. Almost 4% were healthcare workers. History of contact with a COVID-19 patient was indicated by 40% of patients. Table 1 shows the demographic and relevant characteristics of patients.

Table 1:. Demographic and relevant background characteristics of COVID-19 patients (n = 4141)

Variables	N	%
Country		
Iraq	1438	34.7
Pakistan	1199	29.0
Sudan	1011	24.4
Somalia	230	5.6
Morocco	123	3.0
Egypt	71	1.7
Yemen	69	1.7
Age (year)		
<40	1193	28.8
40-59	1571	37.9
>60	1377	33.3
Sex		
Male	2641	63.8
Female	1500	36.2
Profession		
Non-healthcare workers	3994	96.5
Healthcare workers	147	3.5
History of contact with COVID-19 patient (yes)	1690	40.8
Smoking		
Never	3537	85.4
Ever	604	14.6

Comorbidities and Clinical Manifestations

The most common symptoms on admission were fever (77.2%), followed by cough (72%), and shortness of breath (17%). Other common clusters encompassing musculoskeletal symptoms (myalgia or arthralgia or backache or fatigue) were reported by 37.6% of patients. A cluster of enteric symptoms was less common in this study (9.6%). Comorbidities were reported by nearly half of patients, with hypertension being the most common comorbidity (24.7%), followed by diabetes (22.7%). Multiple comorbidities were also reported in almost half of the subjects (52%) (Table 2).

Table 2: Distribution of study participants by clinical manifestations and comorbidities

Variables	N (4141)	%
Comorbidities		
No co-morbidity	2408	48.2
Hypertension	1021	24.7
Diabetes mellitus	939	22.7
Heart diseases	303	7.3
Renal disease	140	3.4
Asthma	111	2.7
Respiratory Diseases (COPD [a] and other respiratory diseases)	61	1.5
Malignancy	62	1.5
Immune compromising Conditions	45	1.1
Liver disease	22	0.5
Symptoms		
Asymptomatic	124	3.0
Fever	3198	77.2
Cough	3009	72.7
Shortness of breath	2224	53.7
Musculoskeletal manifestations	1557	37.6
Sore throat	683	16.5
Headache	664	16.0
Loss of taste or smell	474	11.4
Chest pain	458	11.1
GIT /enteric symptoms (Nausea/vomiting / Diarrhea / Abdominal pain)	364	8.8
Sputum production	156	3.8
Nasal congestion	118	2.8
Conjunctival congestion	37	0.9
Hemoptysis	36	0.9
Other symptoms	134	3.2

[a] Chronic obstructive pulmonary disease

Factors Associated with COVID- 19 Severity and Mortality

Of all patients, 27.6 % had mild disease, 22.7% had moderate disease, 28.9% had severe disease, and 20.7%had critical disease. The **bivariate** analysis had shown that increased age, non-health professions, ever smoking, and comorbidity history particularly hypertension, diabetes mellitus, heart diseases, and respiratory diseases were significantly associated with severe or critical COVID-19. Whereas mortality was consistently associated with the aforementioned factors in addition to the male sex, cerebrovascular disease, and malignancy (Table 3).

Table 3: Bivariate analysis of factors associated with COVID- 19 severity and mortality

Variable	Severity			Mortality		
	Mild-	Sever-	P-	Survivors	Deaths	P-

	moderate		critical		value					value
	N	%	n	%		n	%	N	%	
Sex					0.447					0.005
Male	1318	49.9	1323	50.1		2132	80.7	509	19.3	
Female	767	51.1	733	48.9		1263	84.2	237	15.8	
Age					<0.001					<0.001
<40	849	71.2	344	28.8		1115	93.5	78	6.5	
40-59	779	49.6	792	50.4		1334	84.9	237	15.1	
>= 60	457	33.2	920	66.8		946	68.7	431	31.3	
Working in Healthcare Setting					<0.001					<0.001
Non-healthcare workers	1965	49.2	2029	50.8		3254	81.5	740	18.5	
Healthcare workers	120	81.6	27	18.4		141	95.9	6	4.1	
Positive History of contact with COVID-19 patient:	1116	66	574	34	<0.001	1456	86.2	234	13.8	<0.001
Smoking					<0.001					0.292
Ever	228	37.7	376	62.3		486	80.5	118	19.5	
Never	1857	52.5	1680	47.5		2909	82.2	628	17.8	
Comorbidities	592	34.2	1141	65.8	<0.001	1237	71.4	496	28.6	<0.001
Hypertension	353	34.6	668	65.4	<0.001	714	69.9	307	30.1	<0.001
Diabetes Mellitus	319	34	620	66	<0.001	650	69.2	289	30.8	<0.001
Heart Diseases	91	30	212	70	<0.001	190	62.7	113	37.3	<0.001
Renal Disease	25	17.9	115	82.1	<0.001	108	77.1	32	22.9	0.129
Asthma	50	45	61	55	0.257	91	82	20	18	0.999
Respiratory Diseases	21	34.4	40	65.6	0.012	38	62.3	23	37.7	<0.001
Malignancy	21	33.9	41	66.1	0.009	43	69.4	19	30.6	0.009
Immunocompromising conditions	12	26.7	33	73.3	0.001	39	86.7	6	13.3	0.411
Liver Disease	8	36.4	14	63.6	0.188	16	72.7	6	27.3	0.257
TB [a]	19	33.9	37	66.1	0.013	42	75	14	25	0.171
Cerebrovascular disease	8	42.	11	57.	0.471	12	63.	7	36.	0.032

	1	9		2	8

[a] Tuberculosis

The multiple logistic regression indicated that increased age and smoking were significantly associated with severity (p<0.001). Patients older than 60 years were three times more likely to develop a severe or critical form of COVID-19 compared to patients younger than 40 years. Patients with ever smoking history were 10 times more likely to develop severe or critical disease course compared to non-smokers (OR (odds ratio) = 9.7; 95% CI: 5.1, 18.5, P<0.001). Not having a history of contact with COVID-19 patients (OR = 2.8; 95% CI: 2.4, 3.2, P<0.001) and being non-healthcare workers (OR = 2; 95% CI: 1.2, 3.1, P=0.004) were also significantly associated with developing a severe form of COVID-19. Of comorbidities, renal diseases (OR = 3.3; 95% CI: 2.1, 5.2, P<0.001), heart diseases (OR = 1.7; 95% CI: 1.3, 2.2, P<0.001), diabetes (OR = 1.4; 95% CI: 1.2, 1.7, P<0.001) and hypertension (OR = 1.2; 95% CI: 1,1.5, P = 0.026) were associated with increased odds of severe disease (Table 4).

Increasing age was a strong predictor of mortality in hospitals as the older age group (>60 years) was associated with an increased odds of death by almost four times compared to the younger age category (OR = 4; 95% CI: 3.1, 5.3, P<0.001). The history of contact with COVID-19 patients and being non-healthcare workers had higher odds of mortality. Female sex was associated with lower odds of mortality (OR = 0.8; 95% CI: 0.7, 1.0, P = 0.022). Comorbidities associated with high odds of morality included respiratory diseases (OR = 2.1; 95% CI:1.2,3.7, P = 0.009), heart diseases (OR = 1.8; 95 % CI: 1.4, 2.3, P<0.001), malignancy (OR = 1.8; 95% CI: 1.0,3.3, P = 0.041) and diabetes mellitus (OR = 1.6; 95% CI: 1.3,1.9, P<0.001). Renal diseases and smoking history had no significant association with mortality (Table 4).

Table 4: Multiple logistic regression of factors associated with COVID-19 severity and mortality

Covariates	Factors associated with COVID-19 severity			Factors associated with COVID-19 mortality			
	OR[a]	95% CI	P-value	OR	95% CI		P-value
Sex (female vs. male)	*			0.8	0.7	1	0.022

	OR^a				OR^a			
Age (year)								
<40								
40-59	2	1.7	2.4	<0.001	1.9	1.5	2.5	<0.001
>60	3.1	2.6	3.8	<0.001	4	3.1	5.3	<0.001
Profession								
Healthcare workers								
Non-healthcare workers	2	1.2	3.1	0.004	2.4	1	5.6	0.039
History of contact with COVID-19 patient (no vs. yes)	2.8	2.4	3.2	<0.001	1.4	1.2	1.7	<0.001
Diabetes Mellitus (yes vs. no)	1.4	1.2	1.7	<0.001	1.6	1.3	1.9	<0.001
Hypertension (yes vs. no)	1.2	1	1.5	0.026	1.3	1.1	1.6	0.003
Heart Diseases (yes vs. no)	1.7	1.3	2.2	<0.001	1.8	1.4	2.3	<0.001
Renal Disease (yes vs. no)	3.3	2.1	5.2	<0.001	*			
Respiratory Diseases (yes vs. no)	*				2.1	1.2	3.7	0.009
Malignancy (yes vs. no)	*				1.8	1	3.3	0.041
Symptomatic (yes vs. no)	*				4.5	1.6	12.6	0.004
Smoking (ever vs. never)	9.7	5.1	18.5	<0.001	*			

^{a} Odds ratio

*Not entered in the model because the variable is not statistically significant

Discussion

Principal results

The data of a cohort of COVID-19 patients hospitalized in seven different countries were collected and analyzed. The proportion of hospitalized patients with severe or critical illness in this study (49.6%) is remarkably higher than what is being reported from other parts of the world on hospitalized COVID-19 patients [22–25]. To our knowledge, only one study from Wuhan reported a severity profile as high as 49.1% [26]. However, given that the study was conducted among hospitalized patients rather than in the community, these proportions are not a true representative of the COVID-19 severity spectrum in this region. At the beginning of the pandemic, the healthcare facilities used to admit COVID-19 patients of different severity for the sake of isolation and treatment of those patients. Later, with the increase in the number of patients, the healthcare facilities in most of these countries started to reserve the already limited hospital beds to treat the more severe cases which in turn shifted the majority of mild-moderate cases to be treated at home.

We found older age, diabetes mellitus, hypertension, and heart diseases to be associated with both severity and mortality. Furthermore, ever smoking and renal diseases were associated with severity but not mortality, while male gender, respiratory diseases (COPD or other respiratory diseases), and malignancy were associated with mortality but not severity. The latter category is of special importance, given the fact that these patients might die even if they do not experience severe or

critical illness. The majority of these findings are consistent with previous studies on COVID-19 severity and/or mortality [27–31].

What is Already Known on This Topic

Unraveling the pathophysiology of COVID-19 is still a work in progress. Nevertheless, the role of Angiotensin-converting enzyme 2 (ACE2) receptors is widely recognized as a key player in the disease process. ACE2 is a metallopeptidase that is expressed in various human organs [32] and is thought to be the cell entry point for SARS-Cov-2 [33]. Among others, it has been found on cell membranes of the nasal epithelium, alveolar epithelial cells of the lungs, the small intestine enterocytes, vascular endothelial cells, and cardiovascular system cells [32–35]. It is believed that negative regulation of the renin-angiotensin system (RAS) is a main function of ACE2. RAS has been linked to lung injury [36,37] which has led to concluding that ACE2 has a protective effect on the lungs [38,39] and that its preexisting deficiency might lead to a more severe or even fatal COVID-19 [40].

Older patients, males, and patients with type 2 diabetes mellitus were frequently found to have severe or fatal COVID-19 in epidemiological studies. Interestingly, they were also found to have lower ACE2 expression which might help explain why they are disproportionately affected by COVID-19 poor outcomes [41–43]. Furthermore, age (the earliest and most widely recognized predictor of COVID-19 severity and mortality) showed the strongest correlation with low ACE2 expression [41].

In addition to ACE2 down-regulation, other biological and non-biological factors might help explain some of our findings. For example, differences in the biological and molecular level in older patients (as compared to younger ones) might have their contribution to the disease course [44]. In particular, two cardinal features of the aging immune system are probably the culprits: immune senescence (a general decline in the overall performance of the immune system, innate and acquired) and inflamm-aging (a system-wide persistent pro-inflammatory status) [44–46]. However, some have argued that age-associated comorbidities, rather than age itself, are the major factor behind these findings [47]. However, in this paper, we found that age is an independent risk factor on top of the comorbidities from the multiple logistic regression (Table 4).

Diabetes mellitus is another risk factor where the dysregulated immune response is thought to play a role in a patient's susceptibility to critical COVID-19 outcomes. Similar to aging, diabetic patients are in a state of low-grade chronic inflammation [48]. Furthermore, diabetes is associated with reduced activity of natural killer cells as well as impaired cell-mediated adaptive immunity (chemotaxis, phagocytosis, cytokine secretion, and T cell abnormalities) [48].

The fact that an overactive RAS is a key aspect of the pathogenesis of CVD (heart diseases and Hypertension) [49,50] might explain the association between CVD and fatal COVID-19. An already existing abnormal cytokine profile in patients with these comorbidities can be part of the explanation as well [51–53] Knowing that cytokine storm is frequently linked to severe and fatal COVID-19 strengthens the biological plausibility of this explanation [8,54].

Similar to CVD, some renal diseases are characterized by an overactive RAS [55] and linked to dysregulated cytokine function as well as pro-inflammatory status [56,57]. Although patients with renal diseases were more likely to have severe illness in our study, we found no association with mortality. This is inconsistent with previous reports [58,59] which might be explained by differences in renal disease definitions and severity levels of the studied subjects. These same reasons might explain why, unlike other studies [60], we found no association between liver disease and critical COVID-19 outcomes.

The defective local physiological function of the respiratory system in patients with COPD and other respiratory diseases could explain their predisposition to worse COVID-19 outcomes. Conversely, asthma was not associated with COVID-19 severity nor mortality. The evidence in the literature on asthma has been inconclusive [61].

Comparison with Prior Work

Despite the fact that smoking is probably underestimated in our study due to associated stigma, particularly among women, we were able to find an association with severity. However, this same underestimation might be the reason why, unlike previous reports [17], we could not find an association with mortality. Another reason is the fact that in our study, due to small cell size, we combined former and current smokers under the same category while in other studies mortality was found to be associated with current, rather than former smokers [17].

Unexpectedly, we also found that not working in a healthcare setting and not having a history of contact with a known COVID-19 case to be associated with both severity and mortality. These findings should be interpreted with caution, though, patients with a known COVID-19 contact history might be better informed and more likely to seek help early and thus less likely to suffer from critical outcomes.

There is also the possibility that the history of contact is underreported mainly for two reasons. First, the stigma around the disease may prevent many people from telling everyone around them thus many people may not realize that they had been in contact with a COVID-19 patient.

Second, the societies in the EMR region are among the most social in the world, and being friendly to strangers is the social norm. In Iraq, for example, religious mass gatherings where strangers often

socialize without observing social distancing is a frequent occurrence. There is a decent possibility that some of the patients in this study might, unknowingly, had come in contact with pre-symptomatic or mild COVID-19 cases during one of these events.

Similar to our study, a meta-analysis by The American Journal of Emergency Medicine [62] found that healthcare workers (HCWs) were less likely to have a severe or critical disease or die of COVID-19. The proposed explanation by the authors seems to hold for our study as well: that HCWs tend to come from a younger age demographic and have fewer comorbidities [62,63]. Further analysis of the characteristics of HCWs in our study revealed that only 4.8% of them were aged 60 years or older, while the majority 60.5% (89/147) were aged less than 40, and 34.7% (51/147) aged between 40 and 59 years. Also, only 4.1% (6/147) had comorbidities.

What This Study Adds

Almost a year has passed since the COVID-19 pandemic started and still the best intervention we have to fight it is nonpharmaceutical measures. There is no definite treatment to date and although good news on effective vaccines is emerging, it might take a few years until enough number of the population could access a vaccine. That is why, in the hospital setting, it is still imperative to identify which patients are at higher risk of developing severe disease or dying of COVID-19. Although many studies reported on this from around the world, to our best knowledge, this is the first large multicenter study coming out of the EMR region.

Limitations

This study has its limitations. First, the study was conducted in a hospital setting which limits our ability to generalize our findings to the general population. Second, given that in many hospitals in the selected countries hospital admissions were reserved for the most severe cases, our study might be biased toward more severe outcomes. Finally, some variables might be underreported due to the inability of the HCWs in the overwhelmed facilities to collect all data for all patients.

Conclusions

This study reports on risk factors of COVID-19 severity and mortality in the seven countries. In a hospital setting, healthcare providers should be more attentive to older patients, men, smokers, and patients with certain comorbidities (DM, HT, heart diseases, COPD, malignancy, and renal diseases) as they were shown to be more likely to suffer from severe and/or fatal COVID-19 in our study.

Acknowledgment

Mohammed V University in Rabat, Morocco), Hind EZZINE (PhD student, Mohammed V University in Rabat, Morocco), Alaa Eid, MD (Ministry of Health and Population, Cairo, Egypt), Ehab kamal, MD(Ministry of Health and Population, Cairo, Egypt), Mohamed Hassany, MD(Ministry of Health and Population, Cairo, Egypt), Hanaa Abu El Sood, MPH(Ministry of Health and Population, Cairo, Egypt), Dr. Anwar Ahmed (ER consultant, Minstry of Health ,Sudan)

Abbreviations List

Abbreviation	Definition
EMR	Eastern Mediterranean Region
HT	Hypertension
SARS-CoV-2	Severe Acute Respiratory Syndrome Corona Virus2
WHO	The World Health Organization
IHME	The Institute for Health Metrics and Evaluation
CFR	case-fatality rate
DM	diabetes mellitus
CVD	cardiovascular diseases
COPD	chronic obstructive pulmonary disease
FETP	Field Epidemiology Training Program
BBH	Benazir Bhutto Hospital
PIMS	Pakistan Institute of Medical Sciences
HCW	healthcare worker
ICU	Intensive Care Unit
PCR	Polymerase Chain Reaction
OR	Odds ratio
ACE2	Angiotensin-converting enzyme 2
RAS	renin-angiotensin system
GHD	Global Health Development

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