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ICU admission of COVID-19 patients: Identification of risk factors

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ABSTRACT

Background: The WHO has declared COVID-19 as a global pandemic with a rapidly increasing number of patients at a rate exceeding the limits of health-care resources. Some people seem to be at higher risk of worse prognosis and increased mortality. Identifying these vulnerable groups is a necessity.

Aim of study: To identify the risk factors associated with ICU admission in COVID-19 patients.

Methodology: We present a retrospective study where the clinical data of patients with laboratory-confirmed COVID-19 infection were collected from Ain-Shams University Isolation-Hospital records on admission from 10 April 2020 to 30 July 2020 to identify risk factors in patients requiring ICU admission during hospital stay.

Results: Of 323 subjects diagnosed by the RT-PCR as positive COVID-19, 62 (19.2%) of which were admitted at the ICU. The mean age of the subjects was 46.6 ± 16 years. Significant morbidities were associated with higher age groups (p value 0.000), smokers (p value 0.004), Cairo-residents (p value 0.009), being a health-care provider (p value 0.001) and hypertensive patients (p value 0.000).

Conclusions: Elderly, smokers, diabetic and hypertensive need further attention during disease course. Our results call for further investigations of risk factors for COVID-19 severity; preferably on large prospective cohorts, to increase their validity.

1. Introduction

By the end of 2019, reports of a novel respiratory disease-causing virus in Wuhan, China, had spread around the world. The WHO named this novel coronavirus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. In March 2020, the WHO declared COVID-19 as a global pandemic [2]. The virus is transmissible from human to human [3] and the number of infected people increases at an exponential rate, spreading not only in China but also all over the world. Typical symptoms of COVID-19 are fever, cough, myalgia, and fatigue, while headache, sputum production, hemoptysis and diarrhea are less common. In the course of disease, some patients develop pneumonia with characteristic findings on chest CT [3]. Severe cases are transferred to the intensive care unit (ICU) and frequently require mechanical ventilation. Mortality rate is estimated between 3.4% and 11% [4].

The rise in the number of infected subjects is expected and if not being well controlled, Covid-19 will exceed the limits of health-care resources. Some people seem to be at a higher risk of serious disease progression and increased mortality. Preexisting chronic illnesses are identified as a risk factor exerting a more drastic effect on the disease course as reported by several studies [1,4]. These subjects should be given special protection measures against infection since there is no definitive treatment up to the present moment. Moreover, the efficacy of the available vaccines is still under evaluation and their manufacturing and distribution may take a long time to reach all countries around the world. Hence, identification of vulnerable population and the risk factors for severe and fatal disease progression is a must [1]. Targeting the vulnerable subjects early through vaccination is likely to minimize future deaths and preserve the strength of the health service by preventing infections [5].

The main objective of this study is to identify the risk factors associated with ICU admission of COVID-19 patients, hence applying proper preventive measures to patients having these risk factors.

2. Methodology

Ethical approval for the current study protocol was obtained from Ain Shams University Faculty of

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Medicine Research Ethics Committee (REC) FWA 00017585.

2.1. Patients and setting

This is a retrospective study where the clinical data of patients with laboratory-confirmed COVID-19 infection were collected from El-Obour Hospital records. This hospital belongs to Ain Shams University Hospitals and was adopted for isolation of COVID-19 patients.

Patients were considered to have a definite diagnosis of COVID-19 if they were laboratory-confirmed using reverse transcription polymerase chain reaction (RT-PCR). From 20 April 2020 to 30 July 2020, 338 patients were admitted at Ain Shams University Hospitals, of them 323 patients had COVID-19 RT-PCR positives.

The following intrinsic risk factors for ICU admission were collected: age, gender, hypertension, diabetes mellitus, chronic liver disease, and chronic kidney disease (CKD). Extrinsic risk factors for ICU admission included smoking, being a health-care worker, residence zone as Cairo or another governorate. Risk factors were considered only if they occurred prior to the onset of the symptoms of COVID-19. Finally, we investigated the administration of specific and non-specific treatment and the fate of all patients.

2.2. Statistical analysis

Initial comparisons between COVID-19 patients with ICU admission and those without the need for ICU admission were done using the student's t-test for continuous variables and Pearson's Chi-square test for categorical variables. The adjusted risk factors for ICU admission were obtained using the logistic regression analysis. The dependent variable was the presence and absence of IVU admission in all the patients. All variables described previously were considered as possible candidates for the final model. The initial multivariable model construction consisted in the preliminary selection of variables using a manual purposeful selection method and a relatively large significance level (alpha approximately 0.25). Subsequently, the resulting model was reduced using a likelihood ratio test with a significance level of 0.05. All statistical analyses were performed using the Statistical Package for Social Science (SPSS) version 20.0.

3. Results

A total of 323 subjects were diagnosed by the RT-PCR as positive COVID-19, 62 (19.2%) of which were admitted at the ICU of El-Obour Hospital. The mean age of the subjects was 46.6 + 16 years (median age was 47 years and ranged from 10 to 85 years). Only 21
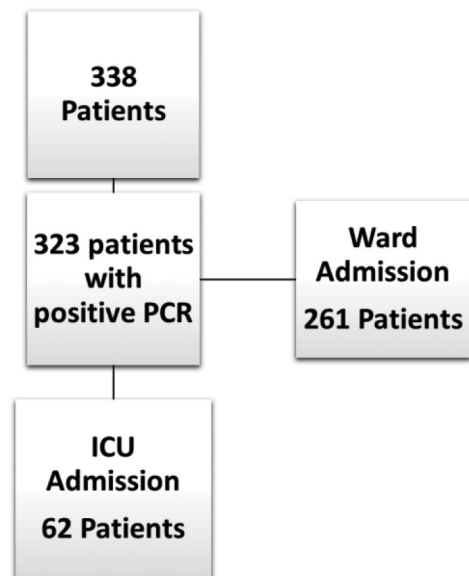

Figure 1. Flow chart of patients' recruitment.

Table 1. Presenting symptoms of COVID-19 patients.

Symptom	Number	Percentage
Asymptomatic	36	11.1
Fever	127	39.3
Sore throat	1	0.3
Cough	124	38.4
Cough and Dyspnea	18	5.6
Diarrhea	6	1,9
Melena	1	0.3
Diabetic ketoacidosis	1	0.3
Fever and cough	3	0.9
Fever and diarrhea	5	1.5
Sore throat and bone aches	1	0.3
Total	323	100

(6.5%) were smokers and 302 (93.5%) were non-smokers. Most of the patients (total number 302; 93.5%) reported contact with a confirmed case or cases of COVID-19 before diagnosis and hospital admission. Figure 1

Table 1 shows that fever was the most common presenting symptom (total number 127; 39.3%), followed by cough (total number 124; 38.4%).

Table 2 shows the univariate association between ICU admission and different postulated independent variables. At the univariate level, ICU admission was more prevalent among the following patients: higher age groups, current smokers, non-healthcare workers, living in Cairo, hypertensives, diabetics and having chronic kidney diseases.

From the risk factors significantly associated with ICU admission in the univariate analysis, the multivariable analysis identified only three: age, smoking and living in Cairo (Table 3). Diabetes mellitus was found to be a potential risk factor (p value 0.06), but it was excluded from the final model.

Table 2. Factors associated with ICU admission in the univariate analysis [a.]

COVID-19 Patients Variables	ICU admission (n = 62)	Ward admission (n = 261)	OR (95% CI) [b]	P value [3]
Age in years	57.9 ± 16	44 ± 15.3	1.06 (1.04–1.08)	0.000*
Gender (male)	36 (58.1)	135 (51.7)	1.29 (0.74–2.26)	0.369
Smoker	9 (14.5)	12 (4.6)	3.52 (1.41–8.79)	0.004*
Healthcare worker	9 (14.5)	94 (36)	0.30 (0.14–0.64)	0.001*
Residence (Cairo)	46 (74.2)	228 (87.4)	0.42 (0.21–0.82)	0.009*
Hypertension	25 (40.3)	40 (15.3)	3.73 (2.03–6.86)	0.000*
Diabetes mellitus	23 (37.1)	33 (12.6)	4.08(2.17–7.66)	0.000*
Chronic liver disease	0 (0)	2 (0.8)	–	0.652
Negative	53 (85.5)	247 (94.6)	3.0 (1.23–7.28)	0.029
Chronic kidney diseases Positive	7 (11.3)	9 (3.4)		
On Dialysis	2 (3.2)	5 (1.9)		

[a]Quantitative data are expressed as mean ± SD; Number in parentheses adjacent to the actual number indicates percentage of cases.
[b]Student's t-test for continuous variables and Pearson's Chi-square test for categorical variables.

Table 3. Factors associated with ICU admission in the multivariable analysis.

Risk Factor	Odds Ratio	95% confidence interval	P value
Age	1.06	1.04–1.08	0.000*
Smoking	3.33	1.24–8.90	0.017*
Living in Cairo	0.239	0.11–0.53	0.000*

4. Discussion

COVID-19 has rapidly affected mortality worldwide [4]. There is an urge to understand who is mostly at risk of severe outcome, prolonged disease course and ICU admission. Early detection of those patients is crucial to regulate treatment plans and accurately identify the severity of patients' condition. Owing to the rapid increase in the spread of disease and the rise in the mortality rates, countries all over the world have started vaccination strategies to protect their citizens. Identification of the high-risk group subjects is a corner stone in prioritizing patients for vaccination. Our study included 323 patients. The mean age of the participants (total number 323) was 46.6 (SD 16.3) years and ranged between 10 and 85 years. Of the 323 COVID-19 patients, 171 (52.9%) were males and 152 (47.1%) were females. Only 21 (6.5%) were smokers and 302 (93.5%) were non-smokers. Only 62 (19.19%) patients required ICU admission.

These results are in alliance with **Qun Li and collaborators** results. They conducted a study to analyze the epidemiological data of the first 425 confirmed COVID-19 patients in Wuhan. Their results revealed that the male sex was the predominant sex among cases [6].

These results could be attributed to the fact that sex hormones play an important role in various immunoinflammatory responses. Estrogen hormone stimulates both innate and adaptive immune responses, producing a vigorous cellular and humoral immune response. This results in swifter clearance of pathogens and higher resistance to infection among females. Moreover, estrogen hormone reduces the expression of SARS-CoV-2 functional receptor, angiotensin-converting enzyme 2 [7]; hence, this hinders the virus ability to enter target cells. On the other hand, testosterone has a deleterious effect on the immune system. The decrease in testosterone level with aging is coupled with an increase in the inflammatory cytokines, antibody levels, natural killer cells counts, CD4/CD8 ratios, and a reduction in regulatory T cells level [8–10].

Immune response is divided into innate and adaptive immune response. Aging is characterized by failure of sufficient progression to adequate adaptive immune response which results in hyperfunctioning of innate immunity. This explains the occurrence of hyperinflammation, cytokine storm and coagulation leading to multiorgan failure during COVID-19. Moreover, aging is also always associated with chronic illnesses, such as diabetes and cardiovascular or lung disease resulting in a state of sustained activation of the innate immunity, making these subjects not only at a higher risk of developing severe illness but also at an increased risk of death once infected [11]. In this study, the higher age group was a highly significant variable (P 0.000), OR 1.06 (CI 1.04–1.08) . The mean age of the ICU patients was (57.9 ± 16y) compared to (44 ± 15.3y) in non-ICU population. Similarly, higher age group was identified as a risk factor by **Turcotte and collaborators** (70.2 vs. 62.6 y, p value .009) [12]. In addition, **Noor and Islam** noticed that old age was associated with higher morbidity and mortality (>65 years vs. <65 years) [RR 3.59, 95% CI (1.87–6.90), p < 0.001] [13].

Tobacco smoking has been identified as a significant risk factor for infections of the respiratory system via alteration of the structural and immunologic host defenses. Smokers have five times incidence of getting influenza infection and twice as likely to have pneumonia. Smoking is also likely to increase the risk of infection because of the repeated hand-to-mouth movements that smoking involves. It may therefore be an important factor in worsening the impact of SARS-CoV-2 [14].

In the current research, 9 patients out of 21 patients (42.86%) with smoking history required ICU admission during their hospital stay [OR 3.52 (CI 1.41–8.79), P 0.004]. **Liu and collaborators'** study suggested

that severe cases had a significantly higher number of patients with a smoking history than stable cases (27.3% *vs.* 3.0%, *P* = 0.018) [15].

Hopkinson and collaborators used UK users of the Zoe COVID-19 Symptom Study app (a not-for-profit initiative that was launched at the end of March 2020 to support vital COVID-19 research. The app was launched by health science company ZOE with scientific analysis provided by King's College London) which collected baseline data between 24 March 2020 and 23 April 2020 including smoking status,14 potential COVID-19 symptoms and history of hospital attendance. They reported that current smokers were more likely to report symptoms suggestive of COVID-19 [16].

Moreover, a metanalysis performed by Reddy RK and his co-workers concluded that any state of smoking either current or former state is associated with severe COVID-19 and worse in-hospital outcomes [17].

OpenSAFELY is a secure analytics platform for electronic health records in the National Health Service (NHS) in England, which is created to deliver urgent results during the global COVID-19 emergency. It is successfully delivering analyses across more than 58 million patients' full primary care NHS records. According to **open safely collaboratives**, both current and former smoking were associated with higher risk of severe disease course adjusted in models for age and sex only, but in the fully adjusted model there was weak evidence of a slightly lower risk of severe COVID-19 in current smokers (fully adjusted HRs 0.88, CI 0.79–0.99) [18]. These conflicting data suggest that although smoking is an identifiable risk factor for more severe disease course in hospitalized patients with COVID-19, the percentage of smokers in hospitalized COVID-19 patients are lower expected from the overall population smoking prevalence.

Chronic illness such diabetes and hypertension are identifiable risk factors for morbidity and mortality via facilitation of viral entry and impairment of the immune response. This occurs either as a direct consequence of the disease or because of its medication. In our study HTN and diabetes are significantly associated with more disease progression and worse outcomes [OR 3.73 (CI 2.03–6.86) P 0.000, OR 4.08 (CI 2.17–7.66) P 0.000], respectively. Similarly, Wang and collaborators observed that 22.2% of patients requiring ICU care had diabetes, compared to 5.9% of non-ICU patients (p = .009) [19].

In a retrospective observational study on COVID-19 patients admitted to Huo Shen Shan Hospital, a COVID-19 isolation hospital in Wuhan China, hypertensive patients had a two-fold increase in the relative risk of mortality compared to non-hypertensive patients [4.0% vs. 1.1%, 95% confidence interval (CI) 1.17–3.82, P = 0.013] [20].

Health workers (HCW) are defined as "all people involved in actions aiming is to enhance health". This includes doctors, nurses, midwives, paramedical staff, hospital administrators and support staff and community workers [21]. Health-care workers (HCWs) can be exposed to SARS-CoV-2, both inside and outside the workplace, thus increasing their risk for infection. During the first wave of this pandemic, HCW in low-income and middle-income countries struggled with shortage of PPE, increased workload, long working hours, inadequate training, and infection control polices, severe mental and psychological stress and fears of transmitting the disease to their families [22].

In the ongoing study, 103 HCWs were admitted to our hospital, 9 of them (9.57%) were admitted to ICU unit [OR 0.30 (CI 0.14–0.64) p value 0.001].

Kambhampati and collaborators reported that a substantial proportion of HCWs with COVID-19 had indicators of severe disease: 27.5% of HCWs were admitted to an ICU for a median of 6 days, and 15.8% required invasive mechanical ventilation [23]. This can be related to high viral load exposure and severe physical fatigue and exhaustion.

Surprisingly, anaesthetists and intensivists, who are expected to be at high risk of SARS-CoV-2 infection because they perform high-risk procedures which are more likely to spread bioaerosols, and because they treat the sickest patients, do not have higher rates of acquiring COVID-19 infection compared to non-ICU members [24]. Shah et al. reviewed health-care data in >150,000 Scottish health-care workers and hospital admissions with COVID-19 between March and June. Data revealed a two- to four-fold increased risk of infection for health-care workers in patient-facing, but not in non-patient-facing roles and the wider population [25]. Shields et al. reported that housekeeping staff and those working in acute (33%) or general medicine (30%) had more than double the risk of infection compared with those working in ICU (15%): working in ICU was associated with an odds ratio of 0.28 [2627]. This data can explain why ICUs are fully supplied with PPE and ICU staff strictly follow infection control protocols and are more experienced in handling PPE. However, this point was not studied in the present research.

Cities are the residence to majority of the world's population and are centers of socioeconomic growth and activities. However, overcrowded cities make humans vulnerable to various stressors, such as natural and man-made disasters. The recent pandemic has brought the urban vulnerability to pandemics to light. Cairo is the capital of Egypt and Cairo is by far the largest city in Egypt. A population of over 9 million spread over 3 085 km^2 and additional 9.5 million inhabitants living in close proximity to the city of Cairo, like many other megacities, suffer from high levels of pollution and traffic [5]. In our study, using multivariate analysis revealed that living in Cairo was associated

with a significantly increased risk in acquiring COVID-19 infection, hospital and ICU admissions [OR 0.239, CI 0.11–0.53, p value 0.000].

Limitations of the current study include being a retrospective study, thus we could not divide the HCW into subgroups, professions or subspecialties, as it was not documented in the medical files. Besides, the patients' medication of their chronic illnesses, DM and/or HTN, prior to hospital admission was not recorded so the current study results could not assess whether the increased risk of mortality and morbidity among those patients was due to the disease itself or due to its medication. Moreover, it is a single-center study. Data need to be compared with other centers for better validation of the data. In addition, Obour hospital is an isolation hospital located in east Cairo so it serves mainly Cairo residents. This magnifies the fact that urban areas were associated with higher rates of infection in our results.

5. Conclusion

Identification of patients at higher risk for complication and mortality is crucial during COVID-19 pandemic. Elderly, smokers, diabetic and hypertensive need further attention during disease course. HCWs should adhere strictly to infection control guidance at all the time in health-care facilities to reduce transmission of SARS-CoV-2. This includes proper use of recommended personal protective equipment, hand hygiene, and physical spacing. High-risk groups and HCW must have priority to receive COVID-19 vaccinations Our results call for further investigation of risk factors for COVID-19 severity; future studies should preferably be performed on large prospective cohorts, to increase their validity.

Disclosure statement

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Authors' contributions

MF, SF and MM designed the study. ST, SF, MM, AH and SR shared in the sample collection. AO performed the analysis and grading of the CT images. MF did the statistical analysis. SF and MF wrote the draft. RS performed a critical review of the manuscript. All authors reviewed and approved the final version. All authors read and approved the final manuscript.

Availability of data and materials

All the data needed to support the current findings could be found in a supporting sheet.

Consent for publication

Not applicable.

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