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Research Article

COVID-19 infection in an intensive care unit in Tunisia: Risk factors of mortality

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Abstract

Introduction: Identification of COVID-19 patients at high risk of mortality is crucial to improve patient management. Our study aimed to identify mortality risk factors at the COVID-19 Intensive Care Unit (ICU), in Mahdia.

Methods: We conducted a prospective study including patients admitted to the COVID-19 ICU at University Hospital Tahar Sfar Mahdia (September 2020 to February 2021). We used "The RAPID CORE CASE REPORT FORM" developed by the World Health Organization.

Results: A total of 119 patients were included (60.5% male). The average age was 61.9 ± 12 years. During their stay, 51.8% of them had invasive ventilation, 31.3 % required vasopressors intake and 50.9% required a prone position.

The mortality rate was 47.1%. Severe acute respiratory distress syndrome and Health Care Associated Infections (HAI) were associated with a higher risk of mortality (64.9% vs 17.8%; $p < 0.001$ and 81.1% vs 18.2 %; $p < 0.001$ respectively). Mortality was higher among intubated patients (79.7% vs 14.5%; $p < 0.001$). The mean Acute Physiology and Chronic Health Evaluation II (APACHII) score were higher in deaths than in survivors ((15.02 ± 7.6 vs 10.63 ± 5.31; $p = 0.02$). Low oxygen saturation on admission was associated with a higher risk of mortality (91.1% ± 6.44 vs 86% ± 11.25; $p = 0.004$).

Binary logistic regression showed increased odds of mortality with health-acquired infection (OR, 7.96 [95% CI, 2.28 - 27.7], severe acute respiratory distress syndrome (OR, 4.04 [95% CI, 1.11 - 14.73]) and invasive ventilation (OR, 12.23 [95% CI, 3.31 – 45.2]).

Conclusion: Interventions preventing the risk factors are needed to improve the prognosis of Covid-19 patients.

Introduction

Mortality related to COVID-19 reflects the full burden of the pandemic [1]. Currently, a total of 623,893,894 cases have been reported worldwide, among them 6,553,936 death cases [2]. The actual numbers are believed to be even higher due to testing shortages [3]. Besides, the number of infected people and mortality rate is higher, especially due to the emergence of new variants of the virus [4]. As these variants may be associated with higher rates of transmission [5], they may cause more severe disease and higher rates of death or they may reduce the effectiveness of current vaccines [6].

Mortality surveillance during the current pandemic is essential to formulate an evidence-based response [7]. However, perceivable global data analyses for COVID-19 mortality risk factors are lacking [8]. In fact, COVID-19 causes clinical, biological and radiological symptoms ranging from mild or asymptomatic to severe [9,10]. Patients with severe symptoms needed admission to intensive care units [11].

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Approximately 15% - 20% of COVID-19 patients will develop severe pneumonia and about 10% of these will die if not properly managed [12].

In fact, older age (≥65 vs <65 years old) and gender (male vs female) were found to be mortality risk factors for COVID-19 [13]. In addition, hypertension, cardiovascular diseases (CVDs), diabetes, chronic obstructive pulmonary disease (COPD) and cancer were also associated with a higher risk of mortality [13].

In Tunisia, the Ministry of Health confirmed the country's first case of coronavirus (COVID-19) using Polymerase Chain Reaction (PCR) on Monday, March, 2nd 2020 [14]. During the next two months, out of 173 patients (17.8%) were admitted to the hospital, among them 47 were admitted to intensive care units [15]. A total of 634 (61.6%) patients have recovered and 45 (4.4%) patients died between February 2020 to February 2021, [14]. Tunisian analyses of the prognostic factors of the disease in patients with COVID-19 showed that older age, imported cases and being symptomatic were associated with a longer duration of illness [16].

Given these data, timely identification of COVID-19 patients at high risk of mortality is crucial to improve patient management and resource allocation in hospitals. Indeed, prophylactic management will not only save lives but also mitigate the otherwise overwhelming healthcare burden [17].

The aim of this study was to identify mortality risk factors at the COVID-19 Intensive Care Unit (ICU) in the region of Mahdia (Tunisia).

Methods

Study design and participants

We conducted a prospective study among all COVID-19 patients admitted to the Intensive Care Unit (ICU) of the University Hospital Tahar Sfar Mahdia from September 2020 to February 2021. Patients included in this cohort were diagnosed with COVID-19 infection based on a PCR-positive test from a naso or oropharyngeal swab or had a chest computed tomography scan compatible with the diagnosis of COVID-19 pneumonia.

Measurement tool and data collection

We used "The RAPID CORE CASE REPORT FORM" (CRF) developed by the WHO [18]. This global COVID-19 anonymized clinical data platform enables State Parties to the International Health Regulations (IHR) (2005) to share with WHO anonymized clinical data related to patients with suspected or confirmed infections with SARS-CoV-2.

This observation booklet was designed to collect data from the clinical examination, the interview with the patient and the patient's medical record at the hospital. It has three modules:

Module1: To be completed on the first day of admission to the health structure.

Module 2: To be completed daily during the hospital stay as many days as the resources allow it.

Module 3: To be completed at the time of final discharge from the health structure or death of the patient.

In fact, for each patient, we collected the clinical inclusion criteria, demographic data, date of onset of symptoms, vital signs on admission, comorbidities, pre-admission and long-term treatments, signs and symptoms on admission, treatment received during the first 24 hours after the admission, treatment received in intensive care units during the first 24 hours and biological analyzes. During the daily monitoring, we collected the vital signs, clinical assessment, biological analyzes and treatment received during that day. At the time of discharge or the death of the patient, we collected the results and dates of the diagnostic tests (scenography or pathogen detection tests), clinical or biological complications and the treatment received during the last 24 hours. For each patient, we calculated the Acute Physiology and Chronic Health Evaluation II (APACHE II). In fact, APACHE II is a severity-of-disease classification system. It is applied within 24 hours of admission of a patient to (the ICU): an integer score from 0 to 71 is computed based on several measurements; higher scores correspond to more severe disease and a higher risk of death [19].

Statistical analyses

Data entry and analysis were conducted using SPSS; Version 23.0. Qualitative variables were represented by effectiveness and percentages. Quantitative variables were represented by means and standard deviations (SD). Chi-square and Student Tests were used to compare percentages and means, respectively.

A binary logistic regression analysis was used to estimate the crude likelihood of mortality related to COVID-19 infection. A p - value less than .05 was considered statistically significant.

Ethical considerations

To ensure anonymity and confidentiality, no names or other identifiers were used.

Results

General characteristics of the study sample

From September 2020 to February 2021, 119 patients were enrolled (60.5% male) with an average age of 61.9 ± 11.9, among them, 75.6% had at least one medical history.

Table 1 shows the medical history of COVID-19 patients admitted to ICU during the survey. As indicated in Table 2, the most common symptom on admission was shortness of breath (83%). Oxygen saturation during the 24H of admission ranged from 54% to 100%. Patients who had a chest scan on admission (n = 37), presented pulmonary damage ranging from 15% to 95%. About 80.7% of patients had a corticosteroid intake, 66.4% were under antibiotics and 91.6% needed oxygen.

During their stay, 51.8% of patients had invasive ventilation, 31.3% required vasopressors intake and 50.9% required a prone position. The mean stay duration was 17.8 days ± 13.13 (ranging from 2 to 66 days) (Table 2).

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Table 1: Medical History of COVID-19 patients included in the study sample (n = 119).

Medical condition	Effective	Percentage (%)
Co-morbidities ≥ 2	90	75.6
Cardiovascular diseases	69	39.88
Chronic renal pathology	4	2.31
Chronic pulmonary disease	10	5.78
Chronic neural pathology	11	6.35
Diabetes	50	28.90
Obesity	12	6.93
Active cancer	2	1.11
Dyslipidemia	15	8.67

Table 2: Clinical and biological characteristics during the first 24H of admission.

Feature	Total (n = 119)
Shortness of breath	93 (83%)
Cough	83 (71.6%)
Fever	80 (68.4%)
Oxygen saturation (median [IQR])	88.6 ± 9.4
Oxygen saturation < 90%	41 (34.4%)
Respiratory rate > 24 per min	85 (71.4%)
Heart rate >120 beats per min	4 (3.3%)
Systolic blood pressure < 100mmHg	1 (0.8%)
Diastolic blood pressure < 60mmHg	3 (2.5%)
Temperature ≥ 39 °C	27 (22.6%)
Pulmonary damage on chest scan	60.4 ± 19.2%
Corticosteroid intake	96 (80.7%)
Antibiotic intake	79 (66.4%)
White Blood cells (median [IQR])	17142.8 ± 2530
< 4.0 × 10^3/µL	6 (5.04%)
> 12.0 × 10^3/µL	51 (42.85%)
C-reactive protein (mg/L) (median [IQR])	149.9 ± 102
> 150 mg/L	46 (38.6%)
Alanine aminotransferase (U/L) (median [IQR])	48.5 ± 39.98
> 40 U/L	23 (19.3%)
Aspartate aminotransferase (U/L) (median [IQR])	47.5 ± 35.63
> 40 U/L	24 (20.1%)
Creatinine (median [IQR])	92.7 ± 85.66
Urea (median [IQR])	8.9 ± 6.76
Lactatemia	2.2 ± 0.86

Factors associated with mortality among COVID-19 patients admitted to the ICU

The overall mortality rate was 47.1%. Table 3 summarizes the results from univariate analyses. In fact, severe acute respiratory distress syndrome and health-acquired infection (HAI) were associated with a higher risk of mortality (64.9% vs 17.8%; $p < 0.001$ and 81.1% vs 18.2 %; $p < 0.001$ respectively).

Mortality was also higher among patients who were obese (50.5% vs 16.7%, $p < 0.01$) and those having low oxygen saturation on admission (91.1% ± 6.4 vs 86% ± 11.2; $p = 0.004$) or had have invasive ventilation (79.7% vs 14.5%; $p < 0.001$). The Acute Physiology and Chronic Health Evaluation II (APACHII) mean score was significantly higher in deaths (15.02 ± 7.6) than in survivors (10.63 ± 5.31) (Table 3).

Multivariable logistic regression analysis showed increasing odds of mortality with severe acute respiratory distress syndrome (ORa = 4.04 [95% CI, 1.11-14.73]), HAI (ORa, 7.96 [95% CI, 2.28-27.7]) and invasive ventilation (ORa, 12.23 [95% CI, 3.31–45.2]) (Table 4).

Table 3: Mortality among COVID-19 patients admitted in the intensive care unit: Results from univariate analyses (n = 119).

Factors	Survivors (n = 63)	Non Survivors (n = 56)	*p - value*
Hypertension	25 (39.7%)	23 (41.1%)	*0.8*
Diabetes	27 (42.9%)	23 (41.8%)	*0.9*
Dyslipidemia	8 (12%)	7 (12.5%)	*0.9*
Respiratory rate	26.9 ± 4.2	28.5 ± 5.4	*0.1*
Age	60.5 ± 11.7	63.5 ± 12.07	*0.1*
Gender			*0.6*
Male	37 (58.7%)	35 (62.5%)	
Female	26 (41.3%)	21 (37.5%)	
Urea level	7.8 ± 6.3	9.9 ± 7.02	*0.1*
Hospital acquired infection	10 (18.2%)	43 (81.1%)	*<0.01*
Severe acute respiratory distress syndrome	26 (41.3%)	48 (85.7%)	*<0.01*
Invasive ventilation	12 (20.3%)	47 (85.5%)	*<0.01*
APACHII	10.6 ± 5.3	15.02 ± 7.6	*<0.01*
Oxygen saturation during the first 24h	91.1 ± 6.4	86 ± 11.2	*<0.01*
Obesity	10 (15.9%)	2 (3.6%)	*<0.01*

Table 4: Mortality risk factors associated with COVID-19 infection: Results from the binary logistic regression.

Associated factors	*p - value*	ORa*	CI 95%
Severe acute respiratory distress syndrome	*0.001*	4.04	1.11 - 14.73
Hospital acquired infection	*0.001*	7.96	2.28 - 27.70
Invasive ventilation	*0.001*	12.23	3.31 - 45.20

*ORa: Adjusted Odds Ratio.

Discussion

The present study used data obtained early in the course of COVID-19 infection in order to identify mortality risk factors among patients hospitalized in the intensive care unit of the region of Mahdia in Tunisia. After multivariate logistic regression analyses, we found that factors related to COVID-19 mortality were healthcare-associated infection, severe acute respiratory distress syndrome and invasive ventilation.

The overall mortality rate was 47.1% among patients hospitalized in our ICU. This rate is falling within the range described in previous reports such as a study carried out in Mexico City (49.2%) [20]. However, it is important to note that several factors such as infections, and underlying comorbidities could interfere with the mortality rate related to COVID-19. Therefore, patients with COVID-19 infection presented a heterogeneity in clinical presentation and disease courses [21].

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As a result, factors associated with mortality are not always readily apparent which hardens the management and care of these patients [21]. In addition, several studies have defined a prediction model and risk scores mortality in COVID-19 [3,21].

In our study, the majority of patients admitted to ICU were males (60.5%) with a lower risk of mortality compared to women (37.5% vs 62.5%). Our results are not in line with those found in Iran and China. Indeed, the male sex presented a higher percentage of hospitalized patients in COVID-19 units in Iran (56%) [20,22]. Added to that, it increased the odds of COVID-19 mortality in China (OR = 1.97, 95% CI = 1.29, 2.99) [23]. This disparity in sex ratio may be multifactorial. The difference in immune system function between males and females could be an important determinant [24,25]. Other differences including steroid hormones and sex organs could also play a crucial role in pathogenesis. However, there is no sufficient clinical data to show that SARS-CoV-2 can enter the testis and regulate COVID-19 severity and mortality in males [26].

We found that HAIs were associated with a higher risk of mortality (OR, 7.96 [95% CI, 2.28 - 27.7]). In fact, the incidence of HAI was 49,1%, which had a significant impact on hospital mortality (81.1% of patients who died in the ICU had at least an HAI). Similar results were found in a study conducted at the University Hospital of Madrid (the main cause of death in 33% of cases in the ICU) [27]. It was reported that patients had long average stay (17.8 days ± 13.13), with multiple central venous catheters and they had higher inflammatory markers. All these factors contributed to an increased risk of infection from cross-contamination of organisms between patients and within an individual patient [27,28].

Invasive ventilation increased the risk of mortality related to COVID-19 by 12.23 [95% CI, 3.31 – 45.2] in our sample. Although invasive mechanical ventilation is used to save lives, 50% of patients aged 85 and above who were ventilated in the United States died [29]. Indeed, aspects of human physiology are also universal and mortality in patients placed on ventilators who are in their 80s and 90s or with severe comorbidities has always been very high [30]. This could be explained by the old age (61.9 ± 11.9) but also the comorbidities in our study sample (75.6% had at least one medical history).

We found that the APACHII mean score was significantly higher in deaths. Accordingly, it was associated with ICU mortality in Madrid (OR 1.1, CI 95% 1.01 – 1.19; $p = 0.017$) [31]. Among the ICU scores, the APACHII score could predict the death of COVID - 2019 patients with a sensitivity of 96.1% and a specificity of 86.3% [32].

In our survey, low oxygen saturation on admission was associated with a higher risk of mortality (91.1% ± 6.4 vs 86% ± 11.2; $p = 0.004$). Our findings are in line with those found in New York City [3]. In fact, decreased pulse oxygen saturation (SpO2) (93% vs 95%, $p < 0.001$) was significantly associated with ICU admission. Another study conducted in Peru suggested oxygen saturation as a predictor of mortality related to Covid-19 [33]. It was also reported that the patient's minimum oxygen saturation value was the strongest predictive feature of mortality. In line with global epidemiological observations, respiratory failure is the most common feature of critical illness and death in patients with COVID-19 [21].

Based on what was quoted above, we recommend that we start preventing some of these mortality risk factors. One of the main objectives of our study is to sensitize healthcare professionals about the importance of preventing HAI. Carrying out training about effective preventive measures in the ICU was one of our actions. In addition, developing a mortality risk score adapted to our local situation would improve patient management and resource allocation in hospitals. Especially with the emergence of the next wave and the importance of infected and seriously ill patients compared to the hospital's capacities in our country.

The present study has some limitations. First, the number of observed patients was to some extent small which limits the statistical power of this explorative survey. However, our study was exhaustive including all patients admitted to the ICU of the University Hospital of the region of Mahdia. Second, the study population was from one city. This may limit the generalizability of our results to a wider population. Besides, it makes mortality rates hard to compare, since criteria for hospitalization in ICU may vary among cities. Further studies in other hospitals are required to identify independent predictors of mortality for patients with COVID-19 in Tunisia.

Conclusion

Nosocomial infection, severe acute respiratory distress syndrome, and invasive ventilation were associated with a higher risk of mortality among COVID-19 patients. On one hand, these predictors could help clinicians identify patients with a poor prognosis at an early stage to reduce mortality related to COVID-19 and streamline the use of limited medical resources. On the other hand, interventions are urgently needed to prevent these factors in order to improve the prognosis of Covid-19 patients.

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