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ORIGINAL RESEARCH

High Mortality Rate in Adult COVID-19 Inpatients in Eastern Sudan: A Retrospective Study

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Aim: The current pandemic of coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory coronavirus syndrome 2 (SARS-CoV-2). It is a global public health concern that has resulted in the rapid growth in the number of infected patients with significant mortality rates. Hence, we conducted a retrospective study in Gadarif Hospital to evaluate the presenting manifestations, mortality rate, and the risk factors associated with mortality in hospitalized patients.

Methods: A retrospective study was conducted at Gadarif Hospital in Eastern Sudan. Medical files of the patients admitted during the period between April and July 2020 were reviewed. All the files of the adult patients (aged 18 or above), of both sexes, who had a confirmed COVID-19-positive status via laboratory testing using PCR and who were admitted during this period were reviewed. The data extracted included patients' demographics and initial clinical presentation, symptoms, signs, and the laboratory and radiographic findings. The data were analyzed using SPSS v22.

Results: Eighty-eight patients were admitted with COVID-19. The median (interquartile) age was 62 (55.00–70.00) years old, and 72 (81.8%) of them were males. Most patients (75%) experienced a one-week duration of symptoms. A fever (87.5%), cough (80.68%), and shortness of breath (77.27%) were the most common presenting symptoms. Following a clinical assessment, both the systolic and diastolic blood pressure were found to be normal in most patients, at 92.05% and 89.77%, respectively. An oxygen saturation of less than 90% was seen in 71.59% of patients. The general mortality rate was 37.5% and most deaths occurred during the first 24 h of admission (21/33 [63.64%]). There was no significant difference in the death rate between females and males (5/16 [31.3%] vs 28/72 [38.9%], $P = 0.776$). There was no significant difference in the body mass index, tobacco use, or education level between the patients who died and those who survived. A logistic regression showed that being older (AOR = 1.05, 95% CI = [1.01, 1.10]) and having a lower PO_2 level (AOR = 1.11, 95% CI = [1.04, 1.16]) were associated with mortality.

Conclusion: The general mortality rate was 37.5%, and the risk factors that could predict increased mortality in hospitalized COVID-19 positive cases included old age and a lower PO_2 level.

Keywords: COVID-19, SARS-CoV-2, risk factors, Gadarif, Eastern Sudan

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Introduction

Coronavirus disease-19 (COVID-19) was initially identified in Wuhan, China in late December 2019 and it subsequently gained pandemic status across the globe.[1] African countries, including Sudan, were not exempt from the pandemic in 2020.[2] The COVID-19 infection spread rapidly in many countries to become a pandemic.[3] The reported case fatality rate was 6.23%, with a significant variation in that rate in

some Sudanese cities.[4] Fever, cough, shortness of breath, besides a history of recent contact with COVID-19-positive patients or recent travel, were the main presentations.[5]

The real-time polymerase chain reaction (RT-PCR) test is a standard diagnostic test to detect viral nucleotides via an oropharyngeal swab, nasopharyngeal swab, bronchoalveolar lavage, or tracheal aspirate.[6] Increased levels of inflammatory markers, such as a high white blood count[7] and a higher D-dimer level,[8] are used as supporting tools for diagnosing COVID-19 infections. Moreover, radiological features of the chest are very important findings that can suggest COVID-19 pneumonia[9] with a high degree of diagnostic accuracy.[10] Interestingly, ground-glass opacities were reported in 87% and 97% of common and severe type patients, respectively. Hence, a chest computed tomography has essential role in diagnosis and prognosis of COVID-19 infection.[11] A COVID-19 infection has many complications that are considered as independent risk factors for mortality.[12,13] Other factors can increase the rate of morbidity and mortality, such as a weak healthcare system and non-adherence to restrictive preventive means, including distancing or wearing protective masks.[4]

All the factors mentioned above may affect the mortality rate at the national and international levels, and the rates obtained for the United States of America at (6%)[14] and (65.4%),[15] and for Italy at 0.007% and 0.005%, vary considerably.[16] There is a scarcity of published data on the epidemiology of COVID-19 in Sudan.[4] To the best of the author's knowledge, there are no published data on the manifestations, mortality rate, and risk factors for COVID-19 mortality in Eastern Sudan. The objective of the present study is to describe the patients' epidemiology and to identify the risk factors associated with mortality for this disease in a hospital in Eastern Sudan.

Methods

Study Area

Gadarif State is situated at a mean altitude of 496-m above sea level, has a population of 1,727,401 residents, covers an area of 75,000 km^2, and lies between latitudes 14 and 16 North and longitudes 33 and 36 East. It is 400 km from the capital of Sudan on the Ethiopian border. Gadarif Hospital is a 170-bed tertiary care facility that serves as a referral center in Gadarif State.

Participant Recruitment and Study Design

A retrospective study was conducted at Gadarif Hospital in Eastern Sudan. Medical files of the patients admitted during the period between April and July 2020 were reviewed. All the files of the adult patients (aged 18 or above), of both sexes, who had a confirmed COVID-19-positive status via laboratory testing using PCR and who were admitted during this period were reviewed. Patients who had negative or equivocal PCR test results or who were suspected cases were excluded from the study. Patients were managed according to the COVID-19 case-management protocols released by the Federal Ministry of Health of the Republic of Sudan during the epidemic. The confirmed cases were classified according to severity, as follows:

1. Uncomplicated illness: Patients with an uncomplicated upper respiratory tract infection.
2. Mild pneumonia: Patients with pneumonia without symptoms of severe pneumonia.
3. Severe pneumonia: Patients with fever or suspected respiratory infection plus one of the following:

- Respiratory rate equal to or more than 30 breaths per minute.
- Severe respiratory distress.
- SPO_2 of less than 90% in room air.
- Confusion or drowsiness.
- Systolic blood pressure of less than 90 mm/Hg or diastolic blood pressure of less than 60 mm/Hg.

Acute respiratory distress syndrome (ARDS) was classified as new or worsening respiratory symptoms within 1 week of the known clinical insult.

- Chest imaging was carried out when the origin of the edema was not fully explained by cardiac failure and the oxygen was less than 90% in room air.

Management as early supportive therapy and monitoring:

- Supplementary oxygen therapy was given immediately to patients with severe acute respiratory insult (SARI) and respiratory distress, hypoxia, or shock.
- Conservative fluid management was in place for patients with SARI when there was no evidence of shock.
- An empirical antimicrobial was given to treat all likely pathogens causing SARI.

- Systemic corticosteroids were given for the treatment of viral pneumonia or ARDS outside of clinical trials unless they were indicated for another reason.
- Patients with SARI were monitored for signs of clinical deterioration, and supportive care and intervention were immediately given.

Management of hypoxemic respiratory failure and ARDS:

- Recognizing severe hypoxemic respiratory failure when a patient with respiratory distress was failing with standard oxygen therapy.
- Endotracheal intubation should be performed by a trained and experienced provider using airborne precautions.
- Implementing mechanical ventilation using lower tidal volumes (4–8 mL per kg of predicted body weight) and a lower inspiratory pressure of less than 30cmH_2O. For patients with severe ARDS, prone ventilation for more than 12 h per day is recommended.
- Computerized tomography chest scans of COVID-19 patients reveal areas of consolidation and ground-glass opacity with bilateral peripheral involvement in multiple lobes progressing to "crazy-paving" patterns and consolidation.

In the absence of a vaccine and an effective antiviral chemotherapy, we adopted a local protocol for management in patients based on World Health Organization and ministry of health recommendation. Inpatients were isolated, paracetamol was given to control fever and oxygen supply or mechanical ventilation according the status of the patient. Chloroquine, its derivative hydroxychloroquine with or without azithromycin for the treatment of COVID-19 in hospitalized patients to combat the pandemic. Later dexamethasone was added to the protocol to improve the outcome.

Data Collection

The data extracted included patients' demographics and initial clinical presentation, symptoms, signs, and the laboratory and radiographic findings.

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences software, version 22.0. Normality was checked using the Shapiro–Wilk test. Frequency tables and percentages were generated for all the major variables of interest. Categorical variables were presented as percentages in tables, while comparisons between such variables were done using the Chi-square test. The associations between the variables and mortality were estimated through binary logistic regressions. Covariates (variables) with a P value of less than 0.2 from the binary logistic regression were selected for the construction of multivariate models by considering crude associations between mortality and the covariates. A backward elimination (likelihood ratio, LR) was then performed to adjust the model for covariates. The adjusted odds ratios (AORs) and the 95% confidence intervals (CIs) were computed. A P value of less than 0.05 was considered statistically significant.

Ethics

The study received ethical approval from the Research Board at the Faculty of Medicine, University of Gadarif, Sudan. The reference number is 2020 ref13. As the data were collected retrospectively, patient consent was not required by the Research Board at the Faculty of Medicine, University of Gadarif, Sudan. Patient data were reserved confidential and used only for research purposes. This study was conducted in accordance with the Declaration of Helsinki.

Results

Eighty-eight patients were admitted with COVID 19. The median (interquartile) age was 62 (55.00–70.00) years and 72 (81.8%) of them were males.

Most of the patients (75%) had a one-week duration of their symptoms. A fever (87.5%), cough (80.68%), and shortness of breath (77.27%) were the most common presenting symptoms. Less frequent symptoms were a sore throat (19.31%), headache (26.14%), chest pain (12.5%), and 3.41% had insomnia, abdominal pain, and diarrhea (Table 1).

Following clinical assessments, both the systolic and diastolic blood pressure were found to be normal in most patients, at 92.05% and 89.77%, respectively. An oxygen saturation of less than 90% was seen in 71.59% of patients. Moreover, a higher number of patients with diabetes mellitus died compared to those who did not have diabetes. There was no difference in the rate of hypertension, bronchial asthma, and chronic kidney disease between the patients who died and those who did not die (Table 2).

The general mortality rate was 37.5%. Most of the deaths occurred during the first 24 h following admission

Table 1 The Number and (%) of Symptoms and Signs Among Patients with Covid-19 in a Hospital in Eastern Sudan

	Total 88	Discharged 55	Died 33	*P* value
Fever	77 (87.5)	47 (85.5)	30 (90.9)	0.526
Cough	71 (80.7)	43 (78.2)	28 (84.8)	0.580
Sore throat	17 (19.3)	11 (20.0)	6 (18.2)	1.00
Headache	23 (26.1)	12 (21.8)	11 (33.3)	0.317
Shortness of breath	68 (77.3)	39 (87.9)	29 (87.9)	0.073
Insomnia	3 (3.4)	3 (5.5)	00 (0.0)	0.372
Chest pain	11 (12.5)	4 (7.3)	7 (21.2)	0.059
Abdominal pain	3 (3.4)	2 (3.6)	1 (3.0)	0.879
Diarrhea	3 (3.4)	3 (5.5)	0 (0.0)	0.289
Psychiatric symptoms	1 (1.1)	0 (0.0)	1 (3.0)	0.375

Table 2 Comorbidities in Patients with Covid-19 in a Hospital in Eastern Sudan

Variables	Total 88	Discharged 55	Died 33	*P* value
Diabetes mellitus	18	6 (33.3%)	12 (66.7%)	0.004
Hypertension	22	14 (63.6%)	8 (34.4%)	0.899
Bronchial asthma	7	3 (42.9%)	4 (57.1%)	0.263
Chronic kidney disease	6	5 (83.3%)	1 (16.3%)	0.275
Cardiovascular diseases	7	3 (42.9%)	4 (57.1%)	0.263
Other chronic lung disease	5	4 (80%)	1 (20%)	0.405

(21/33 [63.64%]). There was no significant difference in the death rate between females and males (5/16 [31.3%] vs 28/72 [38.9%], $P = 0.776$).

There was no significant difference in the Body Mass Index, tobacco use, marital status, education level, employment, residency, or income between the patients who died and those who survived.

The white blood count, blood urea level, D-dimer level, and positive chest radiological findings were significantly higher in patients who died compared with those who did not (Table 3).

A D-dimer level on admission that was greater than 2.0µg/mL was detected in 8/33 (24.2%) vs 16/55 (29.1%) patients ($P = 0.621$). A logistic regression showed that being older (AOR = 1.05, 95% CI = [1.01, 1.10]) and having a lower PO_2 level (AOR = 1.11, 95% CI = [1.04, 1.16]) were associated with mortality (Table 4).

Discussion

In this study, a fever, cough, shortness of breath, headache, and sore throat were the most common symptoms of a COVID-19 infection. This is consistent with previous studies in different populations,[17,18,] These symptoms might reflect the host immune response to viral infection rather than damage to the airway.[19] In the current study, 81.8% of the patients were males. Similar findings have been reported in previous studies.[5,20] In contrast, some other studies have shown female predominance.[21,22] The low susceptibility of females to COVID-19 infection has been extrapolated to the differences in innate immunity, steroid hormones, and factors related to sex chromosomes.[23] Moreover, transmembrane serine protease 2 (TMPRSS2), which is regulated by androgen, and the angiotensin-converting enzyme 2 (*ACE2)* gene on the X-chromosome, result in higher levels of ACE2 or ACE1/ACE2 rebalancing, and they might both play a role in favoring the outcome of COVID-19 infection among females.[24] Likewise, several other genes involved in inflammation are located on the X-chromosome, including a high number of immune-related genes that regulate the innate and adaptive immune responses to infection.[24]

This study documented a general mortality rate of 37.5%, which is higher than the general case fatality rate (6.23%) that was recently reported for Sudan.[4] However, higher mortality rates were also found in North Darfur (31.7%) and Central Darfur (60%) in Sudan.[4] This extreme variation in mortality in Sudan might be related to the lack of hospitals, under-reporting the actual number of cases due to a lack of testing facilities, and could also be attributed to the partial success of the implemented

Table 3 Clinical and Biochemical Characteristics of Patients with COVID-19 in a Hospital in Eastern Sudan

	Total 88	Discharged 55	Died 33	*P* value
Age, years	62 (55–70)	60 (50–70)	65 (60–78)	0.006
Body Mass Index, kg/m^2	25.23 (23.32–27.68)	26.12 (23.45–28.37)	24.76 (23.11–27.41)	0.345
Systolic blood pressure, mm Hg	120.00 (110.00–31.50)	122.00 (120.00–140.00)	112.00 (105.00–127.50)	0.003
Diastolic blood pressure, mm Hg	76.00 (70.00–82.00)	78.00 (70.00–85.00)	70.00 (64.00–80.00)	0.036
Mean blood pressure, mm Hg	92.1 (83.0–97.1)	93.3 (86.0–100.0)	85.3 (77.6–93.3)	0.007
SPO_2 on admission	87.00 (76.25–92.00)	89.00 (86.00–93.00)	89.00 (66.00–80.00)	< 0.001
White blood cells, cells × 10 ^{9}/l	1,105 (8,525–13,000)	9,000 (7,000–12,000)	12,000 (9,250–14,800)	0.001
Neutrophils, cells × 10 ^{9}/l	8,895 (6,330–11,018)	7,200 (4,830–10,080)	9,840 (7,354–12,580)	0.028
Lymphocytes, cells × 10 ^{9}/l	1,437 (852–2,698)	1,440 (840–3,120)	1,440 (833–2,442)	0.007
Platelet count, 10 3/μL	238,000 (189,250–300,500)	250,000 (189,000–320,000)	232,000(190,500–283,500)	0.773
Hematocrit, %	39.00 (37.00–42.00)	39.00 (37.00–41.00)	39.00 (36.50–42.00)	0.917
Blood urea, mg/dL	50.50 (35.25–66.00)	40.00 (31.00–60.00)	62.00 (52.00–67.50)	< 0.001

Table 4 Multivariate Analysis for Factors Associated with Mortality Among Patients with Covid-19 in a Hospital in Eastern Sudan

Variables	Non-Adjusted			Adjusted		
	OR	95% CI	*P*	OR	95% CI	*P*
Age, years	1.03	0.98–1.09	0.128	1.05	1.01–1.10	0.045
Mean blood pressure, mm Hg	0.97	0.92–1.02	0.234	–	–	–
SPO_2 on admission	1.09	1.02–1.16	0.010	1.11	1.04–1.16	0.001
White blood cell, cells × 10 ^{9}/l	1.01	1.00–1.00	0.218	–	–	–
Blood urea, mg/dL	1.01	0.99–1.02	0.484	–	–	–
Diabetes mellitus	4.60	1.11–19.04	0.035	0.73	0.96–14.22	0.057

preventive measures by the government.[4] On the other hand, the mortality rate in our study was markedly higher than that reported in different studies across the globe: Italy (0.007%, 0.005%),[15] India (2 to 3%),[25] the United States of America (6%),[13] and France (22.8%).[26] Many explanations have been proposed for the considerable variation in the mortality rate in different parts of the world. One study pointed to a link between the mortality rate and the economic status of countries. High-income countries and the Sub-Saharan region had the highest and the lowest number of COVID-19 deaths, respectively.[27] Southeast Asia, East Asia, and the Oceania region had the least number of cases per million population when compared to high-income countries (63.86 vs 3050.60).[27] The lowest mortality rates were in southern Italy, mainly in Molise (0.007%) and Basilicata (0.005%), and this was explained by these forested areas having immune-protection attributes due to the emission of immuno-modulating bioactive volatile organic compounds and the provision of dietary sources of bioactive compounds.[15] This can also be explained by possible host genetic determinants for COVID-19 infection, which is reflected in the variation in susceptibility, transmission of the disease, and its severity globally.[28] Another factor is related to the different subtypes of SARS-CoV-2 viral strains that might affect the susceptibility, transmission, and the severity of morbidity and mortality.[29,30] It is worth mentioning that the exacerbation of the multiple disease burden has put further strain on national healthcare systems, especially in developing countries.[4,31]

In the current study, being older (AOR = 1.05) and having a lower PO_2 level (AOR = 1.11) were associated with COVID-19 mortality. Many studies have reported age as a significant risk factor for mortality. There are age-related changes in this geriatric population, such as changes in lung anatomy and muscle atrophy, which negatively affect their physiological functions, reduce their lung reserves, reduce the airway's ability to clear viruses, and impair the defense barrier function.[32] One previous study reported no significant differences in age in in-hospital mortality.[33] Low oxygen saturation at presentation was significantly associated with high mortality. This

finding aligns with a similar finding in some clinical studies, where it is considered an independent risk factor for mortality.[11,34] Severe hypoxemia was associated with considerably higher levels of inflammatory markers, such as higher white blood counts and c reactive protein levels. In addition to acute inflammation of the respiratory system, this can occur in response to a respiratory virus or a secondary bacterial infection.[35] The latter syndrome is due to systemic endothelial injury, which presents clinically as pleural effusions, edema, intra-abdominal hypertension, intravascular fluid depletion, third-space fluid loss, and hypotension.[36] Many efforts are needed in Sudan (besides implementing restrictive preventive measurements) until a vaccine against COVID-19 is available to reduce the morbidities, mortalities, and financial burden.

Conclusion

The general mortality rate was 37.5%, and the risk factors that predict increased mortality in hospitalized COVID-19 positive cases included old age and lower PO_2 levels.

Disclosure

The authors report no conflicts of interest for this work.

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