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Epidemiological and clinical presentations of hospitalized COVID-19 patients in Libya: An initial report from Africa

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1. Introduction

In late December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in Wuhan, a city in the Hubei Province of China, as the cause of severe viral pneumonia [1,2]. This viral pneumonia spread rapidly worldwide, resulting in the declaration of a pandemic by the World Health Organization in February 2020; the disease received the name novel coronavirus disease 2019 (COVID-19) [3].

Full genomic sequencing of SARS-CoV-2 indicated that this coronavirus belongs to a severe acute respiratory syndrome virus subgenus. Therefore, it was designated as SARS-CoV-2 by the Coronavirus Study Group of the International Committee on Taxonomy of Viruses [1,4]. By March 22, 2021, around 123 million cases of COVID-19 and >2.72 million deaths have been reported worldwide [5]. The presenting symptoms of COVID-19 include symptoms such as fever, dry cough, and fatigue. However, the disease can affect systems, including the gastrointestinal, respiratory, and nervous systems [6,7]. The primary cause of death in COVID-19 is acute respiratory distress syndrome (ARDS). It is estimated that >20% of patients infected with COVID-19 require hospitalization [8–10].

A 73-year-old man who returned to Libya from Saudi Arabia after a religious event was diagnosed as the first case of SARS-CoV-2 infection in Libya on March 24, 2020 [11]. By March 22, 2021, >152,000 cases and >2506 deaths have been officially reported in Libya [12,13]. This is the number of cases confirmed by the Libyan Ministry of Health. However, the fragility of the healthcare system and political disputes during the civil war in Libya may have hindered the reporting of the actual number of cases. In particular, inadequate healthcare infrastructure and an open border with neighboring countries put the country at a higher risk of spreading the disease. Therefore, it is estimated that the actual number of cases is higher than officially reported [14–17].

Until late March 2021, there was no COVID-19 vaccine available in Libya and many other countries, despite advances in vaccination in many parts of the world. The civil war and political disputes in Libya have led to delays in the vaccination process [18–20]. In addition, these issues led to an inadequate government response to control the pandemic, which increased human-to-human transmission. On February 24, 2021, the Libyan health authorities announced the discovery of the SARS-CoV-2 variant from the B.1.1.7 lineage, also known as 20I/501Y.V1, or the UK variant, which has a higher mortality rate worldwide, among 23 out of 88 samples [21,22]. Thereafter, on March 17, 2021, the Libyan Ministry of Health announced the discovery of the South African strain, known as the 20H/S01Y.V2 or B.1.351 variant among 15 out of 32 samples [23]. However, as the Libyan health authorities are unable to perform variant testing and advanced genomic analysis locally, the tests are limited with increased costs and detection time, which pose challenges for Libyan authorities in detecting and controlling the pandemic among communities.

Current knowledge about COVID-19 has been based on observation of cases from China, Italy, Spain, France, and the USA, where the majority of cases have occurred [8,24–26]. However, to the best of our knowledge, only a few case series report patients’ clinical characteristics with COVID-19 in Africa. This study aimed to determine the epidemiological, clinical, and laboratory characteristics of hospitalized COVID-19 patients in Libya. In addition, we intend to describe the outcomes of confirmed cases, as these results will educate the global community about the clinical presentation of COVID-19.

2. Materials and methods

2.1. Study design and participants

This was a retrospective, descriptive, multi-center study that included hospitalized patients with COVID-19 treated at several centers in the western part of Libya from March 24, 2020, to December 3, 2020. Public centers involved were hospitals or isolation centers that managed patients with COVID-19. Patients who spent <24 h in the hospital, patients files with >30% missing data and those with negative results or suspected cases were excluded from the final analysis. The initial diagnosis was based on the rapid advice guidelines for diagnosis and treatment [27]. In addition, data regarding the number of laboratory-confirmed cases, deaths, and the number of tests performed were obtained from the official announcements of the local health authorities. However, only patients with COVID-19 confirmed using SARS-CoV-2 real-time reverse transcriptase chain reaction (RT-PCR) were included in the study [28,29]. According to the World Health Organization guidelines, the Libyan National Center for Disease Control (NCDC) performed laboratory testing on suspected cases and their contacts, using real-time RT-PCR assays for the detection of SARS-CoV-2.

The medical records of the patients were retrieved and analyzed by the authors. Data related to demographics, initial clinical presentation, comorbidities, hospitalization, laboratory findings, recent travel history, complications, and outcomes were reviewed. Most of the patients had had no contact with people from Wuhan and did not have a recent history of travel to China or other countries. The reporting of the study follows the Strengthening the Reporting of Observational Studies in Epidemiology statement [30].

2.2. Statistical analysis

Frequency, percentage, and median with interquartile range were used to present descriptive data. Laboratory measurements were presented as categories. The chi-square (χ2) test was used to compare the categorical variables between the groups. Non-normally distributed data were compared using the Mann–Whitney U test to determine if there were differences between the two groups for continuous variables. P-values <0.05 were considered statistically significant. Statistical analyses were performed using SPSS version 25.0 (IBM SPSS Statistics; IBM Corp., Armonk, NY, USA).

3. Results

All cases were confirmed using a nasopharyngeal swab for real-time RT-PCR. Only 1207 patients who met the inclusion criteria were included in the study. The study included 811 (67.2%) men and 396 (32.8%) women. Their median (interquartile range [IQR]) age was 56 (40–64) years. None of the study participants had recently traveled or lived in Wuhan. There was no significant difference between men and women in the study characteristics except for smoking history (higher among men). Table 1 shows an overview of the study population characteristics, symptoms, underlying diseases, complications, ICU admission, and outcomes.

Diabetes mellitus (490, 40.6%), hypertension (414, 34.3%), chronic kidney disease (114, 9.4%), and lung disease (103, 8.5%), were the predominant comorbidities. The most reported symptoms were anorexia, which presented in 1008 (83.5%), followed by fatigue (983, 81.4%), myalgia (876, 72.6%), and fever or feeling feverish (823, 68.2%). Additionally, gastrointestinal symptoms such as diarrhea and/
Table 1
Characteristics of study population adults.

| Characteristics               | Total (n = 1207) | Women (n = 596) | Men (n = 611) | p-value |
|-------------------------------|------------------|-----------------|---------------|---------|
| Age, Median (IQR)            | 56               | 57 (39.6–64)    | 56 (36–94)    | 0.9     |
| Age ranges, years            | (40–64)          | (41–64)         |               |         |
| ≥60                           | 560 (46.4%)      | 219 (48.2%)     | 341 (68.2%)   | 0.371   |
| <60                           | 647 (53.6%)      | 377 (51.8%)     | 270 (31.8%)   |         |
| Symptoms:                    |                  |                 |               |         |
| Fever                        | 823 (68.2%)      | 329 (66.8%)     | 494 (80.6%)   | 0.148   |
| Fatigue                      | 908 (76.4%)      | 465 (84.1%)     | 443 (72.6%)   | 0.001   |
| Dry cough                    | (81.4%)          | 257 (80.6%)     | 200 (45.4%)   |         |
| Headache                     | 766 (64.9%)      | 339 (68.1%)     | 427 (69.7%)   |         |
| Sputum production            | (63.5%)          | 234 (62.8%)     | 100 (62.3%)   |         |
| Underlying comorbidities:    |                  |                 |               |         |
| Acute kidney injury          | 27 (2.2%)        | 11 (3.5%)       | 16 (2.6%)     | 0.621   |
| Shock                        | 170 (14.1%)      | 79 (13.7%)      | 91 (14.7%)    | 0.148   |
| Chronic kidney disease       | 114 (9.5%)       | 50 (8.4%)       | 64 (10.5%)    | 0.697   |
| Liver disease                | 108 (9.0%)       | 50 (8.4%)       | 58 (9.5%)     | 0.914   |
| Anosmia and dysgeusia        | (9.4%)           | 0 (0%)          | 9 (1.5%)      | 0.220   |
| GI symptoms                  | 117 (9.7%)       | 33 (28.1%)      | 84 (13.8%)    | 0.001   |
| Underlying morbidity:         |                  |                 |               |         |
| Diabetes mellitus            | 490 (40.6%)      | 151 (30.3%)     | 339 (55.3%)   |         |
| Hypertension                 | 414 (34.3%)      | 132 (26.8%)     | 282 (46.2%)   | 0.039   |
| Cardiovascular disease       | (34.3%)          | 95 (22.7%)      | 247 (39.8%)   |         |
| Lung disease                 | 25 (2.1%)        | 7 (1.8%)        | 18 (2.9%)     | 0.335   |
| Chronic kidney disease       | 103 (8.6%)       | 29 (7.3%)       | 74 (11.9%)    | 0.914   |
| Liver disease                | 82 (6.8%)        | 20 (6.4%)       | 62 (10.1%)    | 0.152   |
| HIV infection                | 140 (11.6%)      | 49 (3.5%)       | 91 (14.7%)    | 0.148   |
| Neurological diseases        | 87 (7.2%)        | 2 (0.5%)        | 85 (13.7%)    | 0.001   |
| History of Smoking           | 103 (8.6%)       | 29 (7.3%)       | 74 (11.9%)    | 0.914   |
| Outcome and complications    | 52 (4.3%)        | 19 (4.8%)       | 33 (5.4%)     | 0.041   |
| Shock                        | 70 (5.8%)        | 24 (6.1%)       | 46 (7.5%)     | 0.786   |
| Acute cardiac injury         | 173 (14.3%)      | 57 (14.4%)      | 116 (18.8%)   | 0.966   |
| Acute respiratory            | (14.3%)          | 11 (2.8%)       | 105 (17.3%)   | 0.261   |
| Acute kidney injury          | 44 (3.6%)        | 67 (16.9%)      | 33 (4.4%)     | 0.342   |
| Distress syndrome (ARDS)     | (4.3%)           | (10.2%)         | (3.4%)        |         |
| Acute kidney injury          | 190 (15.7%)      | 45 (11.4%)      | 145 (23.8%)   | 0.469   |
| ICI admission                | (15.7%)          | (15.2%)         | (15.2%)       |         |
| Death                        | 149 (12.3%)      | 53 (58.1%)      | 96 (15.8%)    |         |

a Significant at p < 0.001.

Gl, gastrointestinal; HIV, human immunodeficiency virus; ICI, intensive care unit.

Table 2
Clinical laboratory tests of all patients with COVID-19.

| Variable                        | All patients (1207) | Survivor (n = 1058) | Non-survivor (n = 149) | p-value |
|---------------------------------|---------------------|---------------------|------------------------|---------|
| White blood cell count, x 109/L| 63/729 (6.6%)       | 43/582 (7.4%)       | 20/147 (13.6%)         | <0.001**|
| Neutrophil count, x 109/L       | 605/729 (83%)       | 503/582 (86.4%)     | 102/147 (69.4%)        | <0.001**|
| Lymphocyte count, x 109/L       | 339/729 (48.3%)     | 223/582 (38.3%)     | 116/147 (78.9%)        | <0.001**|
| D-dimer, µg/mL                 | 119/561 (21.2%)     | 97/416 (17.7%)      | 22/415 (35.3%)         | <0.001**|
| Creatinine, µmol/L             | 263/328 (82.3%)     | 187/201 (81.2%)     | 81/127 (63.8%)         | <0.001**|
| Alanine, µmol/L                | 432/563 (76.7%)     | 375/456 (82.2%)     | 57/107 (53.3%)         | <0.001**|
| Aminotransferase, U/L          | 131/563 (75.3%)     | 81/457 (73.1%)      | 50/107 (53.3%)         | <0.001**|
| Lactate dehydrogenase, U/L     | 72/406 (21.2%)      | 48/280 (15.2%)      | 24/126 (19.8%)         | <0.001**|
| Total bilirubin, mmol/L         | 453/565 (79.8%)     | 374/457 (81.8%)     | 57/107 (84.6%)         | <0.001**|
| Aspartate aminotransferase, U/L | 352/563 (62.5%)     | 295/456 (64.7%)     | 57/107 (53.3%)         | <0.001**|
| Blood urea nitrogen, mmol/L    | 267/514 (53.3%)     | 195/380 (51.3%)     | 72/134 (51.3%)         | <0.001**|
| Creatinine, µmol/L             | 450/485 (92.8%)     | 366/389 (94.1%)     | 84/96 (87.5%)          | <0.001**|
| Hypersensitive troponin        | 202/292 (69.2%)     | 143/217 (68.3%)     | 59/121 (62.9%)         | <0.001**|
| Procalcitonin, ng/mL           | 47/348 (14.6%)      | 32/219 (16.6%)      | 15/129 (51.2%)         | <0.001**|
| a Significant at p < 0.05.     |                     |                     |                        |         |
| a Significant at p < 0.001.    |                     |                     |                        |         |
significantly lower in the deceased group. We found no significant differences between deceased and survived individuals in the blood levels of procalcitonin, lactate dehydrogenase and blood urea nitrogen.

3.1. Complications and disease severity

A total of 190 (15.7%) patients were admitted to the intensive care unit. 173 (14.3%) patients developed ARDS, while 70 (5.8%) developed circulatory shock and hypotension. Acute cardiac injury was present in 27 (2.2%) patients, and 45 (3.7%) developed arrhythmia. Acute kidney injury occurred in 44 (3.6%) patients. Of the patients admitted during the study period, 149 (12.3%) died. Extracorporeal membrane oxygenation (ECMO) devices and facilities are not available in Libya.

4. Discussion

This study reported an epidemiological overview of a cohort of 1207 laboratory-confirmed hospitalized patients with COVID-19 treated between March 24, 2020, and December 3, 2020. None of the patients lived in Wuhan or had been to Wuhan. This information may provide insight into disease transmission and the clinical course in Libya. As shown in Fig. 1, there was an increased incidence of cases during this period. In addition, the low number of screening tests concerns, given the current international situation of COVID-19. The Libyan Health Authorities are incapable of performing >5000–6000 SARS-CoV-2 tests per day, despite the ongoing increase in deaths. Inadequate contact tracing and the Libyan Ministry of Health’s inability to detect new variants due to the higher costs and time taken for detection compared with those in other countries. Detecting these variants is warranted, as several recent studies have shown that the new variants have the ability to reinfect, and therefore, may reduce the efficacy of vaccines [31,32].

Patient characteristics were not significantly different based on sex apart from smoking history (significantly higher in men). Approximately two-thirds of the study population had at least one comorbidity, such as diabetes mellitus (40.6%) or hypertension (34.3%). The comorbidity rates among Libyan patients are higher compared to those from other countries, where 10%–20% of patients had diabetes mellitus, and 15–30% had hypertension [8,28].

The latest projections from the Institute for Health Metrics and Evaluation (IHME) model on COVID-19 in Libya, which modelled the situation in Libya until March 2021, estimated that 13% of the Libyan population had been infected with COVID-19 till March 2021. Compared to that in the previous weeks, an increase in the daily death rate was observed on March 4, 2021, with an estimated effective R of 1.23, which is greater than that in 1 in 20 countries [33]. The report also outlined COVID-19 as the second leading cause of mortality after ischemic heart disease. This warrants significant government and international organizations’ significant intervention to help Libya tackle the pandemic’s catastrophic consequences. Mitigating the pandemic’s effect requires implementing many strict regulations such as the universal mandatory wearing of masks, which is estimated to prevent 470 deaths by July 1, 2021, compared to the current scenario, according to the IHME model. Other issues are the absence of a mandatory restrictions policy and the absence of vaccines till late March 2021, which have resulted in a surge of COVID-19 cases and deaths, especially after discovering new variants. This has resulted in marked stress on the available beds and inadequacy of isolation centers that admit and treat COVID-19 patients.

Data on laboratory tests were not available for all patients. However, among those whose tests were available, we observed high levels of lymphopenia, especially in non-survivor patients, which has been reported as a predictor of disease severity [34,35]. Platelet count was significantly lower in non-survivors, where about half of them had thrombocytopenia. Compared with the non-survivors, it was found that only one-third of survivors had low platelets (p-value = 0.001); this supports the idea that low platelet count was associated with COVID-19 disease severity, more extended hospital stay, low probability of survival, and subsequent long term mortality [36–40]. Another finding is D-dimer’s elevation, especially in non-survivor patients. The D-dimer levels were significantly higher than the survivor group, which is consistent with reports of previous studies that used D-dimer to predict
mortality and complications in patients with COVID-19 [8,41]. Lactate dehydrogenase was found to be highly elevated in patients with COVID-19. However, no significant differences were found between the survivors and non-survivors in our study. We also observed a higher absolute monocyte count among patients with COVID-19, with higher values in the non-survivors than in survivors, which may support the idea of the monocyte count’s potential role. This may also support the recent findings that SARS-CoV-2 induces immunoparalysis by affecting monocytes and macrophages [43]. Creatine kinase and creatine kinase MB were higher than normal among patients with COVID-19, with higher values in non-survivors than in survivors, which might explain the initial fatigue and weakness induced by COVID-19. According to a recent systemic review and meta-analysis of 14 studies [44], where elevated creatine kinase levels were associated with poor outcomes. We observed an increase in liver function tests levels, which may indicate liver damage. We observed higher values among the non-survivor group than the survivor group, which is consistent with recent studies indicating derangement of liver function tests associated with severe COVID-19 [45]. Further, the high troponin level was associated with increased mortality, consistent with the findings of recent studies that showed that higher troponin was associated with a longer hospital stay and death [46].

On March 13, 2020, the Libyan government suspended schools and implemented a series of restrictions and regulations, such as closing airports and local borders, controlling the spread of the disease, and decreasing the risk of transmission. However, the government allowed schooling in early 2021 without implementing enough protective measures and without imposing strong restrictions, which we believe is one of the causes of the surge in COVID-19 cases in Libya. Except for mandatory negative testing for departures, the absence of strict travel restrictions such as isolation of visitors/arrivals and travel limitations to specific countries could be the main reasons behind the increase in COVID-19 cases and the detection of new COVID-19 variants. Another important issue is the inability of local laboratories to detect new variants, as their testing kits are being imported from overseas in a limited amount due to financial, technical and logistic constraints in Libya. These issues make Libyan people more vulnerable to the pandemic and increase hospital beds’ stress and, consequently, the death rate. The low number of tests due to healthcare infrastructure difficulties and weak surveillance system, and the ongoing conflict could be the causes of the spread of COVID-19 in Libya [15,16,47].

Fillo et al. investigated the genomic characteristics of SARS-CoV-2 in a small sample of 10 patients in Libya. They identified nine belonging to the SS1 cluster and one to the SS4 cluster, which suggested that the source of infection might be other North African countries, sub-Saharan Africa, the Middle East or South East Asia. Thus, with regards to COVID-19, there are concerns about the status of vulnerable communities, such as immigrants from Africa, especially since Libya has a route to Europe across the Mediterranean sea. This also shows that the ongoing conflict has led to the uncontrolled spread of the COVID-19 pandemic in Libya from other countries [48]. Moreover, as immigrants are at risk of contracting and transmitting the virus, and given the local difficulties may put them at risk for severe disease. Therefore, international and regional organizations’ interventions may be necessary to protect immigrants and reduce the burden of COVID-19 on African countries [49].

Since May 2020, the local government has started a repatriation plan for Libyans in other countries. They are at a higher risk of transmitting the disease, as these countries had a large number of cases. Therefore, travelers returning from other countries pose a threat, especially under the Libyan health sector’s current fragile condition [50,51]. This massive repatriation without specific restrictions can have devastating consequences, as the local authorities are unable to provide places to quarantine those who return, as in other countries. Another issue is the absence of nationwide restrictions in Libya, which has resulted in a surge of cases and increased mortality rates. Therefore, there is an urgent need for the government to mitigate these issues by implementing restrictions, including travel restrictions; reducing social gatherings; quarantining those who come from countries with reported new variants; and implementing social distancing measures to reduce the risk of COVID-19 transmission [52,53]. However, Libya is poorly equipped to control and effectively manage the COVID-19 pandemic. Factors such as inadequate training, low levels of preparedness, reduced intensive care capacity, and lack of vital tools to combat COVID-19, including a shortage of mechanical ventilators and the lack of extracorporeal membrane oxygenation devices or facilities in Libya, may worsen the outcomes of those who become ill.

4.1. Limitations

We were unable to include all the cases. However, our study focused on the hospitalized cases in Libya. In addition, there were no data about therapeutic options, as most of the cases were managed symptomatically without specific protocol. We tried to include the officially confirmed cases in several hospitals and isolation centers in Libya and ensure to obtain the majority of the cases with complete data. As no single electronic database available that covers all quarantine and isolation centers in Libya. Another limitation is the relatively small number of patients, and the inclusion of only the Libyan western region, which may not be representative of the nationwide population. Further studies with larger sample sizes and adequate distribution of study participants are needed in the future.

5. Conclusion

Our study suggests age, comorbidities, and laboratory derangement as risk factors for mortality in patients with COVID-19. Therefore, there is a need for urgent plans and determined efforts for patients with COVID-19, especially those with older age and comorbidities. There is also a need to improve healthcare facilities and increase patients’ daily testing capabilities suspected of COVID-19. In addition, there is a need for adequate preventive and quarantine measures for Libyans who arrive from other countries, as they may pose a life-threatening challenge for the local population, especially with the discovery of new variants.

Declaration of interests

The authors declare that they have no competing interests or relationships with industry or organizations.

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Conflicts of interest

A conflicting interest exists when professional judgement concerning a primary interest (such as patient’s welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry). It may arise for the authors when they have financial interest that may influence their interpretation of their results or those of others. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patient applications/registrations, and grants or other funding.

Ethical approval

Ethical approval was obtained from the Bioethics Committee at the Biotechnology Research Center in Libya (Reference number: BEC-BTRC-13-2020). The medical records were anonymized and de-identified through sampling and review processes.
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CRediT authorship contribution statement

Muhammed Elhadi: Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Supervision. Ahmed Abdulhakim Momen: Conceptualization, Validation, Investigation, Data curation, Writing – original draft, Writing – review & editing. Ahmed Alsoufi: Software, Validation, Investigation, Data curation, Writing – review & editing. Ahmed Misherghi: Conceptualization, Investigation, Writing – original draft, Writing – review & editing. Ahmed Zaid: Conceptualization, Methodology, Writing – review & editing, Supervision. Osama Mohamed Ali Senussi Abdulhadi: Investigation, Writing – review & editing. Ahmed Elhadi: Software, Validation, Investigation, Writing – original draft, Writing – review & editing, Visualization. Hamza Bilaid Omar Elfandi: Investigation, Data curation, Writing – review & editing. Abdullahi Muhammad Salam Alshammar: Investigation, Data curation, Writing – review & editing. Ahmed Khalifa Hadreize: Investigation, Writing – review & editing. Mohamed Tawfik Abdul-Salam Elbutali: Investigation, Data curation, Writing – review & editing. Mohamed Abdulma Almahdi El Bibas: Investigation, Data curation, Writing – review & editing. Abdulhamed Amer Mohamed Benaser: Investigation, Data curation, Writing – review & editing. Mohamed Mahfud Rajab Zendah: Investigation, Data curation, Writing – review & editing. Alauldin Ali Mohammed Makhlof: Investigation, Data curation, Writing – review & editing. Mohamed Abdulahel Abdulhamed: Investigation, Data curation, Writing – review & editing. Mahmoud Mohamed BenSuleiman: Investigation, Data curation, Writing – review & editing. Aesol Amer Ann: Investigation, Data curation, Writing – review & editing. Mosab Abdelrazak A. Shaban: Investigation, Data curation, Writing – review & editing. Hazem Abdulkarem Faraj: Conceptualization, Writing – original draft, Writing – review & editing.

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