

Original article

Complications Linked to Acute COVID-19 Phase during its Second Wave Era

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ABSTRACT

Numerous global studies have documented the multi-systemic complications associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. However, there is a scarcity of research exploring SARS-CoV-2-related complications in Libya, specifically in Zawia city. Therefore, this study aimed to screen and identify complications of acute COVID-19 in 176 SARS-CoV-2 infected patients in Zawia city, Libya. As part of a past retrospective cohort study, 176 randomly selected volunteers who tested positive for SARS-CoV-2 between December 1, 2020, and February 28, 2021, in Zawia city participated in this research. Participants completed a questionnaire designed for COVID-19 patients, and the collected data were analyzed to achieve the objectives of this study. In the current study, we found that 73.9% of the COVID-19 patients were mild to moderate cases, while 26.1% were severe cases. Moreover, our recent research revealed that 90.9% of the COVID-19 patients experienced complications during the acute phase of the disease. The reported complications during this phase included psychological disorders (90%), pneumonia (35.6%), brain fog (19.4%), multi-joint pain (18.8%), hearing deficit (8.1%), acute respiratory failure (5.6%), acute cardiac injury (3.8%), thrombotic lesions (1.9%), and vision impairment (1.9%). Overall, our findings indicate that most of COVID-19 participants had mild to moderate disease, with approximately one quarter experiencing severe illness. Furthermore, the vast majority of patients had complications during the acute COVID-19 phase, with psychological disorders being the most commonly reported, followed by pneumonia. While rare, fatal complications such as acute respiratory failure, acute cardiac injury, and thrombotic lesions were observed in some participants.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is an extremely infectious disease. It was first discovered in Wuhan, China in late 2019, and spread rapidly throughout the world, resulting in a global pandemic [1-3]. SARS-CoV-2 transmission is mainly through respiratory droplets and it primarily manifests as flue like symptoms (fever, fatigue, headache, sore throat, cough, breathlessness) [4-7]. The clinical presentation varies from asymptomatic infection to a severe or life threatening one that requires admission to

intensive care unit (ICU) for assisted invasive therapy such as mechanical ventilation for those complicated by severe acute respiratory distress syndrome (ARDS) [8]. The World Health Organization (WHO) has given the term “mild COVID-19 disease to symptomatic patients without evidence of viral pneumonia or hypoxia, moderate disease to patients who have had clinical signs of pneumonia (fever, cough, dyspnea and fast breathing) but no signs of severe pneumonia (i.e. Oxygen saturation $\geq 90\%$ on room air) and severe disease to patients who have had clinical signs of pneumonia plus one of the following: Oxygen saturation $< 90\%$ on room air, respiratory rate > 30 breaths/min in adults and children > 5 years old; ≥ 60 breaths/min in children < 2 months old; ≥ 50 in children 2–11 months old; and ≥ 40 in children 1–5 years old or signs of severe respiratory distress (such as accessory muscle use, inability to complete full sentences, and, in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs)” [9].

Furthermore, various studies have shown that SARS-CoV-2 infection affects not only the respiratory system, but also all other systems in human body. It was reported that COVID-19 complications are multi-systemic including pulmonary (pneumonia, acute respiratory distress syndrome (ARDS) and acute respiratory failure.), cardiovascular (acute myocardial injury, myocarditis, cardiac arrhythmias, endothelial dysfunction, dysautonomia and thrombotic events), neurological (ischemic stroke, Seizures, hemorrhagic stroke and Hypoxic ischemic brain injury), gastrointestinal (liver injury, gastrointestinal bleeding, acute pancreatitis), renal (acute renal injury), endocrine (diabetic ketoacidosis, thyroiditis), haematological complications (deep venous thrombosis, bleeding events and disseminated intravascular coagulation), dermatological (herpes zoster) and others (Multiple organ dysfunction syndrome, Sepsis, shock) [10-13]. Pulmonary complications are the most common reported sequelae and acute respiratory failure is the primary cause of COVID-19 mortality [8,10]. The development of these complications involves several key pathogenic mechanisms. These mechanisms include direct viral toxicity resulting in tissue damage, endothelial cell damage resulting in thrombo-inflammation, dysregulation of the immune response, and disruption of the renin-angiotensin-aldosterone system (RAAS) [14].

Libya is one of African countries that hardly affected by SARS-CoV-2 pandemic since its first appearance in March 2020, and as of 7 October 2023, over 500 thousand confirmed cases of COVID-19 have been documented with more than 6 thousand mortalities across the country [15]. However, there is a paucity of conducted research studies on acute COVID-19 related complications in Libya, and to the best of our knowledge, there are no published studies screened the complications of acute phase of COVID-19 in Zawia city, which is located 46 kilometers west of the capital, Tripoli, Libya. Therefore, this study aims to investigate the severity of SARS-CoV-2 infection in 176 COVID-19 patients in Zawia city, to determine the percentage of complicated COVID-19 cases, to identify the various types of acute COVID-19 complications in them. Knowing that the guidelines established by the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), and the Royal College of General Practitioners (RCGP) have classified COVID-19 disease into 3 phases: i) Acute COVID-19 which includes the signs and symptoms of SARS-CoV-2 infection up to 4 weeks from the onset of first symptoms, ii) ongoing symptomatic COVID-19 (post-acute COVID-19) includes the signs and symptoms of COVID-19 that continue for more than 4 weeks from the onset of first symptoms and may persist up to 12 weeks, and iii) post-COVID-19 syndrome, PCS in which COVID-19 signs and symptoms continue for more than 12 weeks [16]. Hence, it is important to emphasize that the scope of our current research is primarily centered on the complications of acute COVID-19 phase i.e., the complications that arise during the first 4 weeks of the disease onset, but not beyond.

METHODS

Study design and participants

This research paper is a continuous work of the retrospective cohort study that was conducted about COVID-19 pandemic in Zawia city, Libya [17] and it involved 176 randomly chosen volunteers who had infected with SARS-CoV-2 during the period from 1st December 2020 to 28th February 2021 in Zawia city (during the 2nd wave of SARS-CoV-2 epidemic in Libya). The participants' consents were obtained prior starting of this research as it has been mentioned previously [17]. In our initial publication from this study, we reported that the mean age of the 176 COVID-19 patients was 45.06 years (SD 17.7), with 58.5% of them being female [17]. A questionnaire was prepared consisting of three parts. The first part contained demographic characteristics of participants, including age, gender, socioeconomic status and educational level. The second part was comprised of several questions that cover the full history of COVID-19 disease in the participated volunteers, including whether the individual had previous contact with a relative or friend infected with SARS-CoV-2, consistent use of protective measures prior to infection, international travel history preceding infection, methods of confirming SARS-CoV-2 infection, experienced symptoms, severity and duration of illness, complications during the acute phase of COVID-19, pre-existing health conditions, and the development of long-

term COVID-19 effects. The final section of the questionnaire focused on the therapeutic approaches employed to address this infection, encompassing pharmaceutical drugs, traditional Libyan herbal medicine, as well as combined therapy methods. The questionnaire tool was reviewed by two researchers to evaluate the relevancy, the clarity and the adequacy of all questions. The information was collected either from the patient or from his/her close relative through phone calls or social media resources.

Statistical analysis

The collected data were categorized and statistically analyzed using Excel-software, version 16 (Microsoft Corporation, USA). The analysis was performed by means of descriptive statistics. Categorical variables are presented as numbers and percentages (n, %) and normally distributed continuous variables are presented as mean (standard deviation [SD]).

RESULTS

As shown in Table (1), of the total 176 COVID-19 patients involved in the current study, 130 (73.9%) were mild to moderate COVID-19 cases and only 46 (26.1%) were severe COVID-19 patients.

Table 1. The severity of SARS-CoV-2 infection in 176 COVID-19 patients in Zawia city, Libya

The severity of COVID-19 disease	The number of COVID-19 patients	The percentage of COVID-19 patients
Mild to moderate cases (None severe)	130	73.9%
Severe cases	46	26.1%
The total	176	100%

Figure (1) and Table (2) showed that 90.9% (n=160) of the participated COVID-19 patients had complications during the acute phase of the disease (i.e., during the first 4 weeks from the disease onset) and only 9.1% (n=16) of them did not have any complications. In addition to that, it was found that the most common complications were psychological disorders (90%, n=144) and pneumonia (35.6%, n=57), and the less common complications were brain fog (19.4%, n=31), multi-joint pain (18.8%, n=30) and hearing impairment (8.1%, n=13), while the least reported complications were acute respiratory failure (5.6%, n=9), acute cardiac injury (3.8%, n=6), thrombotic lesions (1.9%, n=3) and vision impairment (1.9%, n=3).

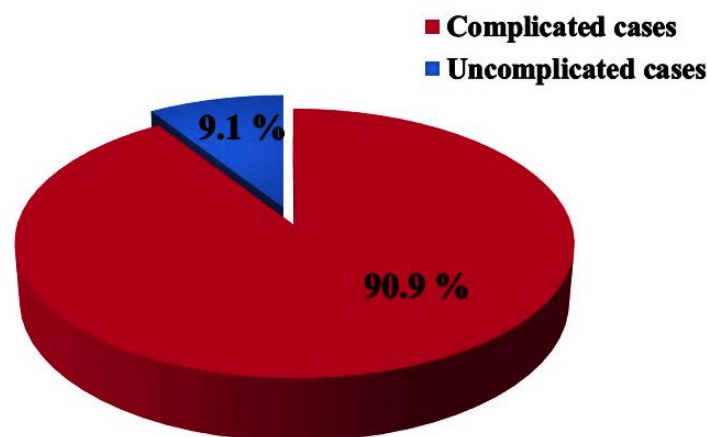


Figure 1. The percentage of complicated and uncomplicated cases among 176 COVID-19 patients during the acute phase of the disease in Zawia city, Libya. Data were expressed in percentages.

Table 2. The percentages of various complications of acute COVID-19 phase among the complicated cases.

Types of acute COVID-19 complications	The number of COVID-19 patients who experienced each complication type	The percentage of each complication type experienced by COVID-19 patients
Psychological disorders	144	90%
Pneumonia	57	35.6%
Brain fog	31	19.4%
Multi-joint pain	30	18.8%
Hearing impairment	13	8.1%
Acute respiratory failure	9	5.6%
Acute cardiac injury	6	3.8%
Thrombotic lesions	3	1.9%
Vision impairment	3	1.9%
Total number of complicated COVID-19 cases	160	-----

DISCUSSION

As it has previously been mentioned, this study is a continuous part of our published study about patients with COVID-19 and its management in Zawia city [17]. The present study showed that approximately three-quarters of the participated COVID-19 patients were mild to moderate cases and only about one-quarter of them were severely ill patients. Interestingly, our findings were consistent with the results of several studies conducted in different countries around the world. [18-20]. Wu *Z et al* reported that 19% of their COVID-19 population study were severe to critically ill cases and 81% of them were mild while Xia L and his colleagues demonstrated that approximately 85% of SARS-CoV-2 infected participants were mild to moderate cases [18-19]. Although most COVID-19 cases are mild to moderate, the fact that it is an infectious and serious disease cannot be denied, as it poses a threat to human life. Furthermore, the current research found that the vast majority of COVID-19 volunteers (90.9%) experienced complications during the acute phase of the disease, with the most common complication being psychological disorders (90%), including depression, anxiety, and insomnia. This result aligns with findings from numerous studies worldwide that have linked SARS-CoV-2 infection to an increased risk of developing psychological disorders [21-24]. A study by Wang M et al found that COVID-19 patients had a high prevalence of psychological problems, with the most common disorders being somatization symptoms (66%), depression (53.4%), anxiety (46.3%), insomnia (42%), and suicidal thoughts (23.2%) [23]. Moreover, Bo *et al* illustrated that a high percentage (96.2%) of hospitalized but clinically stable COVID-19 patients experienced significant posttraumatic stress symptoms.[24]. Thus, SARS-CoV-2 infected patients require psychological support during treatment and isolation, to prevent extreme psychological distress, such as suicide, from occurring. According to our data, pneumonia (35.6%) was the second most common complication of acute COVID-19, after psychological illness. Pneumonia was also the most prevalent organic complication resulting from SARS-CoV-2 infection among acute COVID-19 cases in a recent research study. Data from a systematic review and meta-analysis of COVID-19 complications showed that pulmonary complications, particularly pneumonia, were the most commonly reported organic complications in both 74 case reports/series and 15 observational studies, thereby providing strong support for the current study's findings [10].

The current research identified additional sequelae of acute COVID-19, namely brain fog (19.4%) and multi-joint pain (18.8%). It is noteworthy that the occurrence rates of these two complications were found to be quite similar. The researchers have used the term “brain fog” to describe a wide range of cognitive and memory impairment related symptoms which include forgetfulness, confusion, cloudiness, difficulties with focus, thinking, and communication. [25-27]. Most global COVID-19 studies have shown that brain fog is a criterion for long COVID-19 [28-30]. The term 'long COVID-19' is used when the clinical manifestations of SARS-CoV-2 extend beyond four weeks from the initial symptoms, encompassing both post-acute COVID-19 and post-COVID-19 syndrome [28,30]. However, recent research has revealed that brain fog is one of the reported complications during the acute phase of COVID-19, occurring within the first four weeks of the disease. Hence, it may persist and become a part of long COVID-19 as supported by various studies. Moreover, the present study reported less common acute COVID-19 complications, including hearing impairment (8.1%), acute respiratory failure (5.6%), acute cardiac injury (3.8%), thrombotic lesions (1.9%), and vision impairment (1.9%). Numerous studies have reported these complications, exhibiting similar or divergent frequencies and rates [4,10,31-33]. For instance, Kluge et al. reported that 5% of COVID-19 patients experienced devastating acute respiratory failure due to the development of severe acute respiratory distress syndrome (ARDS) [32]. In another study

by Alonge et al., it was revealed that 1.7% of SARS-CoV-2 patients suffered from acute myopericarditis, and a similar rate was observed for atrial arrhythmias. Additionally, around 2% of these patients were affected by deep venous thrombosis [10]. Furthermore, Italian study reported that 7.7% of hospitalized COVID-19 patients were complicated by thromboembolic lesions at least one time during the disease course [33]. Actually, drawing upon our comprehensive review of the existing literature on the worldwide COVID-19 pandemic, it is evident that the variations in complication rates among various COVID-19 studies can be attributed to several factors [25-33]. These factors encompass differences in study design, study population, country environment, and the specific prevalence of SARS-CoV-2 variants during the study period. Since the emergence of the pandemic in late 2019, a significant number of research studies have been conducted, contributing greatly to our understanding of these variations.

To the best of our knowledge, this current research is one of scarce studies that handles complications of acute COVID-19 phase. In a randomly chosen sample of SARS-CoV-2 infected Libyan patients in Zawia city. However, the recent study had certain limitations, including, a short-term retrospective cohort study but a long-term study would give a better insight about acute COVID-19 complications. It is mostly relied on self-reported data in questionnaire which is subject to bias. Small sample size due to a refusal of several individuals with a positive past history of SARS-CoV-2 infection to participate because of what so called the patient stigma from COVID-19, taking in consideration that this study was conducted during the 2nd wave of COVID-19 in Libya.

CONCLUSION

This retrospective cohort study investigated the severity and complications of acute COVID-19 in 176 SARS-CoV-2 infected patients in Zawia city, Libya. we can conclude that most of the involved COVID-19 patients were mild to moderate cases and only about one quarter of them were severe cases. Furthermore, the majority of COVID-19 cases experienced complications, with psychological disorder being the most prevalent complication during the acute phase of the disease. Pneumonia was the second most common sequelae, followed by brain fog, multi-joint pain, and hearing impairment subsequently. Acute respiratory failure, acute cardiac injury and thrombotic lesions were rare but fatal sequelae in the participated COVID-19 cases. Hence, it is crucial for healthcare professionals to recognize that complications during the acute phase of COVID-19 are multi-systemic, encompassing respiratory, cardiovascular, neurological, and musculoskeletal sequelae. Prompt identification and management of these complications, particularly the severe ones that may lead to loss of life or permanent disabilities, are of utmost importance.

Ethical Issues

Including plagiarism, informed consent, data fabrication or falsification and double publication or submission have completely been observed by authors.

Author Contributions

All the authors substantially contributed to the conception, compilation of data, checking, and approving the final version of the manuscript, and agreed to be accountable for its contents.

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Conflicts of Interest

No potential conflicts of interest were disclosed.

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المضاعفات المرتبطة بالمرحلة الحادة للكوفيد-19 خلال فترة موجة الثانية

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³المركز الوطني للبحوث الطبية, مدينة الزاوية, ليبيا.

المخلص

عدة دراسات أجريت حول العالم قد أفادت بالمضاعفات المتعددة المرتبطة بفيروس سارس-كوف-2 المسبب لمتلازمة الضيق التنفسي الحاد. ومع ذلك، هناك قلة في الأبحاث التي تستكشف المضاعفات المرتبطة بفيروس سارس-كوف-2 في ليبيا، وتحديدًا في مدينة الزاوية. لذا، تهدف هذه الدراسة إلى فحص وتحديد مضاعفات كوفيد-19 الحاد في 176 مريضًا مصابًا بفيروس سارس-كوف-2 في مدينة الزاوية في ليبيا. كجزء من دراسة الاسترجاعية السابقة، شارك في هذا البحث 176 متطوعًا تم اختيارهم عشوائيًا وتبينت إصابتهم بفيروس سارس-كوف-2 بين الأول من ديسمبر 2020 و28 فبراير 2021 في مدينة الزاوية. أكمل المشاركون استبيانًا مصممًا لمرضى كوفيد-19، وتم تحليل البيانات المجمعة لتحقيق أهداف هذه الدراسة. في الدراسة الحالية، اكتشفنا أن 73.9% من مرضى كوفيد-19 كانوا حالات خفيفة إلى متوسطة، بينما كانت 26.1% حالات شديدة. علاوة على ذلك، أوضح البحث الحالي أن 90.9% من مرضى كوفيد-19 تعرضوا لمضاعفات خلال المرحلة الحادة للمرض. والمضاعفات المبلغ عنها خلال هذه المرحلة تشمل الاضطرابات النفسية (90%)، الالتهاب الرئوي (35.6%)، الضبابية الدماغية (19.4%)، ألم في العديد من المفاصل (18.8%)، نقص السمع (8.1%)، الفشل التنفسي الحاد (5.6%)، الإصابة القلبية الحادة (3.8%)، تجلط الأوعية الدموية (1.9%)، وضعف الرؤية (1.9%). بشكل عام، تشير نتائجنا إلى أن معظم مرضى الكوفيد-19 المشاركين في هذه الدراسة كانت لديهم حالة خفيفة إلى متوسطة، وحوالي ربع المرضى عانوا من مرضٍ شديدٍ. علاوة على ذلك، كان لدى غالبية المرضى مضاعفات خلال المرحلة الحادة للكوفيد-19، حيث كانت الاضطرابات النفسية هي الأكثر شيوعًا، يليها الالتهاب الرئوي. ولقد تم ملاحظة مضاعفات قاتلة على الرغم من ندرتها في بعض المشاركين مثل الفشل التنفسي الحاد، الإصابة القلبية الحادة، وتجلط الأوعية الدموية. من الضروري إجراء دراسات بحثية موسعة في مدينة الزاوية لتحديد النطاق الكامل للمضاعفات المرتبطة بالمرحلة الحادة للكوفيد-19. ستوفر مثل هذه الدراسات نصائح قيمة تعزز فهمنا لتأثير الفيروس على الأفراد.

الكلمات الدالة: سارس-كوف-2، كوفيد-19، شدة، مضاعفات، المرحلة الحادة، مدينة الزاوية، ليبيا.