SARS-CoV-2 pandemic and its management in AL-Zawiyah city, Libya.

Entesar A. A. Omran[1*], Osama H. Almajdoub[2], Amina M. Bshaena[2].
[1]Pharmacology Department, Faculty of Medicine,AL-Zawiyah University, AL-Zawiyah, Libya.
[2]Medical Research Center, AL-Zawiyah, Libya.
[*]Correspondence to e.omran@zu.edu.ly

Abstract

The SARS-CoV-2 epidemic has hit Africa hard, with Libya being among the worst-affected nations. However, there were few research studies about this pandemic and its effects in AL-Zawiyah city in particular and Libya in general. This research aimed to study and investigate the COVID-19 disease in AL-Zawiyah city from a variety of perspectives in order to identify and clarify potential risk factors, the most commonly used diagnostic technique, clinical features, various used therapeutic modalities for this disease, and the mortality rate. This research was a retrospective cohort study and it included 176 randomly chosen individuals who had been infected with SARS-CoV-2 during the period from 1st December,2020 to 28th February, 2021 in AL-Zawiyah city. The current study found that the average age of the COVID-19 patients was 45.06 years (SD 17.7), and the most dominant age groups were 15-<45 years (44.3%) and 45-<60 years (36.4%), respectively, and 58.5% of patients were females. Moreover, 76.1% of COVID-19 patients had a positive history of close contact with a COVID-19 patient before they had SARS-CoV-2 infection. The most common clinical manifestations were headache (77.3%), fatigue (73.3%), muscle aches (71.0%), loss of taste or smell (71.0%), fever (67.6%), cough (50.6%), breathing difficulty (49.4%), loss of appetite (42.6%), sore throat (42.0%) and chest pain (36.9%). Only 86.4% of COVID-19 patients were treated by the combined therapy (the traditional Libyan medicine {TLM} and the conventional COVID-19 therapy). Out of 176 COVID-19 patients, 19 (10.8%) died from SARS-CoV-2 infection. We concluded that the individuals with age group fall in 15-<60 years, the female gender and the positive history of close contact with a COVID-19 case are considered the potential risk factors for SARS-CoV-2 infection in AL-Zawiyah city.Our participants' clinical characteristics of SARS-CoV-2 infection were comparable to those reported in numerous studies, with notable differences in the most frequent and least common symptoms between ours and theirs, which might be due to differences in the environment and/or research design.TLM was used widely by our participants for treating this disease with combination by drugs. Although, the recovery percentage was high, the mortality was also very significant and it is six to seven folds higher than that reported by Libyan NCDC.

Keywords: COVID-19, SARS-CoV-2, risk factors, diagnosis, clinical features, therapy, traditional Libyan medicine, mortality, AL-Zawiyah city, Libya.

Citation: A Entesar, Almajdoub O, Bshaena A ,SARS-CoV-2 pandemic and its management in AL-Zawiyah city, Libya.*2021;15(2)*. https://doi.org/10.26719/LJMR.19.049

Received: 06/10/21; **accepted**: 14/10/21; **published**: 31/12/2021

Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the etiological pathogen of the highly contagious and serious coronavirus disease 2019 (COVID-19). It has already affected over 249 million people leading to the death of more than 5 million individuals globally as of November 7, 2021 (1-3).SARSCoV-2 was first discovered in Wuhan city, China in December 2019, thereafter spread widely throughout the world causing a pandemic crisis that frustrating all the globe and it is still posing significanthealth threats and concerns all over the world up to date (4-5). SARS-CoV-2 is a positive-sense single-stranded RNA enveloped virus belonging to beta coronaviruses of Coronavirinae family and Coronaviridae subfamily and order Nidovirales. It is a spherical shaped virus with numerus spike proteins projecting from the surface of the viral envelop giving the virus a crown-shaped appearance, these spikes mediate the viral binding to the host cell membrane either in human or animal body (6-9). In Coronaviridae, seven viruses have been identified to precipitate human infection, four of them produce mild respiratory and gastrointestinal infections while the another three including SARS-CoV-1, MERS and the recent SARS-CoV-2 were reported to cause severe lower respiratory tract infections and categorized as dangerous strains because they resulted in serious pandemics throughout the world (10-11). SARS-CoV-2 is transmitted from animal to human or human to humanand the most common methods of SARS-CoV-2 transmission are inhalation of infectious respiratory droplets and contact with salivary or nasal secretions from the infected person (12). The virus has high affinity for angiotensin converting enzyme 2 (ACE2) receptors that are found on the surface of type-2 pneumocytes and ciliated epithelial bronchial cells and this strongly indicates the involvement of these receptors in the mechanism of viral entry through the lung (13-14).The range of the incubation period of this virus is between 3 to 14 days and its median incubation is 5 days as reported by the researchers (4).

The SARS-CoV-2 causes a disease that ranges from mild to a severe or life-threatening one,it can clinically manifest as a respiratory, digestive or even systemic illness, but it is mainly expressed as a viral flue with or without pneumonia. The COVID-19 symptoms are fever, fatigue, chills, headache, myalgia, dry cough, loss of taste or smell, breathing problems, runny nose and gastrointestinal symptoms (nausea, vomiting, diarrhea and abdominal pain). In addition to symptoms related to central nervous system involvement can be manifested by some patients. Some patients may develop pulmonary pneumonia which worsen if not early diagnosed and/or not appropriately treated resulting in severe respiratory distressthat could end in a respiratory failure. Consequently, the severe hypoxemia causes cardiac arrest and loss of the patient life in the final scenario (15-23). That is why the World Health Organization(WHO) declared a global pandemic state onMarch 11, 2020because it threatens human life especially with a presence of the hazard from the asymptomatic carriers that play as unknown and uncontrollable infectious source to the others (24). Moreover, there are many proposed modes of actions of SARS-CoV-2 which include:

i) hyper-cytokinaemia which precipitate hyper-inflammatory state that might cause destructive multi-organ-failure,ii) immunosuppression and iii) reduction of ACE2 to increase the pulmonary vascular permeability, thereby damaging the alveoli and the lung(25-26).

During the first year of COVID-19 pandemic, no effective vaccine or therapeutic drugs are available for COVID-19 therapy and most of medical researchers throughout the world were trying to design and develop effective and specific vaccines and antiviral drugs in order to overcome this serious disease and prevent its devastating consequences. Therefore, during the meantime, the conventional therapy was applied as a supportive treatment for COVID-19 until the vaccine against SARS-CoV-2 becomes at hand for vaccination of all people in the globe. The conventional SARS-CoV-2 therapy is a combination of the broad-spectrum antibiotics, theantivirals, the corticosteroids, the convalescent plasma and the oxygen therapy (27-32). Currently, many SARS-CoV-2 vaccines have been developed, investigated and distributed to almost all countries of the world.As of today, the vaccination campaign is still going on in order to eradicate this pandemic and limit its spread (33). Actually, we hope that this vaccination campaign will be successful and the people in all world's countries will return to their normal lives as they were before pandemic outbreak.

Libya is one of the countries seriously affected by SARS-CoV-2 virus. On 24 March 2020, Libyan National Center for Disease Control(NCDC) reported the first case of COVID-19, and the disease started to spread widely throughout the whole country. As ofNovember 7, 2021, over 361 thousand confirmed cases have been documented, with above 5thousand deaths across all the cities of the country, and the total number of vaccinated people is over 1.5 million for the first dose and over 499thousand for the second dose of the SARS-CoV-2 vaccine (34). Unfortunately, the conductedstudies about COVID-19 in Libya were very few, especially in AL-Zawiyah city, which is located in the northwest of Libya and west of the capital city, Tripoli, about 46 kilometers, therefore, the main goal of this research is to assess SARS-CoV-2 epidemic in AL-Zawiyah city from many aspects in order to identify the risk factors, the most used diagnostic methods, the average of thesickness period and the clinical profile of SARS-CoV-2 infection in the city. In addition to that, this research study focuses on the types of therapeutic modalities that used in the city and their extent of success in treating patients with COVID-19 through identifying the recovered cases and the death cases from this infectious disease.

Methodology of the study

This research is a retrospective cohort study involved176 randomly chosen volunteers who had infected with SARS-CoV-2 during the last three months of the first pandemic year in AL-Zawiyah city, Libya (from 1st December,2020 to 28thFebruary,2021{during the 2nd wave of SARS-CoV-2 epidemic in Libya}).The consent of the participantswasobtained prior to commencing this research study. A questionnaire was prepared consisting of several questions that cover the full history of COVID-19 disease in the participated volunteers. 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 the phone calls or the social media resources. 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 asnumbers and percentages (n, %) and normally distributed continuous variables are presented as mean (standard deviation [SD]).

Results

The distribution of SARS-CoV-2 infection according to the different age groups of COVID-19 patients

A total 176 COVID-19 patients were involved in this study, the most dominant age group among the participated COVID-19 patients was 15-<45 years (44.3%, n =78), followed bythe age groups 45-<60 years (36.4%, n =64)and60 years old and more (16.5%, n =29).While the least dominantage group was including those who were less than 15 years (2.8%, n =5) (Figure 1A, Table 1). The mean age of all participants was 45.06 years (ranging from 6 to 92 years old, standard deviation ±17.7 years).

Table 1:The distribution of SARS-CoV-2 infection according to the different age groups of COVID-19 patients

The age groups in years	The number of COVID-19 patients	The percentage of COVID-19 patients
0-<15	5	2.8%
15-<45	78	44.3%
45-<60	64	36.4%
≥60	29	16.5%
The total	**176**	**100%**

The distribution of SARS-CoV-2 infection according to the gender type of COVID-19 patients

Our study revealed that more than half of the COVID-19 volunteers were females (58.5%, n =103), while the males only constitute 41.5% (n =73) (Figure 1B, Table 2).

Table 2:The distribution of SARS-CoV-2 infection according to the gender type of COVID-19 patients

The gender type	The number of COVID-19 patients	The percentage of COVID-19 patients
Males	73	41.5%
Females	103	58.5%
The total	**176**	**100%**

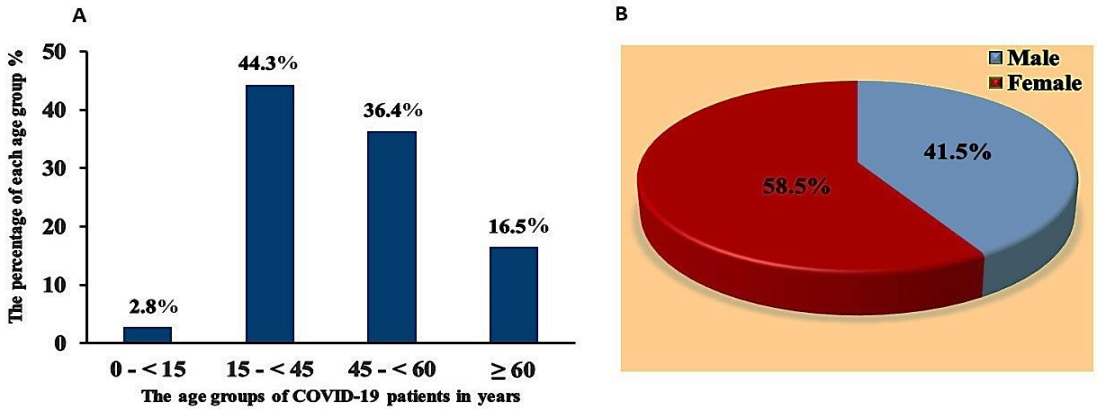

Figure 1: The distribution of SARS-CoV-2 infection; **(A)** according to the different age groups of COVID-19 patients and **(B)** according to the gender type of COVID-19 patients. Data are expressed in percentages (The total number of COVID-19 patients; *n* = 176).

A presence or absence of the past history of close contact with a COVID-19 patient before the infection with SARS-CoV-2

76.1%(n =134) of COVID-19 patients reported having a positive history of close contact with a COVID-19 patient before they had SARS-CoV-2 infection (Figure 2, Table 3).

Table 3:A presence (a positive) or absence (a negative) of the past history of close contact with a COVID-19 patient before the infection with SARS-CoV-2

The past history of close contact with COVID-19 patient before infection with SARS-CoV2	The number of COVID-19 patients	The percentage of COVID-19 patients
A positive history	134	76.1%
A negative history	42	23.9%
The total	**176**	**100%**

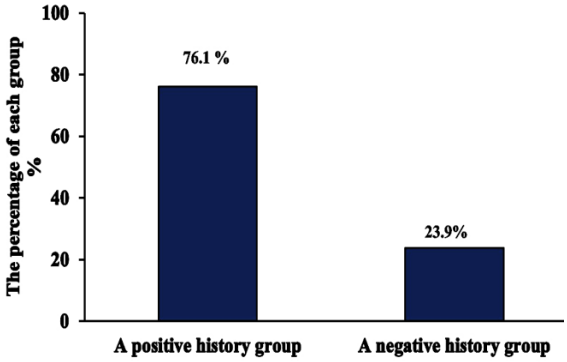

Figure 2: A positive or a negative past history of close contact with a COVID-19 patient before the infection with SARS-CoV-2. Data are expressed in percentages (The total number of COVID-19 patients; *n* = 176).

The different methods that used for diagnosis of SARS-CoV-2 infection

About two thirds (63.6%, n=112) of COVID-19 patients were diagnosed by a real-time reverse transcription polymerase chain reaction test (rRT-PCR) only, 27.8% (n =49) diagnosed by the combined methods (rRT-PCR+ computed tomography{CT}, RT-PCR+ blood antibodiestiters or CT+ blood antibodies titers), and few cases (8.5%, n =15) were only confirmed by blood antibodies titers against SARS-CoV-2 which are immunoglobulins (IgM, IgG and IgA) (Figure 3A, Table 4).

Table 4: The different types of diagnostic methods of SARS-CoV-2 infection and their percentage of use among the COVID-19 patients.

The types of used diagnostic methods of SARS-CoV2	The number of COVID-19 patients who were diagnosed by each method	The percentage of use of each diagnostic method
rRT-PCR	112	63.64%
Blood antibodies titers	15	8.52%
Combined diagnostic method	49	27.84%
The total	**176**	**100%**

The COVID-19 sickness period

Of the total 176 participatedCOVID-19 patients, 155 cases reported their duration of illness with SARS-CoV-2 and only 21 cases did not report their illness duration because of either their inabilities to memorize the exact duration of sickness with this virus (2/176) or the patient-related information were taken from his/her relative since the case was died from this disease (19/176), and the relative of died case was missing this information.

Of the 155 reported COVID-19 patients, 68 (43.9%) recovered within two weeks, 31(20%) cured within three weeks, 30 (19.4%) recovered within one week or less and only 26 (16.7%) takes four weeks or more to recover. Collectively, we noticed 83.3% of the recovered COVID-19 participants were cured within the first 3 weeks from the onset of the disease. (Figure 3B, Table 5).

Table 5: The duration of illness with SARS-CoV-2 among the COVID-19 patients.

The duration of illness with SARS-CoV2	The number of COVID-19 patients	The percentage of COVID-19 patients
≤ 1 week	30	19.4%
2 weeks	68	43.9%
3 weeks	31	20%
≥ 4 weeks	26	16.7%
Total	**155**	**100%**

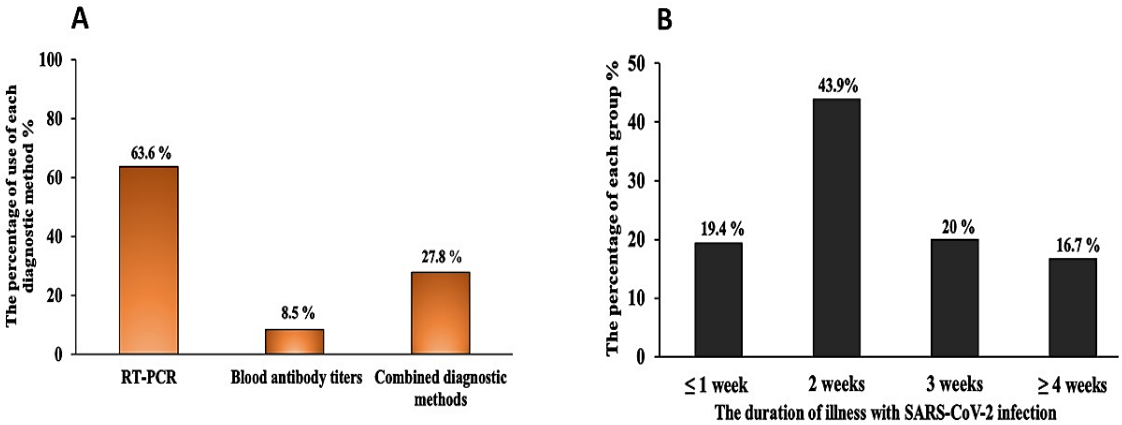

Figure 3: The different types of diagnostic methods of SARS-CoV-2 infection **(A)** and the duration of illness of COVID-19 patients **(B)**. Data are expressed in percentages (The total number of COVID-19 patients; n = 176 in **A** and 155 in **B**).

The clinical manifestations of SARS-CoV-2 infection in COVID-19 patients

According to our study data that are demonstrated in details in the figure 4 and the table6 about the clinical manifestations of SARS-CoV-2 infection in the participated COVID-19 patients, the most common symptoms were headache (77.3%, n =136), fatigue (73.3%, n =129), muscle or body aches (71.0%, n =125), new loss of taste or smell (71.0%, n =125), fever or chills (67.6%, n =119), cough (50.6%, n =89), breathing difficulty (49.4%, n =87), loss of appetite(42.6%, n =75) and sore throat (42.0%, n=74),while the least common manifestations were hearing impairment (7.4%, n =13) and skin rash (1.1%, n =2).

Table 6: The clinical manifestations of SARS-CoV-2 infection in the total 176 COVID-19 patients.

The symptoms or signs experienced by COVID-19 patients	The number of COVID-19 patients who experienced each manifestation	The percentage of each manifestation experienced by COVID-19 patients
Headache	136	77.3%
Fatigue	129	73.3%
Muscle or body aches	125	71.0%
New loss of taste or smell	125	71.0%
Fever or chills	119	67.6%
Cough	89	50.6%
Breathing difficulty	87	49.4%
Loss of appetite	75	42.6%
Sore throat	74	42.0%
Persistent pain or pressure on the chest	65	36.9%
Diarrhea	54	30.7%
Abdominal pain	50	28.4%
Dizziness	38	21.6%
Congestion or runny nose	33	18.8%
Nausea or vomiting	33	18.8%
Joint pain	30	17.0%
Loss the ability to speak or move	30	17.0%
Hearing impairment	13	7.4%
Skin rash	2	1.1%
Total number of COVID-19 patients	**176**	-

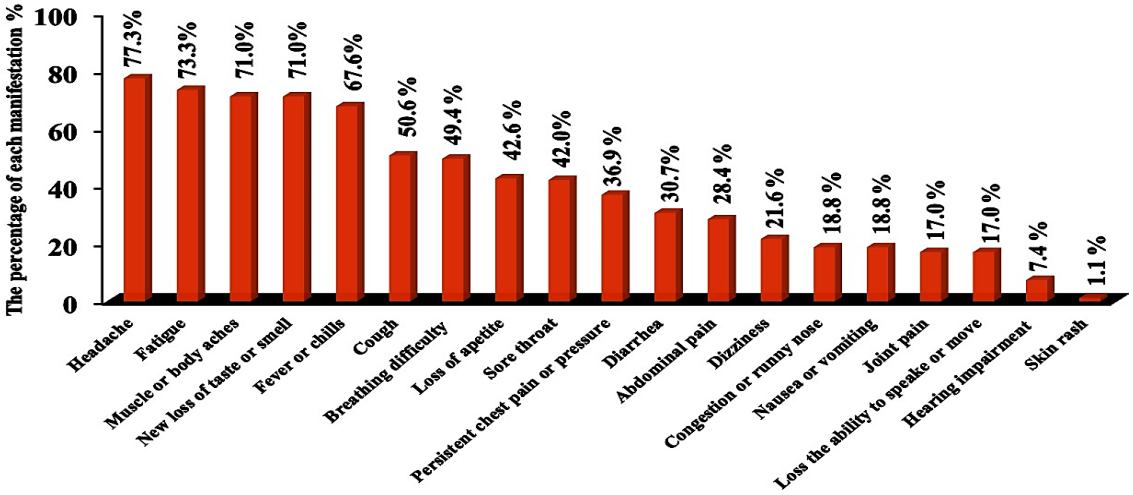

Figure 4: The clinical manifestations of SARS-CoV-2 infection in COVID-19 patients. Data are expressed in percentages (The total number of COVID-19 patients; *n* = 176

Management of SARS-CoV-2 infected patients

The different therapeutic models used by COVID-19 patients

The vast majority of COVID-19 patients (86.4%, n =152) reported that they have used the combined therapy model (the drugs and the traditional Libyan medicine {TLM}) during their infection with SARS-CoV-2, some cases (10.8%, n =19) utilized only the pharmaceutical drugs (The conventional SARS-CoV-2 therapy) and very few patients (2.8%, n =5) reported using only the traditional Libyan herbal medicine and natural products (TLM) to treat themselves from this contagious disease (Figure 5, Table 7).

Table 7: The different therapeutic models used by the COVID-19 patients.

The types of therapy model used by COVID-19 patients	The number of COVID-19 patients who used each therapy model	The percentage of use of each therapy model by COVID-19 patients
Only the pharmaceutical drugs (The conventional SARS-CoV-2 Therapy)	19	10.8%
Only the traditional Libyan herbal medicine and natural products (TLM)	5	2.8%
The combined therapy	152	86.4%
Total	**176**	**100%**

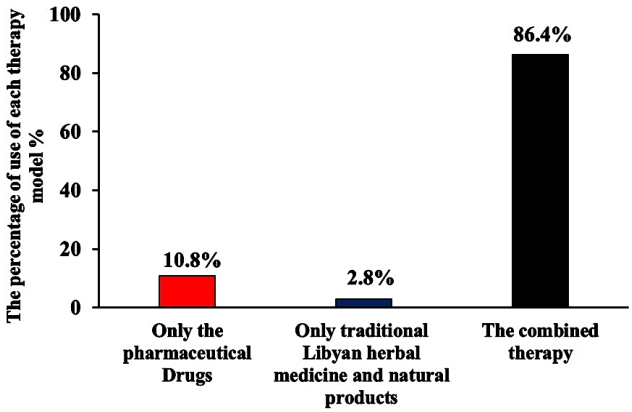

Figure 5: Thedifferent therapeutic models used by COVID-19 patients. Data are expressed in percentages (The total number of COVID-19 patients; *n* = 176).

The medicinal drugs used by COVID-19 patients(The supportive or the conventional SARS-CoV-2 therapy)

In the figure 6 and table 8, we reported the percentage of use of each pharmaceutical drug by the participated COVID-19 patients who had used the drugs either alone or in combination with TLM. Our finding revealed that the most common used drugs were Paracetamol (92.9%, n =159), Zinc supplement (92.9%, n =159), Antibiotics (83.0%, n =142), Vitamin C (79.5%, n =136), Vitamin D (54.4%, n =93), Oxygen therapy (32.7%, n =56) andDexamethasone or its equivalents (32.2%, n =55), while the least used drugs were Fraxiparine (16.4%, n =28), Antitussive drugs (11.1%, n =19), Bronchodilators (10.5%, n =18) and Aspirin (3.5%, n =6).

Table 8: The percentage of use of each pharmaceutical drug by the COVID-19 patients.

Name of the drug	The number of COVID-19 patients who have used each medicinal drug	The percentage of use of each medicinal drug
Paracetamol	159	92.9 %
Zinc supplement	159	92.9%
Antibiotics	142	83.0%
Vitamin C	136	79.5%
Vitamin D	93	54.4%
Oxygen therapy	56	32.7%
Dexamethasone or its equivalents	55	32.2%
Fraxiparine	28	16.4%
Antitussive drugs	19	11.1%
Bronchodilators	18	10.5%
Aspirin	6	3.5%
The total number of patients who have used the drugs either alone or in combination with TLM	**171**	**-**

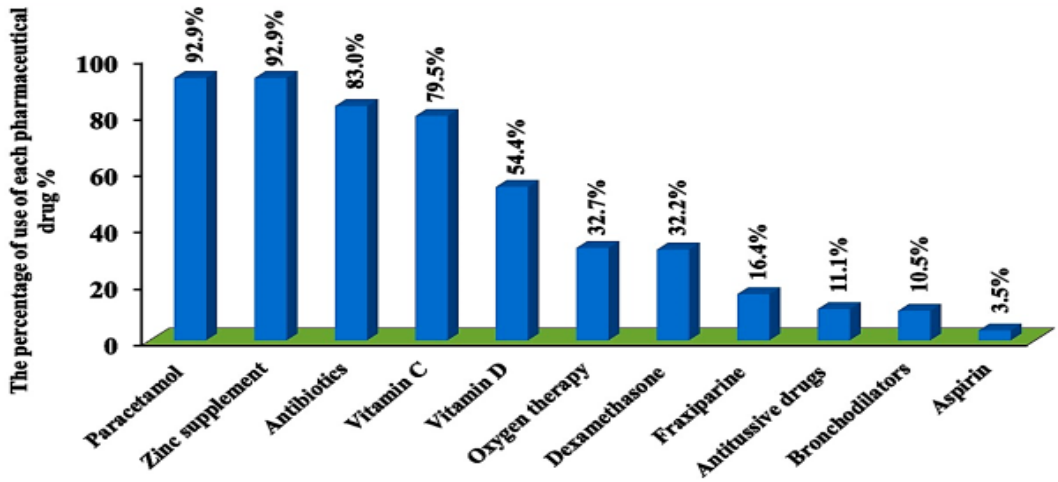

Figure 6: The percentage of use of each pharmaceutical drug by the COVID-19 patients. Data are expressed in percentages (The total number of COVID-19 patientswho have used the medicinal drugs either alone or in combination with the traditional Libyan medicine; n = 171).

The traditional Libyan herbal medicineand natural products (TLM) used by COVID-19 patients

In the figure 7 and table 9, we demonstrated the percentage of use of each traditional Libyan herbal medicine and natural product by SARS-CoV-2 infected participants who had used the TLM either alone or in combination with drugs. It was found that the most common used traditional Libyan herbs and natural products werelemon (92.9%, n =146), honey (76.4%, n =120), thyme (66.2%, n =104), indian installment (59.9%, n =94) , clove beans (46.5%, n =73), green tea (38.9%, n =61), raw onion (36.9%, n =58) and raw garlic (26.1%, n =41), while the least usedtraditional herbs wereground turmeric (16.6%, n =26),ginger (14.6%, n =23), red tea (14.0%, n =22), black seed (13.4%, n =21),artemisia (11.5%, n =18), mint (7.0%, n =11), anisum (6.4%, n =10),fenugreek (5.7%, n =9), chamomile (3.8%, n =6), olibanum (3.2%, n =5), morenga (0.6%, n =1), bee gum (0.6%, n =1) and vinegar (0.6%, n =1).

Table 9: The percentage of use of each traditional Libyan herbal medicine and natural product by the COVID-19 patients.

Name of traditional Libyan herbal medicine or natural products	The number of COVID-19 patients who have used each traditional Libyan herbal medicine or natural products	The percentage of use of each traditional Libyan herbal medicine or natural products
Lemon	146	92.9%
Honey	120	76.4%
Thyme	104	66.2%

Indian installment	94	59.9%
Clove beans	73	46.5%
Green tea	61	38.9%
Raw onion	58	36.9%
Raw garlic	41	26.1%
Ground turmeric	26	16.6%
Ginger	23	14.6%
Red tea	22	14.0%
Black seed	21	13.4%
Artemisia	18	11.5%
Mint	11	7.0%
Anisum	10	6.4%
Fenugreek	9	5.7%
Chamomile	6	3.8%
Olibanum	5	3.2%
Morenga	1	0.6%
Bee gum	1	0.6%
Vinegar	1	0.6%
The total number of COVID-19 patients who have used TLMeither alone or in combination with drugs	**157**	**-**

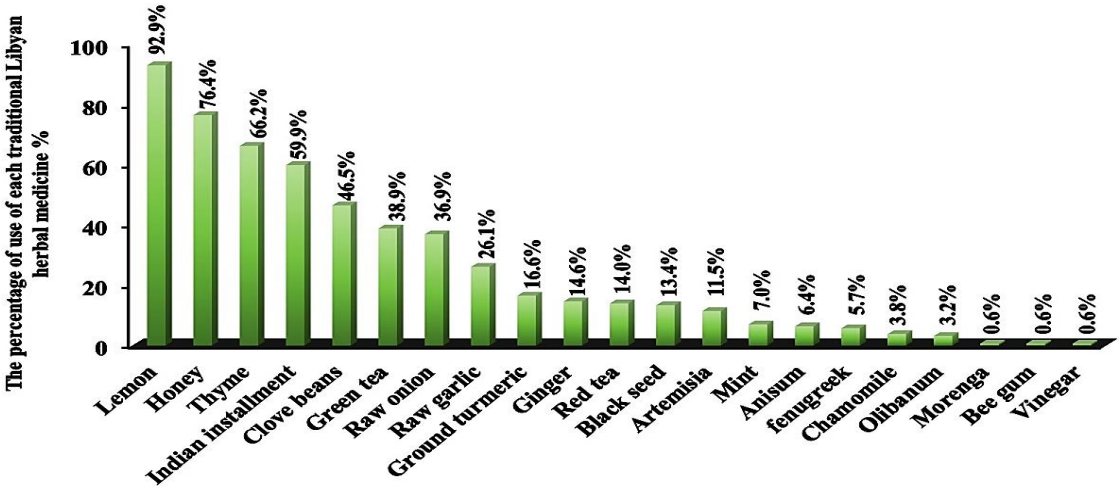

Figure 7: The percentage of use of each traditional Libyan herbal medicine and natural product by the COVID-19 patients. (The total number of COVID-19 patientswho have used the traditional Libyan medicineeither alone or in combination with drugs; $n = 157$).

Therecovery and death from SARS-CoV-2 infection among COVID-19 patients

Among the 176 COVID-19 patients, 157 (89.2%) recovered, while 19 (10.8%) died from SARS-CoV-2. Therefore, although ahigh recovery percentage was achieved,a considerable death percentage was encountered too (Figure 8, Table 10).

Table 10: The percentage of recovered and death cases among the total COVID-19 patients.

Type of the group	The number of COVID-19 patients	The percentage of each group
Recovered cases-group	157	89.2%
Death cases-group	19	10.8%
The total	**176**	**100%**

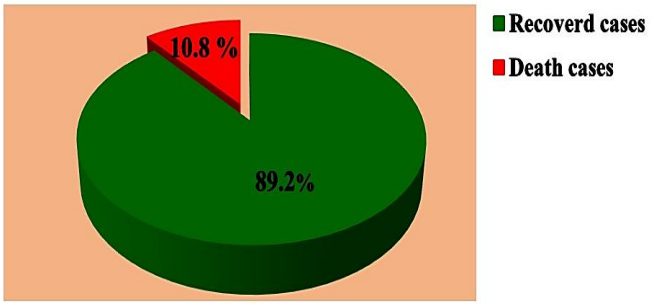

Figure 8: The percentage of recovered and death cases among the total COVID-19 patients. Data are expressed in percentages (The total number of COVID-19 patients; *n* = 176).

Discussion

This is one of the few conducted studies about SARS-CoV-2 pandemic in Libya. In this retrospective study of 176 randomly chosen volunteers of COVID-19 patients from AL-Zawiyah city of Libya, we found that the mean (SD) age of all participants was 45.06 (17.7) years. Thereby we confirm findings from other studies showing that the mean age of their COVID-19 patients was in forties (35-36). Moreover, our study revealed that both of the age groups 15-<45 and 45-<60 years (44.3% and 36.4% of COVID-19 patients; respectively) were found to be the risky age groups for SARS-CoV-2 infection, and they together constitute 80.7% of the participated COVID-19 patients in this study. This is because these two age groups are the most active age groups in Libya, therefore they are more likely to have SARS-CoV-2 infection than the other age groups.To some extent, our data supported Monod *et al.*finding that demonstrated that 75% of COVID-19 infections in USA originated from adults aged 20 to 49 years because they are the most mobile and active age group in USA (37). The difference in the most active age groups between Libya and USA could berelated to the difference in the demographic and the cultural features between these two countries. Worldwide, men were more likely to be infected by SARS-CoV-2 than women (12,35,38-39). However, our findings revealed that the women were the most affected because 58.5% of the participated COVID-19 volunteers in our study were females,

therefore, the females are considered riskier for SARS-CoV-2 infection than males in AL-Zawiyah city, Libya. We think that this discrepancy is due to our Libyan cultural life, where the females are more prone to social collections than males. Furthermore, our research showed that 76.1% of COVID-19 participants have had a contact with a confirmed case of SARS-CoV-2 infection. Similar results were found in a Chinese studies where 72-86% of COVID-19 patients had confirmed Wuhan-related exposure (contact with Wuhan resident or visitor) which was the main source of SARS-CoV-2 epidemic in China and pandemic in the world (5,40).

In this study, the majority of COVID-19 participants (63.6%) reported that their SARS-CoV-2 infection wasconfirmed by rRT-PCR only while a substantial proportion of our involved patients (27.8%) were diagnosed by the combined methods which are rRT-PCR and computed tomography (CT), rRT-PCR and blood antibodies titers or CT and blood antibodies titers against SARS-CoV-2. Our findings are in line with several studies that also illustrated that rRT-PCR based detection of SARS-CoV-2 RNA from the nasopharyngeal swab or otherrespiratory samples is the typical and the standard diagnostic method for SARS-CoV-2 infection (41-44). However, giving the factthat sensitivity ofrRT-PCR test may be not enough for the diagnosis of SARS-CoV-2 infection with the possibility of false negative test results, so the serological assays and the imaging techniques can be used to make a presumptive diagnosis for individuals with a highly suspicious clinical feature of COVID-19. The serological test is used for detection of blood antibodies titers against SARS-CoV-2 while CT is used for detection of the characteristic pulmonary manifestations related to COVID-19 (25,44-45). That is why we noticed 27.8% of our studied patients were diagnosed by multi-methods.In addition to the severity of some cases of our COVID-19 participants that necessitates the uses of multi-diagnostic methods in order to identify the underlying SARS-CoV-2 complications.

Furthermore, we also observed most of our recovered COVID-19 participants (83.3%) were recovered within 1-3 weeks from the onset of the first symptoms and only 16.7% of the recoveredcases takes 4 weeks or more to recover, confirming findings of the United Kingdom-a smartphone application-based study that revealed approximately 90% of its COVID-19 participants were returned to their previous level of health after 3 weeks of the disease onset and around 10% of them had suffered from the persistence of SARS-CoV-2 symptoms beyond 3 weeks from the onset of the symptoms (46). Regarding the clinical manifestations of SARS-CoV-2 infection among our COVID-19 cases, the most common symptoms were headache, fatigue, muscle or body aches, new loss of taste (ageusia) or smell (anosmia) and fever and/or chills followed by cough, shortness of breathing, loss of appetite, sore throat and chest pain or pressure, while the less common symptoms were related to gastrointestinal system (nausea, vomiting, diarrhea and abdominal pain) and joint pain while the very rare symptoms were hearing impairment and skin rash.It was found that the clinical manifestations of SARS-CoV-2 infection among our COVID-

19 participants were consistent with that reported by several studies throughout the world with some differences in the frequencies and percentages of the symptoms between our study and the other studies and between each study and another (5,25,36,39,47-51). For example, fever, cough and dyspnea were more common in Spanish Casas-Rojo JM*et al.*study than ours (fever 84.2% vs. 67.6%, cough 73.5% vs. 50.6%, dyspnea 57.6% vs. 49.4%) while fatigue, anosmia and loss of appetite were less common in Casas-Rojo JM *et al.* study than ours (fatigue 43.6% vs. 73.3%, anosmia 7.1% vs. 71.0%, loss of appetite 19.6% vs. 42.6%) (38). Furthermore, the reported cough and fever by COVID-19 patientsof Chen N *et al*. Chinese studywere higher than that seen in ours (fever 83% vs.67.6% and cough 82% vs 50.6) while headache, muscle ache, sore throatand rhinitisand diarrheawere less common in this Chinese study than that in our records (headache 8% vs. 77.3%, muscle ache 11% vs.71.0%, sore throat 5% vs.42.0%, rhinitis 4% vs. 18.8% and diarrhea 2% vs. 30.7%)(32).The possible explanations for these variations with some studies include the difference in geographical (environmental) factor between Libya and the other countriesin which the studies were conducted and/or the difference in the study design between our study andthe other studies. Libya is characterized by its warmer climate in comparison to western countries and this is highly expected to create some differences in the dominant manifestations of SARS-CoV-2 between Libya and the other colder countries. Moreover, the difference in the study design plays an important role in the discrepancy between our study data and someother studies' data because some studies involved only the hospitalized COVID-19 patient while ours included the SARS-CoV-2 cases with or without history of hospitalization, and this definitely would make a great difference in the dominant features of SARS-CoV-2 infection between our findings and other studies findings, since the hospitalized cases would be more severe than the non-hospitalized one, therefore more respiratory distress symptoms would be seen in these patients (5,25,38,39). The difference in the study design also could include the difference in demographic features (sex, and age) of the studied COVID-19 participants, as some studies might exclude certain age group like those below 18 years but ours didn't, andin some studies the mean age of their participants was more than 60 years while ours was in forties (38,52). Moreover, some studies involved certain people with a specific career like studying SARS-CoV-2 infection among the health workers rather than in the general population of their community while our study was not designed for a specific career group (36,51). All these differences in the study design are expected to generate variations in the SARS-CoV-2 manifestations between our study and the other different studies throughout the globe.

Because of absence of specific antiviral drugs and vaccines especially during the first year of the pandemic appearance, several nonspecific drugs were used as supportive management for this infection and they were called the conventional SARS-CoV-2 therapy. This conventional treatment includes antipyretics, antibiotics,

vitamins, corticosteroids, anticoagulants, oxygen therapy and convalescent plasma, and it was approved by Libyan Health Ministry and recommended to all health facilities and clinics for SARS-CoV-2 management in our country (27-32,56). In this context, we discovered that the vast majority of our COVID-19 patients (97.2%) strictly followed this conventional therapy protocol for treating their infection either by using it alone (10.8%) or in combination with traditional Libyan herbal medicine (86.4%). From this point, we caught up an interesting finding in our study which is that most of our SARS-CoV-2 infected patients (86.4%) have used the combined therapy for treating themselves from this serious pandemic. The combined therapy includes both of the conventional treatment for SARS-CoV-2 and the traditional Libyan medicine (TLM). The main reasons that prompted the majority of our COVID-19 participants to use the combined therapy rather than using the conventional therapy only were several reasons as reported by our COVID-19 patients, and they include: i) at the time of conduction of this study, most of our SARS-CoV-2 patients knew that this new pandemic didn't have either known effective antiviral drug or vaccine yet, ii)They also knew that even the newly developed vaccines are still under trials to prove their success in overcoming COVID-19 pandemic without serious short or long term complication iii) the severe panic state experienced by our COVID-19 participants from this devastating pandemic that frustrating the world and iv) the strong belief of our patients in the role of TLM as immune-modulator or enhancer, thereby helping in treating this infection. We therefore support findings from many Chinese studies revealing that both of the conventional medicine and the traditional Chinese medicine are used for the treatment of patients with infection of SARS-CoV-2 in China according to Chinese clinical guidelines. In addition to that, our data are in agreement with several worldwide studies that highlighted the benefit of using their own traditional medicine as adjuvant therapy to the conventional SARS-CoV-2 therapy (26,53-55).

In regard to the conventional treatment, the most used drugs by our COVID-19 patients were Paracetamol, Zinc supplement, vitamin C, vitamin D and antibiotics. It was reported that supplementation of SARS-CoV-2 infected patients with vitamin C, vitamin D and Zinc might have a supportive therapeuticrole because of their immune-modulatory and antioxidant effects. In addition to that, administration of these nutrients was found to decrease significantly both of SARS-CoV-2 viral load and the time of hospitalization. That is because of Vitamin D interacts with ACE which acts as an entry receptor for SARS-CoV-2 and Zinc reduces viral replication (57-60).83% of our COVID-19 patients received antibiotic therapy and the most used antibiotic was Azithromycin.Some of our patients reported usingantibiotics rather than Azithromycin either they were allergic to Azithromycin or their health didn't improve with this macrolide antibiotic. It had been shown that Azithromycin has antiviral activity against SARS-CoV-2 and immunomodulatory effects that included in its ability to preserve epithelial integrity and reduce cytokine production (61-62). The significantly high percentage of use of

antibiotic therapy by our study participants is considered of extreme concern, especially most of them were mild to moderate COVID-19 cases as they reported. Therefore, antibiotics misusecould bea great issue among our SARS-CoV-2 patients. Antibiotic therapy should be reserved for SARS-CoV-2 patients with secondary bacterial infection or critically ill patients to avoid emergence of antibiotic resistance which affects negatively on many burden diseases (63). Our data revealed that a significant proportion of COVID-19 cases were treated with oxygen therapy (32.7%) and dexamethasone or its equivalents (32.2%). The supplemental oxygen therapy was recommended to COVID-19 patients with signs of severe respiratory distress or to those without signs of severe respiratory distress but with SpO_2 < 90% (63). Corticosteroids (such as Dexamethasone and Methylprednisolone)are anti-inflammatory and immunosuppressive drugs that reduce the secretion of the proinflammatory cytokines. It was illustrated that the increase in the inflammatory cytokines production plays a crucial role in the immunopathogenesis of COVID-19 and it might be excessively secreted resulting in a severe systemic inflammation and consequently multi-organ damage; and this was termed the cytokine storm.However, the systemic use of corticosteroids for COVID-19 patients is still controversial. Some studies showed the positive effects of systemic steroid use for COVID-19 management which included in reducing lung inflammation and hence correcting hypoxemia, reducing the mortality in patient requiring supplemental oxygen and improving the clinical outcomes by controlling the immunothrombosis. On the other hand, several studies reported that systemic administration of corticosteroids impairs the viral clearance, increases the risk of superinfection with bacteria and fungi and increases the risk of having psychosis, diabetes and avascular necrosis. Therefore, clinician must out weight the benefit and the risk of systemic use of steroids in COVID-19 patients. It is highly recommended to use steroids to control cytokine storm in critically ill patients (6,64-68). Furthermore, our research demonstrated that 16.4 % of SARS-CoV-2 infected patients were treated by Fraxiparine (Nadroparin calcium). Nadroparin is a subcutaneous low molecular weight heparin used to treat and preventthe thromboembolic disorders. It is recommended to use a low molecular weight heparin for all hospitalized COVID-19patients as a prophylactic therapy against thromboembolism (63,69).

Several studies reported that using traditional medicine in combinationwith conventional treatment had some beneficial effects, representing in better fever control and more rapid clearance of chest infection and other symptoms. China reported that 85% of COVID-19 patients were treated with traditional Chinese medicine as adjunctive to conventional treatment, based on the observed antiviral effects of many Chinese plants (28,70,71). Interestingly, this was consistent with our results that showing 89.2% of our COVID-19 patient were treated with TLM either alone (2.8%) or in combination with the conventional therapy (86.4%).In this study, the most common used TLMwerelemon, honey,

thyme, indian installment, clove beans, green tea, raw onion and raw garlic. The ground turmeric, ginger, red tea,black seed, artemisia, mint, anisum, fenugreek, chamomile, olibanum, morenga, bee gum and vinegar were also used by some of the involved COVID-19 participants in this study, but their use seems to be less common than the previously mentioned group. Moreover, the vast majority of TLM were used only by oral route except for some of them were also used as aromatherapy in addition to the oral use to disinfect the surrounding environment from microbes as reported by our COVID-19 participants. Many food and herbs are known to display antiviral, anti-inflammatory, antioxidant, antipyretic, immunomodulatory and cytoprotective activities, therefore enhancing the immune system to combat the COVID-19.Many literatures have reported the antimicrobial activity of honey against different pathogens (bacteria, viruses, fungi and protozoa) (72-73).Lemon is a powerful antioxidant and useful for relieving the respiratory symptoms especially sore throat and cough (55,74). Abdul M Gbaj, *et al.* revealed that the thyme has antioxidant, anti-inflammatory and immunomodulatory properties(59). Furthermore, the clove has been reported to have antioxidant, anti-inflammatory, antimicrobial, antibacterial and antifungal properties whilequercetin from onions and green tea has been shown to inhibit the 6LU7 and 6Y2E proteases of SARS-CoV-2 by binding to them(75-77). Several studies reported that the fresh garlic has several activities including antioxidant, antiviral, antifungal, antibacterial and antiprotozoal in addition to antihypertensive,antilipemic, anticancer effects. Therefore, it is used for treatment chronic bronchitis and recurrent upper respiratory infections (78-80). In regard to ginger and curcuma, it was shown that ginger has anti-inflammatory, antioxidant, antipyretic, analgesic, antiviral activities while ground turmeric (curcuma) has activities such as anti-inflammatory, antioxidant, anti-diabetic, hepatoprotective, hypolipidemic, anti-diarrheal, anti-asthmatic, and anti-cancerous drug(55,73).Moreover, mint leaveshave antioxidant activities, anisum is used for fever and cough and for asthmatic patient because of its antispasmodic effect (4,55). Collectively, traditional medicine was used to booster and modulate the immune system, thereby they might contribute in relieving of SARS symptoms and shortening of the disease course as reported by Hsu CH,*et al.* (81). An interesting finding in our study was that no drug-drug, herb-herb or drug- herb interactions have been reported by our COVID-19 participants. Thereby, this is considered as encouraging data for using TLM as adjuvant therapy for COVID-19 patients in Libya.

An important finding in our research was that the mortality among our SARS-CoV-2 patients was 10.8%, approximately six or seven times higher than that reported by Libyan NCDC (1.5-1.6%) for the same study period (34). This highly significant discrepancy could be explained by some reasons including: i) possibly, there aremany unknown numbers of COVID-19 cases that were not reported to Libyan NCDC, ii) possibly, there are many unknown numbers of COVID-19 deaths that were not reported to Libyan NCDC

and iii) since our study was restricted for AL-Zawiyah city, it might be the mortality in this city is much higher than that reported on the level of whole country because of the difference in the disease course or epidemiology in this city that necessitates further and broader retrospective and prospective studies in this city especially and in all over the country generally. On the other hand, our research study is a purely applied field study in which COVID-19 patients were randomly chosen from AL-Zawiyah city without a bias to choose the recovered or the death cases from this pandemic. Therefore, we highly expect that our results are more accurate and reflecting the general facts of this disease in our community, AL-Zawiyah city.WHO reported that "as of 30 January 2021, Libya occupied the 15th place in the list of the cumulative number of cases of COVID-19 in the 22 countries and territories of the Eastern Mediterranean region (EMR). It ranked 12th place in the list of the number of deaths per country/territory in the region. The national case fatality rate in Libya (CFR) increased from 1.4% to 1.6% but remains well below EMR's average CFR of 2.5%. Libya's CFR remains difficult to interpret given the low rates of testing in some parts of the country and its weak mortality surveillance system. By way of comparison, EMR countries with similar or better health care systems and epidemiological conditions have much higher CFRs (Yemen (29%), Syria (6.5%), Sudan (6.1%), Egypt (5.6%) and Tunisia (3.2%))." (82).Therefore, our data strongly support the expectations of WHO thatLibyan's CFR does not reflect the actual reality of deaths from this pandemic in the countrybecause of a weak case reporting system and a weak mortality surveillance system in Libya.

This study had some limitations. Firstly, this is a short term retrospective cohort study. A long term prospective or retrospective study would give us a better insight about COVID-19pandemic in AL-Zawiyah city in particular and in whole Libya in general.Secondly, we mostly relied on self-reported data in our questionnaire which is subject to the bias.Lastly, our sample size was small due to arefusal of several individuals with a positive past history of SARS-CoV-2 infection to participate in our study because of what so called the patient stigma from COVID-19, and this was the major obstacle that limiting our research sample size to only 176 COVID-19 volunteers.Collaboration with health clinics and hospitals would lead to a larger cohort and a more accurate analysis. However, to our knowledge, this research is the first study that handled SARS-CoV-2 infection from several aspects in AL-Zawiyah city, Libya.

Conclusion

This retrospective cohort study investigated SARS-CoV-2 pandemic in AL-Zawiyah city from several aspects, despite of some difficulties and challenges that faced it.Collectively, we can conclude that the individuals with age group falls in 15-<60 years old, the female gender and the positive history of close contact with a COVID-19 case are considered strong risk factors for SARS-CoV-2 infection in our community.AlthoughtherRT-PCR was the most commonly used SARS-CoV-2diagnostic technique, the combined

diagnostic tools were also used significantly either to confirm the diagnosis oridentify the underlying COVID-19 pathological changes and progression.The clinical manifestations of COVID-19 among our participants were identical to that seen in several studies with considerable variations in the most common and least common symptoms between ours and theirs that could be related to the difference in the environmental factor and/or in the study design. Furthermore, the vast majority of the participated SARS-CoV-2 cases were treated by the combined therapy which is using TLM as adjuvant therapy to the conventional SARS-CoV-2 therapy, and the main reason for using the combined therapy is the knowledge of our participants that this disease does not have specific known and effective drugs for treating it. Although the recovery percentage (89.2%) among our COVID-19 cases was high, the mortality percentage (10.8%) was also very considerable. The mortality in our study was six to seven folds higher than that reported by Libyan NCDC, and this difference could be related to the poor registration system for COVID-19 cases and deaths in our country or could be due to the restricted study location to AL-Zawiyah city only, thereby, this mortality could reflect the pandemic situation in AL-Zawiyah city only (A hot COVID-19 spot) rather than in the whole country. Therefore, we need to conduct further and broader studies at the level of AL-Zawiyahcity in particular and the level of the whole country, Libya in general to know the main reasons of this discrepancy.

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.

Acknowledgments

We would like to express my deep gratitude to all COVID-19 volunteers and their families for their cooperation with us that facilitates conduction of this research.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

Authors declare no conflict of interest.

Reference

1. **Rabaan A.A., Al-Ahmed S.H., Al Mutair A., Alhumaid S., Sule A.A., Tirupathi R., Fawzy M., Muhammad J.,*et al.***(2021) *Immunopathogenesis and immunobiology of SARS-CoV-2.* Infez Med. 29(2),167-180.
2. **COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU).**https://coronavirus.jhu.edu/map.html (accessed November 7, 2021).
3. **Dhama K., Khan S., Tiwari R., *et al.*** (2020)*Coronavirus Disease 2019-COVID-19.* Clin Microbiol Rev. 33 (4).
4. **Mputu Kanyinda J.N.** (2020)*Coronavirus (COVID-19): A protocol for prevention and treatment (Covalyse®).* EJMED. 2 (3), 1-4.

5. **Guan W.J., Ni Y.Z., Hu Y., *et al.*** (2020)*Clinical characteristicsof coronavirus disease 2019 in China*. N Engl J Med.382 (18), 1708-20.
6. **Rodriguez-Morales A.J., Katterine Bonilla-Aldana D., Tiwari R., Sah R., Rabaan A.A. and Dhama K.** (2020)*Covid-19, an Emerging Coronavirus Infection: Current Scenario and Recent Developments - An Overview*.J. Pure Appl. Microbiol.14(1),5-12.
7. **Wang L.F. and Eaton B.T.** (2007) *Bats, civets and the emergence of SARS.* Curr Top Microbiol Immunol. **315**,325-44.
8. **Paraskevis D., Kostaki E.G., Magiorkinis G., Panayiotakopoulos G., Sourvinos G. and Tsiodras S.** (2020)*Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event.* Infect Genet Evol.79, 104212.
9. **Xiao K., Zhai J., Feng Y., Zhou N., Zhang X., Zou J.J., Li N., Guo Y., Li X., Shen X.,*et al.***(2020) *Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins. Nature.* 583(7815), 286-289.
10. **Cui J., Li F. and Shi Z.L.** (2019) *Origin and evolution of pathogenic coronaviruses.* Nat Rev Microbiol. 17,181–192.
11. **Khan A., Umbreen S., Hameed A., Fatima R., Zahoor U., Babar Z., Waseem M., Hussain Z.,*et al.***(2021) *In Silico Mutagenesis-Based Remodelling of SARS-CoV-1 Peptide (ATLQAIAS) to Inhibit SARS-CoV-2: Structural-Dynamics and Free Energy Calculations.* Interdiscip Sci. 13(3), 521-534.
12. **Vellingiri B., Jayaramayya K., Iyer M., Narayanasamy A., Govindasamy V., Giridharan B., Ganesan S., *et al.***(2020)*COVID-19: A promising cure for the global panic.* Sci Total Environ. 725:138277.
13. **Zhang H., Zhou P., Wei Y.,*et al.***(2020a) *Histopathologic changes and SARS-CoV-2 immunostaining in the lung of a patient with COVID-19.* Ann Intern Med. 172,629–632.
14. **Xiu S., Dick A., Ju H.,Mirzaie S., Abdi F., Cocklin S., Zhan P. and Liu X.** (2020) *Inhibitors of SARS-CoV-2 entry: current and future opportunities.* JMed Chem. 63,12256–12274.
15. **Munster V.J., Koopmans M., Van Doremalen N., Van Riel D. and de Wit E.**(2020) *A Novel Coronavirus Emerging in China - Key Questions for Impact Assessment.* N Engl J Med.382(8), 692-4.
16. **Yang D. and Leibowitz J.L.** (2015)*The structure and functions of coronavirus genomic 3′ and 5′ ends.* Virus Res. 206, 120-33.
17. **Xu Z., Shi L., Wang Y., Zhang J., Huang L., Zhang C., Liu S., Zhao P., Liu H., Zhu L., Tai Y., Bai C., Gao T., Song J., Xia P., Dong J., Zhao J. and Wang F.S.** (2020) *Pathological findings of COVID-19 associated with acute respiratory distress syndrome.* Lancet Respir Med. 8(4),420-422.
18. **Jin X., L.J.-S., Hu J-H., *et al.***(2020)*Epidemiological, clinical and*

virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. bsg. 69,1002–1009.

19. **Wang Q., Vlasova A.N., Kenney S.P., Saif L.J.** (2019) *Emerging and re-emerging coronaviruses in pigs.* Curr Opin Virol.34, 39-49.
20. **Yeo C., Kaushal S. and Yeo D.** (2020)*Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible?* Lancet Gastroenterol Hepatol.5(4), 335-337.
21. **Gu J., Han B. and Wang J.** (2020) *COVID-19: Gastrointestinal Manifestations and Potential Fecal-Oral Transmission. Gastroenterology.*158(6):1518-1519.
22. **Luo S., Zhang X. and Xu H.** (2020) *Don't Overlook Digestive Symptoms in Patients with 2019 Novel Coronavirus Disease (COVID-19).* Clin Gastroenterol Hepatol. 18(7),1636-1637.
23. **Wang J. and Du G.** (2020*) COVID-19 may transmit through aerosol.* Ir J Med Sci. 189(4),1143-1144.
24. **Tummers J., Catal C., Tobi H., Tekinerdogan B. and Leusink G.**(2020) *Coronaviruses and people with intellectual disability: an exploratory data analysis.* J Intellect Disabil Res. 64(7),475-481.
25. **Huang C., Wang Y., Li X., *et al*.**(2020)*Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.* Lancet. 395 (10223), 497–506.
26. **Li G. and Clercq E.** (2020)*Therapeutic options for the 2019 novel coronavirus (2019-nCoV).* Nat. Rev. Drug Discov. 19, 1449–14150.
27. **Dhawan M., Parmar M., Sharun K., Tiwari R., Bilal M. and Dhama K.** (2021)*Medicinal and therapeutic potential of withanolides from Withania somnifera against COVID-19.* J Appl Pharm Sci. 11(04),006–013.
28. **Yang Y., Islam M.S., Wang J., Li Y. and Chen X.**(2020) *Traditional Chinese Medicine in the Treatment of Patients Infected with 2019-New Coronavirus (SARS-CoV-2): A Review and Perspective.* Int J Biol Sci.16(10),1708-1717.
29. **Jin Y.H., Cai L., Cheng Z.S., Cheng H., Deng T., Fan Y.P., *et al.***(2020) *A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus(2019-nCoV) infectedpneumonia (standard version).*Mil Med Res. 7(1):4.
30. **Wang M., Cao R., Zhang L., Yang X., Liu J., Xu M.,*et al.***(2020)*Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro.* Cell Res. 30(3), 269-271.
31. **Zhang L. and Liu Y.** (2020)*Potential Interventions for Novel Coronavirus in China: A Systemic Review.* J Med Virol.92(5):479-490.
32. **Chen N., Zhou M., Dong X., Qu J., Gong F., Han Y.,*et al.*** (2020*) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.* Lancet.395(10223), 507-513.
33. **Yan Y., Pang Y., Lyu Z., Wang R., Wu X., You C., Zhao H., Manickam**

S., Lester E., Wu T. and Pang C.H.(2021) *The COVID-19 Vaccines: Recent Development, Challenges and Prospects.* Vaccines (Basel). 9(4), 349.

34. **NCDC. Coronavirus COVID-19.***https://ncdc.org.ly/Ar/*(Accessed 8November,2021).
35. **Guan W.-J., Ni Z.-Y., Hu Y., Liang W.-H., Ou C.-Q., He J.-X.,*et al*.** 2020. *Clinical characteristics of 2019 novel coronavirus infection in China.* N. Engl. J. Med. 382,1708– 1720.
36. **Pereckaitė L., Dambrauskienė A., Urbonienė D., Sadauskas S., Petrikonis K., Naudžiūnas A. and Vitkauskienė A.** (2021)*SARS-CoV-2 Seroprevalence in Healthcare Workers of Kaunas Hospitals during the First Wave of the COVID-19 Pandemic. Medicina (Kaunas).* 57(2):148.
37. **Monod M., Blenkinsop A., Xi X., Hebert D., Bershan S., Tietze S., Baguelin M., Bradley V.C., Chen Y., Coupland H., Filippi S., Ish-Horowicz J.,*et al.***(2021) *Age groups that sustain resurging COVID-19 epidemics in the United States.* Science. 371(6536), eabe8372.
38. **Casas-Rojo J.M., Antón-Santos J.M., Millán-Núñez-Cortés J., Lumbreras-Bermejo C., Ramos-Rincón J.M., Roy-Vallejo E., Artero-Mora A., Arnalich-Fernández F., García-Bruñén J.M.,*et al.***(2020) *Clinical characteristics of patients hospitalized with COVID-19 in Spain: Results from the SEMI-COVID-19 Registry.* Rev Clin Esp (Barc). 220(8),480-494.
39. **Richardson S., Hirsch J.S., Narasimhan M., Crawford J.M., McGinn T., Davidson K.W.,*et al.*** (2020)*Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized with COVID-19 in the New York City Area.* JAMA. 323(20),2052-2059.
40. **Wu Z.and McGoogan J.M.**(2020) *Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention.* JAMA. 323(13),1239-1242.
41. **Wang W., Xu Y., Gao R., Lu R., Han K., Wu G. and Tan W.** (2020)*Detection of SARS-CoV-2 in different types of clinical specimens.* JAMA. 323(18),1843–4.
42. **Nalla A.K., Casto A.M., Huang M.W., Perchetti G.A., Sampoleo R., Shrestha L., Wei Y., Zhu H., Jerome K.R. and Greninger A.L.** (2020) *Comparative Performance of SARS-CoV-2 Detection Assays Using Seven Different Primer-Probe Sets and One Assay Kit.* J Clin Microbiol. 58(6):e00557-20.
43. **Sethuraman N., Jeremiah S.S. and Ryo A.** (2020)*Interpreting Diagnostic Tests for SARS-CoV-2.* JAMA.323(22),2249–2251.
44. **Wiersinga W.J., Rhodes A., Cheng A.C., Peacock S.J. and Prescott H.C.** (2020)*Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review.* JAMA. 324(8),782–793.

45. **Chung M., Bernheim A., Mei X., Zhang N., Huang M., Zeng X., Cui J., Xu W., Yang Y.,Fayad Z.A. and Jacobi A.** (2020)*CT imaging features of 2019 novel coronavirus (2019-nCoV).* Radiology.295(1), 202–7.
46. **COVID Symptom Study.***How long does COVID-19 last?* Kings College London, 2020
47. **Mao R., Qiu Y., He J.S.,*et al.***(2020) *Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis.*Lancet Gastroenterol Hepatol. 5(7),667-678.
48. **Wang Y. and Chen Y.,*et al.*** (2020) *Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures.* J Med Virol. 92(6), 568–76.
49. **Rodriguez-Morales A.J., Cardona-Ospina J.A., Gutiérrez-Ocampo E.,*et al.*** (2020)*Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis.* Travel Med Infect Dis.34: 101623.
50. **Dhama K., Patel S.K., PathakM.,*et al.*** (2020c) *An update on SARS-CoV-2/COVID-19 with particular reference to its clinical pathology, pathogenesis, immunopathology and mitigation strategies.* Travel Med Infect Dis 37:101755.
51. **Díez-Manglano J., Solís-Marquínez M.N., Álvarez García A., Alcalá-Rivera N., Maderuelo Riesco I.,*et al.*** (2021) *Healthcare workers hospitalized due to COVID-19 have no higher risk of death than general population. Data from the Spanish SEMI-COVID-19 Registry.* PLoS One. 16(2):e0247422.
52. **Argenziano M.G., Bruce S.L., Slater C.L., Tiao J.R., Baldwin M.R., Barr R.G., Chang B.P.,*et al.*** (2020) *Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series.* BMJ.369:m1996.
53. **Li T. and Peng T.** (2013) *Traditional Chinese herbal medicine as a source of molecules with antiviral activity.* Antiviral Res. 97, 1-9.
54. **Nugraha R.V., Ridwansyah H., Ghozali M., Khairani A.F. and Atik N.***Traditional Herbal Medicine Candidates as Complementary Treatments for COVID-19: A Review of Their Mechanisms, Pros and Cons.*(2020) Evid Based Complement Alternat Med. 2020:2560645.
55. **Silveira D., Prieto-Garcia J.M., Boylan F., Estrada O., Fonseca-Bazzo Y.M., Jamal C.M., Magalhães P.O., Pereira E.O., Tomczyk M. and Heinrich M.**(2020) *COVID-19: Is There Evidence for the Use of Herbal Medicines as Adjuvant Symptomatic Therapy?* Front Pharmacol. 11:581840.
56. **Libyan Health Ministry,***the recommended COVID-19 therapy to all health facilities.*2020.
57. **Zhang J., Xie B. and Hashimoto K.** (2020) *Current status of potential therapeutic candidates for the COVID-*

19 crisis. Brain Behav Immun. 87,59-73.

58. **Jovic T.H., Ali S.R., Ibrahim N., Jessop Z.M., Tarassoli S.P.,*et al*.** (2020) *Could Vitamins Help in the Fight Against COVID-19?* Nutrients 12(9).
59. **Sadawe I.A., Qabaj A.M., Meiqal N.H.,Bensaber S.M., Hamid A.R., Maamar M.S., Hermann A., Gbaj A.M.**(2021)*Single-center clinical study and in-Silico investigation of Thymus capitatus extract as supportive treatment of patients with COVID-19.*Clinical & Community Medicine J. 2 (5), 221-231.
60. **Barati F., Pouresmaieli M., Ekrami E., Asghari S., Ziarani F.R. and Mamoudifard M.**(2020)*Potential Drugs and Remedies for the Treatment of COVID-19: A Critical Review.* Biol Proced Online. 22:15.
61. **Ouassou H., Kharchoufa L., Bouhrim M., Daoudi N.E., Imtara H.,*et al*.** (2020) *The Pathogenesis of Coronavirus Disease 2019 (COVID-19): Evaluation and Prevention.* J Immunol Res. 2020:1357983.
62. **Felsenstein S., Herbert J.A., McNamara P.S., Hedrich C.M.** (2020) *COVID-19: Immunology and treatment options.* Clin Immunol. 215: 108448.
63. **World Health Organization.** (2020) *. Clinical management of COVID-19: interim guidance, 27 May 2020.* https://apps.who.int/iris/handle/10665/332196.
64. **Rabaan A.A., Al-Ahmed S.H., Muhammad J., Khan A., Sule A.A., Tirupathi R., Mutair A.A., Alhumaid S.,*et al.*** (2021)*Role of Inflammatory Cytokines in COVID-19 Patients: A Review on Molecular Mechanisms, Immune Functions, Immunopathology and Immunomodulatory Drugs to Counter Cytokine Storm.* Vaccines (Basel). 9(5):436.
65. **Brown E., Gray R., Lo Monaco S., O'Donoghue B., Nelson B., Thompson A., Francey S.,McGorry P.** (2020) *The potential impact of COVID-19 on psychosis: a rapid review of contemporary epidemic and pandemic research.* Schizophr Res Article 222,79–87.
66. **Horby P., LimW.S., Emberson J., Mafham M., Bell J.,*et al.***(2020) *Effect of dexamethasone in hospitalized patients with COVID-19: preliminary report.* medRxiv.2020: 20137273.
67. **Loo J., Spittle D.A. and Newnham M.** (2021) *COVID-19, immunothrombosis and venous thromboembolism: biological mechanisms.* Thorax. 76(4), 412-420.
68. **Wu C., Chen X., Cai Y.,*et al.***(2020)*Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China.* JAMA Intern Med. 180(7):1031.
69. **Abrial D., Blanc A., Réhailia M., Mismetti P., Bouchut C., Laporte-Simitsidis S., Decousus H., Buisson B.** (2000)*Establishing the dose-dependent daily variations of a low molecular weight heparin (Fraxiparine) through a population*

approach analysis in the rat. Chronobiol Int.17(2):173-85.

70. **National Health Commission of the People's Republic of China.** *Transcript of press conference in 17, February, 2020. http://www.nhc.gov.cn/xcs/s3574/202002/f12a62d10c2a48c6895cedf2faea6e1f.shtml. 2020.*
71. **Leung P.C.**(2007) *The efficacy of Chinese medicine for SARS: a review of Chinese publications after the crisis.* Am J Chin Med. 35, 575-81.
72. **Carter D.A., Blair S.E., Cokcetin N.N., Bouzo D., Brooks P., Schothauer R.,*et al.***(2016)*Therapeutic manuka honey: No longer so alternative.* Front. Microbiol. 7 (569), 1–11.
73. **Oladele J.O., Ajayi E.I., Oyeleke O.M., Oladele O.T., Olowookere B.D., Adeniyi B.M., Oyewole O.I. and Oladiji A.T.** (2020)*A systematic review on COVID-19 pandemic with special emphasis on curative potentials of Nigeria based medicinal plants.* Heliyon. 6(9):e04897.
74. **Patil B. S., Jayaprakasha G.K., MurthyK. N. C.** (2017) *Beyond vitamin C: the diverse, complex health-promoting properties of citrus fruits.* Citrus Research and Technology.38(1),108-121.
75. **Kaur D. and Chandrul K.K.**(2017) *Syzygium aromaticum L.(Clove): A vital herbal drug used in periodontal disease.* IJPBR. 5(2), 45-51.
76. **Zhang D.-H., Wu K.-L., Zhang X., Deng S.-Q., Peng B.** (2020) *In silico screening of Chinese herbal medicines with the potential to directly inhibit 2019 novel coronavirus.* J. Integr. Med.18, 152–158.
77. **Lee H., Lei H., Santarsiero B.D., Gatuz, J.L., Cao S., Rice A.J., Patel K., Szypulinski M.Z., Ojeda I., Ghosh A.K.,*et al.***(2015)*Inhibitor recognition specificity of MERS-CoV papain-like protease may differ from that of SARS-CoV.* ACS Chem. Biol.*10*, 1456–1465.
78. **Amagase H.**(2006)*Clarifying the real bioactive constituents of garlic.* J. Nutr. 136, 716S–725.
79. **EMA (2017b).**"*European Union herbal monograph onAllium sativum L., bulbus,in EMA/HMPC/7686/2013 Committee on Herbal Medicinal Products (HMPC)* (London: European Medicines Agency).
80. **El-Saber Batiha G., Magdy Beshbishy A., G. Wasef L., Elewa Y. H. A., A. Al-Sagan A., Abd El-Hack M. E.,*et al.*** (2020b). *Chemical Constituents and Pharmacological Activities of Garlic (Allium sativum L.): A Review.* Nutrients 12:872.
81. **Hsu C.H., Hwang K.C., Chao C.L., Chang S.G., Ho M.S. and Chou P.**(2006) *Can herbal medicine assist against avian flu? Learning from the experience of using supplementary treatment with Chinese medicine on SARS or SARS-like infectious disease in 2003.* J Altern Complement Med.12, 505-6.
82. **WHO,***Health response to COVID-19 in Libya, WHO update # 23, Reporting period: 24 December 2020 to 31 January 2021.*