http://www.pjbs.org

PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

OPEN ACCESS Pakistan Journal of Biological Sciences

ISSN 1028-8880
DOI: 10.3923/pjbs.2021.663.671

Research Article
Clinical Findings of COVID-19 Patients at High and Average Altitudes in Saudi Arabia

[1]Ahmad El Askary, [1]Mazen Almehmadi, [2]Mustafa Halawi, [3]Layla Ibrahim Al-Hejji, [4]Abdulaziz Ali Al Hajjiahmed, [1]Ziyad Tariq Arab, [1]Faisal Turki Almalki, [1]Muhannad Alenazi, [5]Rokayya Sami and [1]Alaa Shafie

[1]Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Taif University, P.O. Box 11099, Taif 21944, Saudi Arabia
[2]Medical Laboratory Technology, Applied Medical Sciences College, Jazan University, Jazan, Saudi Arabia
[3]Al-Ahsa Health Affairs, Ministry of Health, Al-Ahsa, Saudi Arabia
[4]Reference Lab, Al Hofouf, Al Ahsa Health Cluster, Ministry of Health, Saudi Arabia
[5]Department of Food Science and Nutrition, College of Sciences, Taif University, P.O. 11099, Taif 21944, Saudi Arabia

Abstract

Background and Objective: Coronavirus disease 2019 (COVID-19), also known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), became a global health issue that influenced the lives of billions of people all over the world. The goal of this study was to investigate the clinical findings and routine laboratory evaluations of COVID-19 patients in both average- and high-altitude settings in Saudi Arabia. **Materials and Methods:** A comparative study to explore the clinical characteristics and Laboratory tests results of COVID-19 patients at both high and average altitudes in Saudi Arabia has been conducted. The study included a total number of 103 patients (53 patients comprising the high-altitude group living in Taif, Saudi Arabia and 50 patients comprising the average-altitude group living in Al Ahsa, Saudi Arabia) were included in the study. Patients were diagnosed with SARS-CoV-2-positive by PCR test. Clinical characteristics, laboratory test results and symptoms of adult patients were collected and expressed as mean and standard deviation. Statistical analysis was done using SPSS software to compare between both groups and significance was considered when the p-value is less than 0.05. **Results:** Approximately 55.3% of the total cases were male with a mean age of 40.16±12.47 years. There were highly statistically significant differences between the groups in age, heart rate ($p<0.001$). There were also statistically significant differences between the groups in temperature, SpO_2, fever, myalgia, shortness of breath and loss of smell and taste. **Conclusion:** The current study provides an understanding of the clinical and laboratory investigations of COVID-19 patients in two regions (high altitude and average altitude) in Saudi Arabia.

Key words: Saudi Arabia, COVID-19, high altitude, average altitude, SARS-CoV-2, respiratory syndrome, angiotensin-converting enzyme 2, leucocytic count

Citation: El Askary, A., M. Almehmadi, M. Halawi, L.I. Al-Hejji, A.A. Al Hajjiahmed, Z.T. Arab, F.T. Almalki, M. Alenazi, R. Sami and A. Shafie, 2021. Clinical findings of COVID-19 patients at high and average altitudes in Saudi Arabia. Pak. J. Biol. Sci., 24: 663-671.

Corresponding Author: Rokayya Sami, Department of Food Science and Nutrition, College of Sciences, Taif University, P.O. 11099, Taif 21944, Saudi Arabia

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

A new and evolving respiratory virus was identified at the end of 2019 in Wuhan, the capital of the Hubei province in China[1,2]. The virus causes dangerous pneumonia in infected individuals and is highly contagious, causing the disease to rapidly spread in China and leading to an epidemic. The infection soon showed signs of spreading outside China and a significant number of cases were diagnosed in many other countries with an alarming rate of infection[3-5]. Researchers were able to isolate the virus that causes the infection and, in some cases, leads to the development of the severe acute respiratory syndrome. The virus was determined to be a new strain of the coronavirus family. The viral genome was sequenced and recognized as a betacoronavirus from the same subgenus as a Severe Acute Respiratory Syndrome (SARS), though it was a newly identified strain[6]. The scientists named the new virus severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) and the new respiratory disease caused by the virus COVID-19[7-10]. The viral receptor-binding gene also was identified; it showed high similarity to the SARS coronavirus family as the new SARS CoV-2 virus enters the cell via the same receptor. This receptor is the Angiotensin-Converting Enzyme 2 (ACE2) receptor[6,11]. Most cases of SARS CoV-2 are mild. The clinical picture of COVID-19 infection includes fever, cough and fatigue. The infection is more prevalent in males than females, which may be due to increased exposure. Fever and cough were the predominant symptoms and were found in most cases, with over 90% of patients presenting with more than one symptom. Only a small number of cases progress to severe acute respiratory distress syndrome[7,8]. Previous studies showed that the proportion of fatal or severe infection may vary according to location. Although the serious disease can occur in otherwise healthy people of any age, it is more common in people over the age of 65 or with underlying chronic diseases[12,13]. Chronic diseases that have been associated with the severity of COVID-19 illness and increased risk of mortality include cardiovascular diseases, diabetes mellitus, hypertension, chronic lung diseases, cancer, chronic kidney diseases and obesity[14,15]. The understanding of pathological mechanisms and prediction of severe cases is critical for optimising treatment and prognosis of patients with SARS CoV-2. Understanding pathological laboratory findings can also guide strategies to find a new treatment or vaccine[8]. A healthy blood oxygen level is normally above 95%. The partial pressure of oxygen (PaO_2) is low in high-altitude areas. The PaO_2 may be also altered by ageing[14-16]. Residency in high-altitude regions may cause significant pulmonary changes that may aggravate the condition of COVID-19 patients. The effect of high altitude on outcomes of patients with SARS CoV-2 infection is unclear. The primary laboratory parameters reported in previous studies on COVID-19 that can be correlated to the severity of illness are elevated levels of Total Leucocytic Count (TLC), Lactate Dehydrogenase (LDH), Alanine Transaminase (ALT), Aspartate Transaminase (AST), total bilirubin, prothrombin time (PT), D-dimer test, serum ferritin, C-reactive protein, cardiac troponin and procalcitonin (PCT), as well as decreased levels of lymphocytes and serum albumin[17].

This research aimed to correlate the clinical characteristics and routine laboratory values of COVID-19 patients with severity of illness in average- and high-altitude settings.

MATERIALS AND METHODS

Study area: The study was conducted between October-December, 2020 at the Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Taif University, Saudi Arabia.

Sample collection: The high-altitude group comprised 53 COVID-19 patients residing at high altitude (approximately 1879 m above sea level) in Taif, Saudi Arabia and the average-altitude group comprised 50 COVID-19 patients residing at average altitude in Al Ahsa, Saudi Arabia. Patients were recruited from COVID-19 isolation hospitals in the 2 cities. Ethical approval was obtained from the Taif University Ethics Committee before beginning the study (approval no. 42-0010). Informed consent was obtained from all patients before enrolment in the study. Diagnosis of COVID-19 was established by positive PCR and clinical and laboratory data were collected from patients in the early stage of the disease, between day 5 and day 12 of symptom appearance. Patients were not receiving corticosteroid treatment. Statistical analysis of collected data was done to explore the effect of residing at high altitudes on the presentation of COVID-19.

Statistical analysis: Collected data were statistically analysed using SPSS software version 20.0 (SPSS Inc, Chicago, US). The data were presented as mean±SD. A p-value<0.05 was considered significant.

RESULTS

The age range of the study sample (n = 103) was 15-69 years, with a mean age of 40.16±12.47 years. As shown in Table 1, there was a statistically significant difference

Table 1: Comparison between high altitude and average altitude according to age (years)

Demographic data	High altitude (n = 53)	Average altitude (n = 50)	Total (n = 103)	Test	p-value
Age (years)					
Mean±SD	45.51±10.81	34.37±11.60	40.16±12.47	t = 5.020	<0.001**
Range	21-69	15-54	15-69		
Sex					
Male (%)	24 (45.3)	33 (66.0)	57 (55.3)	$\chi^2 = 3.669$	0.055
Female (%)	29 (54.7)	17 (34)	46 (44.7)		

t: Independent sample t-test, Chi-square test, p-value>0.05 NS: **p-value<0.001 HS

Table 2: Comparison between High altitude and Average altitude according to vital signs

Vital signs	High altitude (n = 53)	Average altitude (n = 50)	Total (n = 103)	t-test	p-value
T (C)					
Mean±SD	37.64±0.96	38.11±0.80	37.86±0.91	-2.681	0.009*
Range	36-39.8	36-39.4	36-39.8		
P (b min^{-1})					
Mean±SD	97.55±13.07	114.86±18.01	102.70±16.57	-3.700	<0.001**
Range	77-125	89-146	77-146		
SpO_2 (%)					
Mean±SD	94.87±3.09	96.61±1.88	95.80±2.65	-3.137	0.002*
Range	84-99	90-99	84-99		

T: Temperature, P: Pulse, SpO_2: Oxygen saturation, *p-value <0.05 S, **p-value<0.001 HS

Table 3: Comparison between high altitude and average altitude according to clinical presentation

Complains	High altitude (n = 53) (%)	Average altitude (n = 50) (%)	Total (n = 103) (%)	χ^2	p-value
Fever	33 (62.3)	42 (84.0)	75 (72.8)	6.141	0.013*
Runny nose	5 (9.4)	8 (16.0)	13 (12.6)	1.006	0.316
Cough	24 (45.3)	29 (58.0)	53 (51.5)	1.666	0.197
Sore throat	10 (18.9)	5 (10.0)	15 (14.6)	1.626	0.202
Chest pain	0 (0.0)	0 (0.0)	0 (0.0)	0.000	1.000
Shortness of breath	23 (43.4)	9 (18.0)	32 (31.1)	7.748	0.005*
Headache	25 (47.2)	22 (44.0)	47 (45.6)	0.104	0.747
Myalgia	25 (47.2)	12 (24.0)	37 (35.9)	6.000	0.014*
Nausea	0 (0.0)	0 (0.0)	0 (0.0)	0.000	1.000
Vomiting	0 (0.0)	2 (4.0)	2 (1.9)	2.162	0.141
Diarrhea	9 (17.0)	11 (22.0)	20 (19.4)	0.414	0.520
Loss of smell and taste	9 (17.0)	0 (0.0)	9 (8.7)	9.303	0.002*

χ^2: Chi-square test, p-value>0.05 NS, *p-value<0.05 S

between groups regarding age (p<0.001). The mean age in the high-altitude group was higher than the mean age in the average-altitude group.

In the total study sample (n = 103), 55.3% of participants were male. There was not a statistically significant difference between groups in sex (p = 0.055). In the high-altitude group, 45.3 were male and 54.7% were female while in the average-altitude group, 66 were male and 34% were female (Table 1).

In the entire study sample (n = 103), the heart rate range in beats per minute (bpm) was 77-146 bpm with a mean of 102.70±16.57 bpm. As demonstrated in Table 2, there was a highly statistically significant difference in heart rate between groups (p<0.001). The average-altitude group demonstrated a higher mean heart rate (114.86±18.01 bpm) than the high-altitude group (97.55±13.07 bpm).

In the study sample (n = 103), the temperature ranged from 36-39.8°C with a mean of 37.86±0.91°C. There was a statistically significant difference between groups in temperature (p = 0.009). The mean temperature in the average-altitude group was higher (38.11±0.80°C) than in the high-altitude group (37.64±0.96°C).

In the study sample (n = 103), oxygen saturation (SpO_2) ranged from 84-99% with a mean of 95.80±2.65%. There was a statistically significant difference between groups in SpO_2 (p = 0.002). The average-altitude group demonstrated a higher SpO_2 (96.61±1.88%) than the high-altitude group (94.87±3.09%).

As shown in Table 3, there was a statistically significant difference between groups in presence of fever (p = 0.013); more patients in the average-altitude group presented with a fever (84.0%) than in the high-altitude group (62.3%).

Table 4: Comparison between high altitude and average altitude according to random blood glucose level

Glucose	High altitude (n = 53)	Average altitude (n = 50)	Total (n = 103)	t-test	p-value
RBS (mmol L^{-1})					
Mean±SD	8.68±4.97	6.70±2.94	7.72±5.16	2.978	0.021*
Range	4.3-31.7	4.6-30.73	4.3-31.7		

t: Independent sample t-test, *p-value<0.05 S

Table 5: Comparison between high altitude and average altitude according to complete blood count (CBC) parameters

CBC	High altitude (n = 53)	Average altitude (n = 50)	Total (n = 103)	t-test	p-value
HGB (g dL^{-1})					
Mean±SD	12.43±1.72	13.42±1.88	12.91±1.85	-2.778	0.007*
Range	6.9-15.7	8.4-17.2	6.9-17.2		
WBC (×10^3 mL^{-1})					
Mean±SD	5.47±3.10	5.36±2.03	5.42±2.62	0.215	0.830
Range	2-22.1	2.5-15.6	2-22.1		
PLT (×10^3 mL^{-1})					
Mean±SD	253.58±99.39	230.12±57.98	242.19±82.40	1.452	0.150
Range	97-594	130-404	97-594		

t: Independent sample t-test, p-value>0.05 NS, *p-value<0.05 S

Table 6: Comparison between high altitude and average altitude according to lactate dehydrogenase (LDH)

LDH (U L^{-1})	High altitude (n = 53)	Average altitude (n = 50)	Total (n = 103)	t-test	p-value
Mean±SD	244.77±99.74	209.67±66.78	227.91±86.90	2.071	0.041*
Range	106-613	135-456	106-613		

t-Independent sample t-test, *p-value<0.05 S

Table 7: Comparison between high altitude and average altitude according to renal function test (RFT)

RFT	High altitude (n = 53)	Average altitude (n = 50)	Total (n = 103)	t-test	p-value
Urea (mmol L^{-1})					
Mean±SD	5.37±9.93	4.17±1.01	4.80±7.18	0.844	0.400
Range	1.7-75	2.6-6.7	1.7-75		
Creatinine (mmol L^{-1})					
Mean±SD	86.42±25.60	78.78±15.91	82.75±21.74	1.793	0.076
Range	2.1-181	46-118	2.1-181		

t: Independent sample t-test, p-value>0.05 NS

Besides, there was a statistically significant difference between groups in the symptoms of shortness of breath (p = 0.005), myalgia (p = 0.014) and loss of smell and taste (p = 0.002). Each of these symptoms was more prevalent in the high-altitude group (43.4 vs. 18.0; 47.2 vs. 24 and 17 vs. 0%), respectively.

As shown in Table 4, there was a statistically significant difference in Random Blood Sugar (RBS) between the high-altitude and average-altitude groups (p = 0.021), with the high-altitude group demonstrating an RBS of 8.68±4.97 mmol L^{-1} and the average-altitude group demonstrating an RBS of 6.70±2.94 mmol L^{-1}.

As Table 5 displays the statistically significant difference between groups in haemoglobin levels (p = 0.007); the mean haemoglobin in the high-altitude group was 12.43±1.72 g dL^{-1} compared to 13.42±1.88 g dL^{-1} in the average-altitude group. This finding regarding haemoglobin level may be explained by the mean age of COVID-19 patients, which was higher in the high-altitude group; also there was increased ratio of female patients in the high-altitude group. There was no statistically significant difference between groups in White Blood Cell count (WBC) (p = 0.830) or Platelet Count (PLT) (p = 0.150).

As shown in Table 6, there was a statistically significant difference between groups in LDH (p = 0.041); the mean LDH in the high-altitude group was 244.77±99.74 U L^{-1} compared to a lower value of 209.67±66.78 U L^{-1} in the average-altitude group.

The data of Table 7 illustrates no statistically significant difference between groups in urea (p = 0.400) and creatinine (p = 0.076) levels. In the high-altitude group, the mean urea level was 5.37±9.93 and mean creatinine level was 86.42±25.60, which were higher than the mean urea level of 4.17±1.01 and mean creatinine level of 78.78±15.91 that were found in the average-altitude group.

The mean AST and ALT levels of the total sample were 28.06±21.86 U L^{-1} and 45.57±31.36 U L^{-1}, respectively. The data of Table 8 shows that there was no statistically significant difference between groups in AST (p = 0.855) and ALT (p = 0.540) levels. The high-altitude group

Table 8: Comparison between high altitude and average altitude according to liver function test (LFT)

LFT	High altitude (n = 53)	Average altitude (n = 50)	Total (n = 103)	t-test	p-value
AST (U L^{-1})					
Mean±SD	27.69±22.90	28.74±20.29	28.06±21.86	-0.184	0.855
Range	7-127	7-81	7-127		
ALT (U L^{-1})					
Mean±SD	43.79±30.49	48.83±33.34	45.57±31.36	-0.617	0.540
Range	15-167	15-167	15-167		

t: Independent sample t-test, p-value>0.05 NS

demonstrated a mean AST of 27.69±22.90 and mean ALT of 43.79±30.49; the average-altitude group demonstrated higher values, with a mean AST of 28.74±20.29 and a mean ALT of 48.83±33.34.

DISCUSSION

COVID-19, the disease caused by the SARS-CoV-2 virus, has caused a pandemic. However, there have been few studies from different geographic regions, including people living at higher elevations. The current study was conducted to compare the clinical features of COVID-19 patients at high altitude with patients at average altitude. Our results revealed a significant difference between patients at high and average altitudes regarding age, heart rate, temperature, SpO_2, fever, myalgia, shortness of breath and loss of smell. Since the beginning of the pandemic, age has been recognized as the key prognostic determinant in COVID-19 patients[18-21], though the age distribution of patients with COVID-19 is variable. In our study, a significant difference in the mean age of our 2 groups was found ($p<0.001$), with a mean age of 45.51±10.81 years in the high-altitude group and 34.37±11.60 years in the average-altitude group. In previous studies in Saudi Arabia, AlJishi *et al.*[22] documented that the mean age of COVID-19 patients was 50 years. In contrast, Alsofayan *et al.*[23] found a mean age of 36 years and Barry *et al.*[24] found a mean age of 44 years for COVID-19 patients in Saudi Arabia.

Regarding gender, the present study found a higher percentage of male COVID-19 patients across the total sample (55.3% male), though differences were noted between groups, with a higher prevalence of males in the average-altitude group (66% male) but a higher prevalence of females in the high-altitude group (54.7% female). In a study conducted by Al Mutair *et al.*[25], 80% of patients were male, while a study by AlJishi *et al.*[22] found that 65.9% of patients were female. Previous researches observed that males had a slower viral clearance in comparison to females[26-28].

In the patients of the high-altitude group, 62.3% had a fever, 43.4% had shortness of breathing, 47.2% had myalgia and 17% experienced loss of smell and taste. In contrast, in the patients of the average-altitude group, 84.0% had a fever, 18% suffered from shortness of breathing, 24% reported myalgia and none lost their sense of smell and taste. These results indicate that the clinical symptoms of COVID-19 were more prominent in patients living at high altitude than in patients living at average altitude.

The results are compatible with previous research by Al Mutair *et al.*[25], in which cough, fever, fatigue and shortness of breath were prominent symptoms of COVID-19. Another study conducted in Saudi Arabia by Barry *et al.*[24] found that the most frequent symptoms of COVID-19 were high temperature (67.7%), cough (60.6%), difficulty in breathing (43.4%), upper respiratory tract symptoms (27.3%), nausea (26.3%), diarrhoea (19.2%) and lost smelling sensation (9.1%). The most common symptoms reported by Jin *et al.*[29] were fever (95.3%) and cough (65.1%), while diarrhoea (16.3%) was not common. Fu *et al.*[30] found that fever (83.3%), cough (60.3%) and fatigue (38.0%) were the most common clinical symptoms. The primary clinical symptoms of COVID-19 patients reported by Li *et al.*[31] was elevated body temperature (88.5%), fatigue (35.8%), cough (68.6%), sputum (28.2%) and shortness of breathing (21.9%). Also, minor findings like headache (12.1%), nausea and vomiting (3.9%) in addition to diarrhoea (4.8%). Shortness of breath was the most common presenting complaint in 55.3% of patients, followed closely by cough and fever in a study by Bahl *et al.*[32]. Most studies on hospitalized patients from Wuhan, as reflected in the findings of Sharma *et al.*[33], revealed that the common symptoms of COVID-19 were fever (83-98%), fatigue (70%), dry cough (59%), anorexia (40%), myalgia (35%), dyspnoea (31%) and sputum production (27%).

In the current study, there was a statistically significant difference between groups in SpO_2 ($p = 0.002$); mean SpO_2 in the high-altitude group was 94.87±3.09% compared to 96.61±1.88% in the average-altitude group. This may be attributed to the hypoxia present at high altitude. Patients with COVID-19 often demonstrate hypoxia without equivalent characteristics of respiratory distress which is defined as silent hypoxia[34].

The heart rate range in the high-altitude group was 77-125 bpm compared to 89-146 bpm in the average-altitude group. The temperature range in the high-altitude group was 36-39.8 and 36-39.4°C in the average-altitude group. Previous research by Ikeuchiet *et al.*[35] showed that at admission, the average body temperature was 37.2°C and the average pulse rate was 84 beats per minute. During admission, 13.0% of patients had a high-grade fever (temperature>38.9°C) and all of them had a pulse rate of fewer than 120 beats per minute.

There was a statistically significant difference between groups in RBS ($p = 0.021$), with the high-altitude group demonstrating a mean RBS of 8.68±4.97 mmol L^{-1} and the average-altitude group demonstrating a mean RBS of 6.70±2.94 mmol L^{-1}. Chen *et al.*[36] has proposed that there could be a close association between the magnitude of COVID-19 and glycemic criteria, including people who do not have diabetes.

They found that blood glucose was significantly higher in patients with severe COVID-19 than those with mild COVID-19. Zhang *et al.*[37] demonstrated that COVID-19 infection resulted in an increase in blood glucose, even in those who had not been diagnosed with diabetes before admission.

There was a statistically significant difference between groups in LDH levels ($p = 0.041$), with a mean LDH in the high-altitude group of 244.77±99.74 U L^{-1} and a mean LDH in the average-altitude group of 209.67±66.78 U L^{-1}. In patients with COVID-19, high LDH levels have been linked to a 6-fold increase in the risk of developing severe disease and a 16-fold increase in the risk of death[38]. In a study by Serinet *et al.*[39], mean LDH was 268.56±140.39 U L^{-1} and Chen *et al.*[40] found that LDH was significantly increased in most patients.

The mean haemoglobin in the high-altitude group was 12.43±1.72 and the mean haemoglobin in the average-altitude group was 13.42±1.88. The mean WBC count in the high-altitude group was 5.47±3.10 and 5.36±2.03 $\times 10^3$ mL in the average-altitude group. The mean PLT in the high-altitude group was 253.58±99.39 and 230.12±57.98 $\times 10^3$ mL in the average-altitude group. A recent study on blood indices in COVID-19-positive individuals revealed that most patients had a normal complete blood count and LDH on admission. None of the patients presented with moderate or severe thrombocytopenia, which is a common finding in other viral illnesses including dengue fever[41]. A meta-analysis on available heterogeneous studies showed that severe cases of COVID-19 were characterised by substantially decreased haemoglobin values compared to mild cases, which confirmed previous evidence gathered from patients with other types of pneumonia[42].

Platelets are at the forefront of COVID-19 pathogenesis, as they release different molecules through different stages of the disease[43]. COVID-19 patients frequently have moderate thrombocytopenia and tend to have improved platelet intake as well as platelet production[44]. Platelet count was significantly reduced in patients with more severe COVID-19[45]

Previous studies have shown normal WBC count in 90% of patients with COVID-19[46]. The majority of the COVID-19 patients studied by AlJishi *et al.*[22] demonstrated normal WBC. About 9% of cases had reduced leucocytic cont, but the proportion of lymphopenia was also as high as 35%[40]. In contrast, Zhongnan Hospital of Wuhan University recorded clinical features of 138 patients with COVID-19 and found that up to 70.3% of them developed lymphopenia with a median lymphocyte count of 0.8×10^9 L^{-1} [47].

In the current study, urea levels ranged from 1.7-75 in the high-altitude group and 2.6-6.7 in the average-altitude group. The mean creatinine was 2.1-181 in the high-altitude group and 46-118 in the average-altitude group. In a study by Hong *et al.*[48], serum creatinine levels were not abnormally high in all cases and Blood Urea Nitrogen (BUN) levels were abnormally high in just 25% of the patients. Similarly, Li *et al.*[49] found that BUN was elevated in 27% of COVID-19 patients, with higher levels of BUN present in 2 patients who died. Serum creatinine was elevated in 19% of the patients, with extremely high levels noted in the patients who died.

The mean AST was 27.69±22.90 in the high-altitude group and 28.74±20.29 in the average-altitude group. The mean ALT was 43.79±30.49 in the high-altitude group and 48.83±33.34 in the average-altitude group. Similar to our results, Chen *et al.*[40] reported that 43 of 99 COVID-19 patients had variable liver enzyme disorders (e.g., ALT and AST) and 1 patient had a significant rise in hepatic enzymes (ALT 7590 U L^{-1}, AST 1445 U L^{-1}), resulting in liver disease. It has been found that 2–11% of patients with COVID-19 had liver comorbidities and 14-53% of patients had abnormal ALT and AST levels during the COVID-19 disease progression[50]. Liver injury is more prevalent in severe cases compared to mild cases of COVID-19.

The study had limitations that warrant mentioning. The sample size was relatively small and thus results of this study may not reflect the true picture of a large cohort. Unfortunately, we were unable to access radiological findings in this study, which would have increased the clinical picture of patients with COVID-19.

CONCLUSION

The current study provides insight into the clinical and laboratory investigations of COVID-19 patients in high and average altitudes in Saudi Arabia. COVID-19 patients at high altitude showed significantly lower blood oxygen levels and higher LDH levels. Also, symptoms of COVID-19 infection like shortness of breathing, myalgia, loss of smell and taste were more prominent in patients living at high altitude.

SIGNIFICANCE STATEMENT

This study discovers the effect of living at a high altitude on the clinical presentation of COVID-19 patients. The possible effect of living at a high altitude on COVID-19 patients is still unclear and this work can add unique knowledge about this point. This study will help the researchers to explore the impact of living at high altitudes on the clinical features of patients with COVID-19 in Saudi Arabia.

ACKNOWLEDGMENT

The authors acknowledge the support of the Deanship of Scientific Research at Taif University through the project (1-441-32). The authors also would like to extend their sincere thanks to all medical staff of King Faisal Hospital in Taif city, Saudi Arabia especially the laboratory staff Ms. Khadijah Hassan and Mr. Turki Al-Malki.

REFERENCES

1. Zhu, N., D. Zhang, W. Wang, X. Li and B. Yang *et al*., 2020. A novel coronavirus from patients with pneumonia in China, 2019. N. Engl. J. Med., 382: 727-733.
2. Chan, J.F.W., K.H. Kok, Z. Zhu, H. Chu, K.K.W. To, S. Yuan and K.Y. Yuen, 2020. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. Emerging Microbes Infect., 9: 221-236.
3. The Lancet, 2020. Emerging understandings of 2019-nCoV. Lancet, 395: 311-311.
4. Bassetti M., A. Vena and D.R. Giacobbe, 2020. The novel Chinese coronavirus (2019 nCoV) infections: Challenges for fighting the storm. Eur. J. Clin. Invest., 50: 13209-13209.
5. Rothe, C., M. Schunk, P. Sothmann, G. Bretzel and G. Froeschl *et al*., 2020. Transmission of 2019-nCoV infection from an asymptomatic contact in germany. N. Engl. J. Med., 382: 970-971.
6. Lu, R., X. Zhao, J. Li, P. Niu and B. Yang *et al*., 2020. Genomic characterisation and epidemiology of 2019 novel coronavirus: Implications for virus origins and receptor binding. Lancet, 395: 565-574.
7. Gibson, P.G., L. Qin and S.H. Puah, 2020. COVID-19 acute respiratory distress syndrome (ARDS): Clinical features and differences from typical pre-COVID-19 ARDS. Med. J. Aust., 213: 54-56.
8. Yang, X., Y. Yu, J. Xu, H. Shu and H. Liu *et al*., 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet, 395: 497-506.
9. Saeidi, A., K. Zandi, Y.Y. Cheok, H. Saeidi and W.F. Wong *et al*., 2018. T-cell exhaustion in chronic infections: Reversing the state of exhaustion and reinvigorating optimal protective immune responses. Front. Immunol., Vol. 9. 10.3389/fimmu.2018.02569.
10. Liu, W.J., M. Zhao, K. Liu, K. Xu, G. Wong, W. Tan and G.F. Gao, 2017. T-cell immunity of SARS-CoV: Implications for vaccine development against MERS-CoV. Antiviral Res., 137: 82-92.
11. Wan, Y., J. Shang, R. Graham, R.S. Baric and F. Li, 2020. Receptor recognition by the novel coronavirus from wuhan: An analysis based on decade-long structural studies of SARS coronavirus. J. Virol., Vol. 94. 10.1128/JVI.00127-20.
12. Qin, L., X. Jing, Z. Qiu, W. Cao, Y. Jiao, J.P. Routy and T. Li, 2016. Aging of immune system: Immune signature from peripheral blood lymphocyte subsets in 1068 healthy adults. Aging, 8: 848-859.
13. Yang, W., Q. Cao, L. Qin, X. Wang and Z. Cheng *et al*., 2020. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multi-center study in Wenzhou city, Zhejiang, China. J. Infect., 80: 388-393.
14. Bärtsch, P. and E.R. Swenson, 2013. Acute high-altitude illnesses. N. Engl. J. Med., 369: 1664-1667.
15. Azad, P., T. Stobdan, D. Zhou, I. Hartley, A. Akbari, V. Bafna and G.G. Haddad, 2017. High-altitude adaptation in humans: From genomics to integrative physiology. J. Mol. Med., 95: 1269-1282.
16. Zeng, J., S. Peng, Y. Lei, J. Huang and Y. Guo *et al*., 2020. Clinical and imaging features of COVID-19 patients: Analysis of data from high-altitude areas. J. Infect., 80: e34-e36.
17. Wang, F., H. Hou, Y. Luo, G. Tang and S. Wu *et al*., 2020. The laboratory tests and host immunity of COVID-19 patients with different severity of illness. JCI Insight, Vol. 5. 10.1172/jci.insight.137799.
18. Bonanad, C., S. García-Blas, F. Tarazona-Santabalbina, J. Sanchis and V. Bertomeu-González *et al*., 2020. The effect of age on mortality in patients with COVID-19: A meta-analysis with 611,583 subjects. J. Am. Med. Directors Assoc., 21: 915-918.

19. Wang, P., J. Sha, M. Meng, C. Wang and Q. Yao *et al*., 2020. Risk factors for severe COVID-19 in middle-aged patients without comorbidities: A multicentre retrospective study. J. Transl. Med., Vol. 18. 10.1186/s12967-020-02655-8.
20. Ashktorab, H., A. Pizuomo, N.A.F. González, E.D.C. Villagrana and M.E. Herrera-Solís *et al*., 2021. A comprehensive analysis of COVID-19 impact in latin America. BMC Infect. Dis., 10.21203/rs.3.rs-141245/v1.
21. Liu, K., Y. Chen, R. Lin and K. Han, 2020. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. J. Infect., 80: e14-e18.
22. AlJishi, J.M., A.H. Alhajjaj, F.L. Alkhabbaz, T.H. AlAbduljabar and A. Alsaif *et al*., 2021. Clinical characteristics of asymptomatic and symptomatic COVID-19 patients in the Eastern Province of Saudi Arabia. J. Infect. Public Health, 14: 6-11.
23. Alsofayan, Y.M., S.M. Althunayyan, A.A. Khan, A.M. Hakawi and A.M. Assiri, 2020. Clinical characteristics of COVID-19 in Saudi Arabia: A national retrospective study. J. Infect. Public Health, 13: 920-925.
24. Barry, M., A. AlMohaya, A. AlHijji, L. Akkielah and A. AlRajhi *et al*., 2020. Clinical characteristics and outcome of hospitalized COVID-19 Patients in a MERS-CoV endemic area. J. Epidemiol. Glob Health, 10: 214-221.
25. Al Mutair, A., S. Alhumaid, W.N. Alhuqbani, A.R.Z. Zaidi and S. Alkoraisi *et al*., 2020. Clinical, epidemiological, and laboratory characteristics of mild-to-moderate COVID-19 patients in Saudi Arabia: An observational cohort study. Eur. J. Med. Res., Vol. 25. 10.1186/s40001-020-00462-x.
26. Xu, K., Y. Chen, J. Yuan, P. Yi and C. Ding *et al*., 2020. Factors associated with prolonged viral RNA shedding in patients with coronavirus disease 2019 (COVID-19). Clin. Infect. Dis., 71: 799-806.
27. Zheng, S., J. Fan, F. Yu, B. Feng and B. Lou *et al*., 2020. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: Retrospective cohort study. BMJ, Vol. 369. 10.1136/bmj.m1443.
28. Pradhan, A. and P.E. Olsson, 2020. Sex differences in severity and mortality from COVID-19: Are males more vulnerable? Biol. Sex Differ., Vol. 11. 10.1186/s13293-020-00330-7.
29. Jin, J.M., P. Bai, W. He, F. Wu and X.F. Liu *et al*., 2020. Gender differences in patients with COVID-19: Focus on severity and mortality. Front. Public Health, Vol. 8. 10.3389/fpubh.2020.00152.
30. Fu, L., B. Wang, T. Yuan, X. Chen and Y. Ao *et al*., 2020. Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. J. Infect., 80: 656-665.
31. Li, L.Q., T. Huang, Y.Q. Wang, Z.P. Wang and Y. Liang *et al*., 2020. COVID 19 patients' clinical characteristics, discharge rate, and fatality rate of meta analysis. J. Med. Virol., 92: 577-583.
32. Bahl, A., M.N. Van Baalen, L. Ortiz, N.W. Chen and C. Todd *et al*., 2020. Early predictors of in-hospital mortality in patients with COVID-19 in a large American cohort. Internal Emergency Med., 15: 1485-1499.
33. Sharma, R., M. Agarwal, M. Gupta, S. Somendra and S.K. Saxena, 2020. Clinical Characteristics and Differential Clinical Diagnosis of Novel Coronavirus Disease 2019 (COVID-19). In: Coronavirus Disease 2019 (COVID-19), Saxena, S. (Ed.)., Springer, Singapore, pp: 55–70.
34. Ottestad, W., M. Seim and J.O. Maehlen, 2020. Covid-19 med stille hypoksemi. Tidsskriftet Den Norske Legeforening, Vol. 140. 10.4045/tidsskr.20.0299.
35. Ikeuchi, K., M. Saito, S. Yamamoto, H. Nagai and E. Adachi, 2020. Relative bradycardia in patients with mild-to-moderate coronavirus disease, Japan. Emerg. Infect. Dis., 26: 2504-2506.
36. Chen, J., C. Wu, X. Wang, J. Yu and Z. Sun, 2020. The impact of COVID-19 on blood glucose: A systematic review and meta-analysis. Front. Endocrinol., Vol. 11. 10.3389/fendo.2020.574541.
37. Zhang, Y., H. Li, J. Zhang, Y. Cao and X. Zhao *et al*., 2020. The clinical characteristics and outcomes of patients with diabetes and secondary hyperglycaemia with coronavirus disease 2019: A single centre, retrospective, observational study in Wuhan. Diabetes Obesity Metab., 22: 1443-1454.
38. Henry, B.M., G. Aggarwal, J. Wong, S. Benoit, J. Vikse, M. Plebani and G. Lippi, 2020. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. Am. J. Emerg. Med., 38: 1722-1726.
39. Serin, I., N.D. Sari, M.H. Dogu, S.D. Acikel and G. Babur *et al*., 2020. A new parameter in COVID-19 pandemic: Initial lactate dehydrogenase (LDH)/lymphocyte ratio for diagnosis and mortality. J. Infect. Public Health, 13: 1664-1670.
40. Chen, N., M. Zhou, X. Dong, J. Qu and F. Gong *et al*., 2020. Epidemiological and clinical characteristics of 99 cases of 2019 novel Coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet, 395: 507-513.
41. Fan, B.E., V.C.L. Chong, S.S.W. Chan, G.H. Lim and K.G.E. Lim *et al*., 2020. Hematologic parameters in patients with COVID 19 infection. Am. J. Hematol., 95: E131-E134.
42. Lippi, G. and C. Mattiuzzi, 2020. Hemoglobin value may be decreased in patients with severe coronavirus disease 2019. Hematol. Transfusion Cell Ther., 42: 116-117.
43. Zaid, Y., F. Puhm, I. Allaeys, A. Naya and M. Oudghiri *et al*., 2020. Platelets can associate with SARS-Cov-2 RNA and are hyperactivated in COVID-19. Circ. Res., 127: 1404-1418.
44. Wool, G.D. and J.L. Miller, 2021. The impact of COVID-19 disease on platelets and coagulation. Pathobiology, 88: 15-27.
45. Lippi, G., M. Plebani and B.M. Henry, 2020. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. Clin. Chim. Acta, 506: 145-148.

46. Han, R., L. Huang, H. Jiang, J. Dong, H. Peng and D. Zhang, 2020. Early clinical and CT manifestations of coronavirus disease 2019 (COVID-19) pneumonia. Am. J. Roentgenol., 215: 338-343.
47. Wang, D., B. Hu, C. Hu, F. Zhu and X. Liu *et al*., 2020. Clinical characteristics of 138 hospitalized patients with 2019 novel Coronavirus–infected pneumonia in Wuhan, China. JAMA., 323: 1061-1069.
48. Hong, X.W., Z.P. Chi, G.Y. Liu, H. Huang and S.Q. Guo *et al*., 2020. Characteristics of renal function in patients diagnosed with COVID-19: An observational study. Front. Med., Vol. 7. 10.3389/fmed.2020.00409.
49. Wang, T., M. Hu, X. Chen, Y. Fu and C. Lei *et al*., 2020. Caution on kidney dysfunctions of COVID-19 patients. MedRxiv, Vol. 2020. 10.1101/2020.02.08.20021212.
50. Zhang, C., L. Shi and F.S. Wang, 2020. Liver injury in COVID-19: Management and challenges. Lancet Gastroenterol. Hepatol., 5: 428-430.