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ORIGINAL ARTICLE

Prediction of Complications and Death in Covid-19 Patients with Deranged Liver Function Tests at Time of Admission and Hospitalization

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ABSTRACT

COVID-19 pandemic has affected millions of individuals globally over the last three years and is spreading continuously. In view of different studies and clinical findings, patients suffering with COVID-19 frequently have deranged liver function tests (LFTs), but the clinical significance of this finding is debatable.

Objective: The present study was aimed to estimate the prevalence, features, and clinical significance of deranged LFTs in COVID-19 infected individuals, who were hospitalized but were not critically ill.

Method: We conducted a cross sectional from May 2021 to December 2021 at The Akbar Niazi Teaching Hospital Islamabd. A total of 250 COVID-19 patients were included in the current study. The patient's blood samples were collected to get laboratory results, which included LFTs. LFTs were performed at the time of admission and every 5 ± 2 day throughout the stay. The outcome measure was either death or transfer of the patients to an intensive care unit.

Results: At the time of admission, 160 patients (64%) showed deranged LFTs. Individuals with deranged LFTs experienced more severe inflammation, swelling, and organ damage than those who didn't. Patients with deranged LFTs had a greater proportion of transfer to the ICU (81 vs 17), hospital stay (17 vs 7 days), and death (17 vs 5) than those with normal LFTs.

Conclusion: The results of the current investigation demonstrated that LFTs data might forecast the degree of illness in patients with COVID-19 infections at the time of admission and during their hospital stay.

Keywords: Covid-19, Liver Function Tests, ICU, Mortality Rate, Pakistan

NTRODUCTION

After the discovery of covid-19 during a recent epidemic in China, (1, 2) now the virus has spread around the world, infecting 250 million individuals and resulted in 5 million death as of Nov, 2021.(3) Infected Patients could present with mild to moderate symptoms, but the majority of individuals will be asymptomatic carrier of the disease. Infected individuals usually present with the prevalent symptoms of cough, fever, and dyspnea.(4) Chest X-rays of the Covid-19 infected individuals typically have ground-glass opacity.(5) COVID-19's major clinical hallmark is pneumonia leading to significantly high mortality rate. The current evidences and findings suggests that COVID-19 is a systemic illness that affects other vital organs including the liver, heart, and kidney.(6) Despite the fact that the lung is the primary site of coronavirus infection, it is important to constantly monitor the cardiac, digestive, kidney, liver, central nervous system, and ocular systems due to the widespread presence of ACE 2 receptors in various organs. (7, 8) An elevation of 14% to 75% was observed in LFTs along with serum albumin and Prothrombin Time values of patients suffering/infected with COVID-19 (9)

The clinical significance of deranged LFTs has been discussed, with few studies linking them to the incidence of COVID-19 pneumonia. (10, 11) Those investigations were limited by the lack of information concerning simultaneous or past usage of hepatotoxic medications. Overall, research examining the frequency, pattern, and clinical significance of LFTs are few, particularly in Islamabad, Pakistan. On a clinical level, it's still unclear whether deranged LFTs should be regarded as a sign of disease severity or not. The goal of this study was to determine the incidence, prevalence, clinical characteristics, and importance of aberrant LFTs in COVID-19 patients who were hospitalized.

MATERIALS AND METHODOLOGY

Selection of the patients: In Islamabad, Pakistan, patients with COVID-19 were assessed in three isolation wards. COVID-19 was identified using a specific primer-based Polymerase Chain Reaction (PCR). Only those patients who were infected with SARS-CoV-2, with age greater than 18 years, and hospitalized were included in the current research. Patients who presented directly to the ER or ICU with a serious infection were excluded from the study.

Collection of data: At the time of admission, previous history and files of the patients were examined, and sign and symptoms with clinical and laboratory parameters were obtained. Medical history was gathered, including infection, symptoms, and medications taken in the 10 days before admission. We took vital indicators such as breathing rate, body temperature, blood pressure, and pulse. Laboratory tests, such as LFTs (ALT, AST, ALP, GGT, and Bilirubin), were performed at the time of admission and every 5 ± 2 day thereafter. The types of medicines given throughout the hospitalization, as well as the dates of their beginning and cessation, were all recorded. Admission to the ICU, acute renal damage, the onset of multi-organ failure, acute liver failure, and death were all recorded throughout the hospitalization.

Statistical Analysis: The mean, median, and standard deviation with range were used to represent continuous variables. Frequencies and percentages were used to present categorical variables. After collection of data, statistical analysis was performed in December 2021, and SPSS 24.0 was used for analysis.

RESULTS

In the current study, we included 250 patients with confirmed COVID-19 infection through PCR. The participants average age was 46 ± 15 years, and 69% (n = 173) were males. The most common comorbidities were fever (83%), hypertension (54%), and atrial fibrillation (13%), and diabetes (10%), at the time of admission. 6% (n = 17) of the patients were diagnosed with COPD, 5% (n = 13) with ischemic heart disease, 4% (n=11) with chronic kidney disease, and 5% (n=13) with chronic liver disease. 39% (n=99) of the patients had used antibiotics in the last 10 days, and 3% (n=18) were using some sort of NSAID. The respiratory rate

was in the 18–24 range, and the mean arterial pressure was 95 (n=11) mmHg. 57% (n = 143) of the patients had symptoms of cough (Table 1).

Table 1: Demographic distribution of patients presenting at OPD

Parameters	N = 250
Age in years m(SD)	46 (15)
Gender male n (%)	173 (69)
Fever n (%)	207 (83)
Hypertension-n (%)	135 (54)
Diabetes-n (%)	25 (10)
Prior use of Antibiotics-n (%)	99 (39)
Pulse m (SD)	79 (11)
Atrial fibrillation-n (%)	33 (13)
COPD -n (%)	17 (6)
Ischemic heart disease-n (%)	13 (5)
CKD-n (%)	11 (4)
CLD-n (%)	13 (5)
Respiratory rate	20 (18-24)
Dyspnea-n (%)	131 (52)
NSAIDs-n (%)	18 (3)
Headache-n (%)	5 (2)
Mean arterial pressure-m (SD)	95 (11)
Cough-n (%)	143 (57)

Legends: Chronic kidney disease (CKD), Chronic Liver disease (CLD), chronic obstructive pulmonary disease (COPD), Non-steroidal anti-inflammatory drugs (NSAIDs)

As far the laboratory parameters are concerned, the mean hemoglobin of the patients was 13.6 g/l with a range of 12.2 to 14.7. C-reactive protein was observed with a mean value of 58 mg/l in patients with Covid-19 infection. LFTs, count of WBCs, and platelets were performed and details are given in Table 2.

Table 2: Lab findings of the patients at the time of Admission

Variables	Lab Results
Hemoglobin (g/l)	13.6 (12.2-14.7)
Albumin (g/dl)-m(SD)	3.4 (0.5)
Lymphocytes (x10^9/L)	0.8 (0.5-1.4)
WBC (x10^9/l)	5.5 (4.2-8.3)
Platelets (x10^9/l)	195 (133-240)
Neutrophils (x10^9/l)	4.4 (2.3-6.5)
Serum creatinine (mg/dl)	0.92 (0.77-1.12)
C-reactive protein (mg/l)	58 (27-110)
AST (u/l)	41 (25-61)
ALP (u/l)	56 (45-84)
Bilirubin (mg/dl)	0.49 (0.38-0.74)
GGT (u/l)	41 (20-69)
ALT (u/l)	34 (17-52)
CPK (u/l)	115 (67-190)
Ferritin (µg/l)	517 (325-978)
Troponin (ng/l)	9 (3-28)

Legends: Alkaline Phosphatase (ALP), Creatine phosphokinase (CPK), Gamma glutamyl transferase (GGT), Aspartate aminotransferase (AST), Alanine transferase (ALT).

Table 3: Characteristics of the patients at time of admission with and without Normal LFTs

Variables	With Normal LFTs (N = 90)	With Deranged LFTs (N = 160)
Age in years – m (SD)	45 (14)	46 (14)
Gender (male) – n (%)	73 (81)	96(60)
Diabetes-n (%)	11 (12)	14 (8)
Atrial fibrillation-n (%)	9 (10)	24 (15)
Hypertension-n (%)	45 (50)	90 (56)
COPD-n (%)	4 (4)	13 (8)
Ischemic CVD-n (%)	2 (2)	11 (6)
CLD-n (%)	4 (4)	9 (6)
Prior use of antibiotics-n (%)	28(31)	71 (44)
CKD-n (%)	3 (3)	8(5)
Pulse– m (SD)	78 (12)	81 (14)
NSAIDs-n (%)	3 (3)	15 (9)

Legends: Chronic kidney disease (CKD), Chronic Liver disease (CLD), chronic obstructive pulmonary disease (COPD), Non-steroidal anti-inflammatory drugs (NSAIDs)

Demographic distribution of parameters with deranged Liver Function Tests: At the time of the admission in the isolation ward, 160 patients had deranged LFTs, with a mean age of 46 ± 14. Out of these 160 patients, 96 (60%) were male. 56% of the patients with elevated LFTs parameters had hypertension, 15% with atrial fibrillation, 8% each with ischemic heart disease and diabetes. 44% of the patients had a previous history of consumption of antibiotics. All these parameters were suggesting more complications in patients with deranged LFTs than with normal LFTs (Table 3).

Characteristics and Laboratory Findings during Hospitalization: Blood samples were collected during hospitalization at 5 ± 2 days intervals. Patients with deranged LFTs at time of admission showed higher variation in AST (22 vs 57 u/l), ALP (49 vs 70 u/l), GGT (19 vs 61), serum troponin (6 vs 16) than those with normal LFTs (Table 4).

Table 4: Laboratory Parameters of the patients during hospitalization with and without deranged LFTs

Variables	Patients with Normal LFTs	Patients with Deranged LFTs
Hemoglobin (g/l)	13.6 (12.3-14.2)	13.4 (12.2-14.7)
WBC (x10^9/l)	5.1 (4.2-7.6)	6.4 (4.4-8.3)
Neutrophils (x10^9/l)	3.4 (2.3-5.8)	4.7 (2.5-6.5)
Lymphocytes (x10^9/l)	0. 6 (0.5-1.1)	0.9 (0.6-1.2)
Platelets (x10^9/l)	170 (144-211)	189 (149-240)
CRP (mg/l)	33 (27-45)	78 (43-110)
Serum creatinine-(mg/dl)	0.90 (0.76-1.09)	0.96 (0.68-1.12)
Bilirubin-(mg/dl)	0.46 (0.35-0.72)	0.61 (0.41-0.86)
AST-(u/l)	22 (15-31)	57 (38-81)
ALP-(u/l)	49 (38-62)	70 (49-84)
ALT-(u/l)	19 (16-24)	51 (25-67)
GGT-(u/l)	19 (15-33)	61 (38-89)
Serum Albumin (g/dl)	3.5 (0.4)	3.2(0.4)
Serum Troponin (ng/l)	6 (5-22)	16 (7-39)
CPK (u/l)	84 (61-145)	1125 (71-225)
Serum Ferritin (µg/l)	378 (190-612)	856 (467-1230)

Legends: Alkaline Phosphatase (ALP), Creatine phosphokinase (CPK), Gamma-glutamyl transferase (GGT), Aspartate aminotransferase (AST), Alanine transferase (ALT).

Endpoint Results of the Patients with Deranged LFTs: During the current study, findings showed that patients with deranged LFTs have more no. of deaths (17 vs 5), prolonged stay at the hospital (17 vs 7 days), and more patients were shifted to ICU (81 vs 17) than those with normal LFTs. (Figure 1)

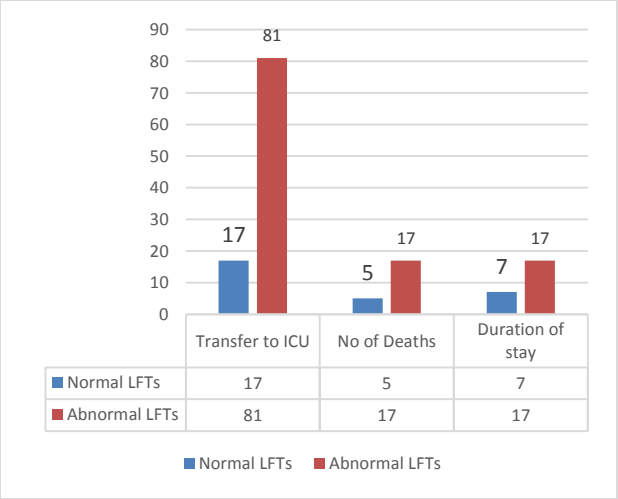

Figure 1: Endpoint result of the patients with Deranged LFTs

DISCUSSION

Deranged LFTs have been seen often in individuals with COVID-19, the clinical relevance and cause of liver damage have yet to be revealed. Patients with severe COVID19 had higher levels of AST and ALT.(12) Most of the studies in the past weren't intended particularly to look at LFTs abnormalities in COVID-19 patients, and they didn't elaborate possible causes such as past liver illness and/or concurrent therapies.(13) in other studies, a complete profile of LFTs was assessed during the stay of the patient, an approach that fails to address the important aspect whether abnormal LFTs have any effect on patients with COVID-19 or not? (14, 15)

The findings of the current study revealed that the deranged LFTs are found in 64% of COVID-19 patients when they were initially admitted in the ward and they are independently related with a outcome of the referral to the Intensive care unit especially when the pattern of change is heterogeneous. On clinical grounds, deranged LFTs at first visit should be regarded as a signal of illness severity, prompting clinicians to actively monitor these patients and prepare for the possibility of fast deterioration of clinical symptoms throughout the hospitalization. This might help forecast the demand for ICU beds, which is important given the shortages that occurred in some areas during the COVID-19 pandemic.(16)

Several causes can induce deranged LFTs in patients suffering from pneumonia with COVID-19. The virus attaches to target cells via ACE-2, which is found in high amounts on the liver and biliary epithelium.(17) As a result, the liver become the most prevalent target site during the viral infection, which could be indicated by variation in LFTs.(18) Autoimmune disease on the other hand, is a possible consequence or alternate mechanism by which the illness might induce liver damage.(19) Although the direct cytotoxic impact remains unknown, we found that patients with deranged LFTs had more severe inflammatory response with neutrophilia, elevated CRP and ferritin level. Patients with deranged LFTs may have a poorer clinical outcome due to widespread inflammation in multi organs caused by COVID-19 infection. Although respiratory failure is indeed the primary predictor of ICU admission or death in patients with COVID19, we discovered that deranged LFTs are linked with the primary outcome.(20)

Our research has both advantages and disadvantages. It is particularly designed to observe the prevalence and clinical significance of LFTs abnormalities ties, as well as the first one conducted in Islamabad, Pakistan. Because we lacked the data of the patients before admission and visit to the hospital, we can't rule out the possibility that some patients with chronic liver disease might have a deranged LFTs before being infected with COVI-19. Some patients with severe complications were directly admitted in ICU, and they have been excluded from the study.

CONCLUSION

Deranged LFTs are prevalent on admission in COVID-19 patients and they are related to systemic inflammation, organ failure, and are an independent predictor of transfer to ICU or death during the hospitalization. They have higher mortality rate and prolonged stay at the hospital with more complications than the individuals with normal LFTs. Patients with deranged LFTs at the time of admission should be actively monitored for a possible poorer prognosis.

Recommendations: Patients with deranged LFTs at the time of admission should be actively monitored for a possible poorer prognosis, a higher mortality rate and prolonged stay at the hospital, than individuals with normal LFTs

Authorship Contribution:

Muhammad Kamran: Substantial contributions to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; Drafting the work

Mahtab Ahmad: Drafting the work, revising it critically for important intellectual content;

Shehla Farhin: the acquisition, analysis, interpretation of data for the work;

Sadia Yasir Khan: the acquisition, analysis, interpretation of data for the work;

Saba Zafar: the acquisition, analysis, interpretation of data for the work;

Tehmina Siddique: the acquisition, analysis, interpretation of data for the work;

Samra Asghar: the acquisition, analysis, interpretation of data for the work;

Sadia Khalil: the acquisition, analysis, interpretation of data for the work;

Amber Shabbir: Final approval of the version to be published; revising it critically for important intellectual content; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Irfan Ullah: Final approval of the version to be published; revising it critically for important intellectual content; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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