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ORIGINAL ARTICLE

Prevalence of Liver Injury in 445 Patients with Corona Virus Disease-19

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ABSTRACT

Background and Aim: Severe acute respiratory syndrome COVID-19 disease patients are susceptible to abnormal liver function and its prevalence varies from 16 to 52%. The present study aimed to assess the incidence of liver injuries in 445 patients with COVID-19 infections.

Methodology: This retrospective study was carried out on 445 COVID-19 infected patients in the department of Gastroenterology, Northwest General Hospital & Research Centre Hayatabad Peshawar and Bacha Khan Medical Complex, Swabi for the duration of six-months from February 2021 to July, 2021. The patient's demographic details, COVID symptoms, laboratory tests, and previous illness history were recorded. COVID-19 was diagnosed through Reverse transcriptase-polymerase chain reaction (RT- PCR) via oropharyngeal and nasopharyngeal swabs. Ethical approval was taken from the institutional ethical committee. SPSS version 21 was used for data analysis.

Results: Of the total 445 COVID-19 infected patients, the incidence of elevated, mild elevated, moderately elevated, and severely elevated Aspartate transaminase (AST) was 208 (46.8%), 47 (10.6%), 10 (2.3%), and 4 (0.9%) respectively. The prevalence of symptomatic abnormal liver was 89% compared to asymptomatic 81% at p=0.001). Moderate, mild, and elevated Alanine transaminase (ALT) was 1.2%, 10.9%, and 29.8% respectively. The incidence of respiratory symptoms and loose stool was 44.2% and 12.3% compared to 30.3% and 3.8% respectively. Abnormal liver patients were more susceptible to severe COVID-19 disease 26.7% compared to 14.2%.

Conclusion: Our study found that patients with COVID-19 had a high rate of liver test abnormalities. The majority of the patients had transaminase elevations that were borderline or mild. Abnormal liver disease patients are more susceptible to symptomatic disease, mortality, and severe COVID-19 disease.

Keywords: Prevalence, COVID-19 disease, Liver Injuries

INTRODUCTION

Coronaviruses are a type of virus that infects the upper respiratory tract, causing mild to severe illnesses ranging from the common cold to pneumonia in severe cases [1]. Severe acute respiratory syndrome COVID-19 disease patients are susceptible to abnormal liver function and its prevalence varies from 16 to 52% [2]. In COVID-19 patients, recurrent gastrointestinal symptoms were observed, which were late-stage symptoms associated with an increase in disease severity [3]. A previous study on the SARS virus found that more than half of the patients had varying levels of hepatopathy, particularly elevated liver enzymes [4]. Another study discovered a high prevalence of abnormal aminotransferase levels in severe COVID-19 patients, which could be due to a non-hepatic cause [5]. Multi-organ dysfunction, full-blown respiratory cases, mild asymptomatic patients, and acute cases of respiratory distress syndrome are caused by COVID-19 [6, 7]. The infection is especially severe in patients with corona artery disease, diabetes, and hypertension. Fever, a dry cough, and tiredness are common clinical symptoms. In addition, serious complaints include shortness of breath and chest pain.

A Chinese based study reported the prevalence of hepatitis B, Aspartate Amino Transaminase (AST), and elevated Alanine Amino Transaminase (ALT) 2.1%, 21.3%, and 22.2% respectively among 1099 patients of confirmed COVID-19. It was also found that abnormal bilirubin were present in 10.5% patients [9]. Another study defined abnormal liver function as ALT > 40 U/L, AST > 40 U/L, GGT > 49 U/L, ALP > 135 U/L, and total bilirubin (TBIL) > 17.1 mmol/L [10]. COVID-19-associated hepatic injury should be defined as ALT or AST levels exceeding three times the upper limit of normal, and ALP, GGT, or TBIL levels exceeding two times the upper limit of normal. Previous research found that elevated ALT varied from 9.6% to 37.6%, elevated AST varied from 14.8% to 36%, the abnormal GGT varied from 13.0% to 24.4%, and abnormal total bilirubin varied from 5.1% to 18% [11, 12]. There is little information available about the liver-associated abnormalities seen in COVID-19 patients. The clinical profile and analysis of 445 COVID-19 patients are presented in this study.

METHODOLOGY

This retrospective study was carried out on 445 COVID-19 infected patients in the department of Gastroenterology, Northwest General Hospital & Research Centre Hayatabad Peshawar and Bacha Khan Medical Complex, Swabi for the duration of six-months from February 2021 to July, 2021. The patient's demographic details, COVID symptoms, laboratory tests, and previous illness history were recorded. COVID-19 was diagnosed through Reverse transcriptase-polymerase chain reaction (RT- PCR) via oropharyngeal and nasopharyngeal swabs. Ethical approval was taken from the institutional ethical committee. Patients' medical records were gathered. Demographic details, symptoms, and a pre-existing illnesses history such as hypertension, coronary artery disease, diabetes, chronic kidney disease, and chronic liver disease were all recorded. Patients' clinical progress, laboratory tests, and outcomes were followed.

Oropharygeal and nasophygeal swabs from suspected COVID-19 patients were gathered. Patient's laboratory tests such as a renal function tests, complete blood count, liver function tests, blood sugar, chest X-ray, and glycosylated haemoglobin. Concurrent viral infection were eliminated using hepatitis B and C tests. Based on the patient's clinical course, ensuing reiteration tests and severity markers such as C-reactive protein (CRP), interleukin 6, procalcitonin, and D – dimer were accomplished. Except for blood sugars and electrolytes, the tests were rarely repeated in uncomplicated and mild cases. Descriptive statistics such as percentages and means were used in our calculations. In addition, for categorical variables, we used the Chi-squared test, and for continuous variables. $P<0.05$ was considered statistically significant.

RESULTS

Of the total 445 COVID-19 infected patients, the incidence of elevated, mild elevated, moderately elevated, and severely elevated Aspartate transaminase (AST) was 208 (46.8%), 47 (10.6%), 10 (2.3%), and 4 (0.9%) respectively as shown in Figure-

2. The prevalence of symptomatic abnormal liver was 89% compared to asymptomatic 81% at p=0.001). Moderate, mild, and elevated Alanine transaminase (ALT) was 1.2%, 10.9%, and 29.8% respectively. The incidence of respiratory symptoms and loose stool was 44.2% and 12.3% compared to 30.3% and 3.8% respectively. Abnormal liver patients were more susceptible to severe COVID-19 disease 26.7% compared to 14.2%. The baseline laboratory findings are shown in Table 1. Figure-1 illustrate the gender distribution. Table 2 shows the clinical characteristics, severity, and outcome. Sore throat, fever, breath shortness, and cough were the prevalent symptoms.

Many patients had elevated alkaline phosphatase and serum bilirubin levels. Figure-3 shows the associations of patient's frequency with severity of COVID-19, elevated transaminase degrees, and mortality.

Table 1: Demographic details of 445 COVID-19 diagnosed patients

Features	Mean ±sd (n=445)	P-value
Age (years)	48.5±2.3	0.01
White blood cell (mm^3)	7100±621	0.002
Hemoglobin (gm/dl)	12.2±1.4	0.201
Platelet (10^9/dl)	1.95±0.23	0.783
Creatinine (mg/dl)	0.78±0.35	0.102
Random blood sugar (rbs) (mg/dl)	142.5±10.5	0.03

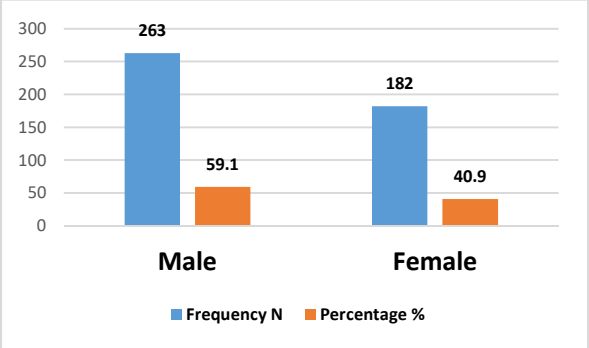

Figure 1: Gender distribution (n=445)

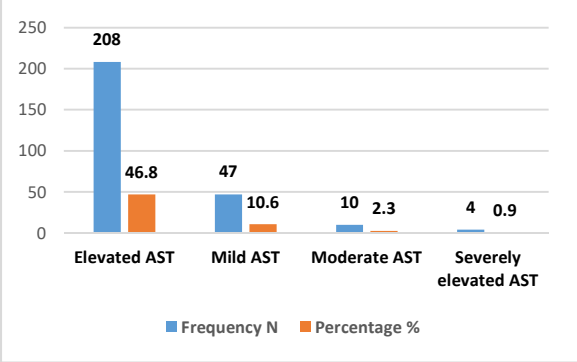

Figure 2: Incidence of elevated Aspartate transaminase (AST)

Table 2: clinical characteristics, severity, and outcome.

Parameters	Frequency N	Percentage %	P-value
Asymptomatic	51	11.5	0.51
Fever	332	74.6	0.001
Sore Throat	58	13.03	0.049
Cough	151	33.9	0.003
Breathlessness	89	20	0.001
Myalgia	47	10.6	0.09
Abdominal Pain	17	3.8	0.576
Headache	33	7.4	0.49
Outcomes			
Survived	423	95.1	0.001
Death	22	4.9	0.001

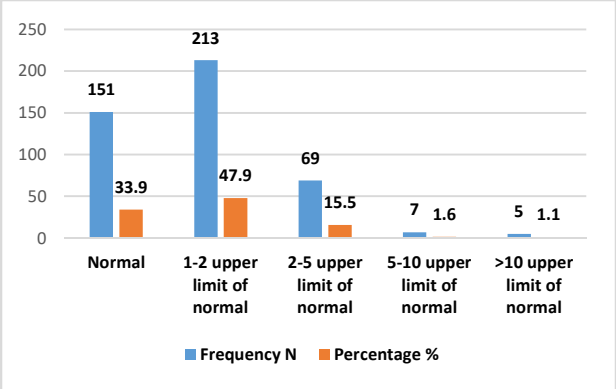

Figure 3: Association of patient's frequency with COVID-19 severity, elevated transaminase levels, and mortality.

DISCUSSION

SARS-CoV-2 is primarily responsible for respiratory illness, which may range from mild symptomatic respiratory disease to acute pneumonia, respiratory related syndromes, and mortality. On the other hand, manifestations of extra-pulmonary disease includes all the organ systems [13, 14]. COVID-19 has been found in non-respiratory samples such as blood, stool, sperm, and ocular secretions. Stool samples were utilized for viral RNA detection. Coronavirus spike protein promotes virus access into cells by binding to the angiotensin converting enzyme 2 (ACE2) receptor. Liver might be infected by receptor bindings with biliary duct among COVID-19 patients. Cytokine storm that case inflammation and damages associated with hypoxia might leads to liver injuries [15, 16]. Drug-induced liver injuries could be caused by various drugs used as treatment such as Lopinavir, Remdesvir, and Tocilizumab. Perforated kupffer cell, hepatic steatosis, infiltrated lymphoctic, congested chronic hepatic, and portal fibrosis were all recorded [17-19].

The prevalence of COVID-19 liver abnormalities varies according to published studies. Most studies used different cut-offs for abnormal values [20]. Guan et al. published a study in which ALT, AST, and bilirubin levels were raised in 21%, 22% and 10.5% among 1099 coronavirus patients respectively [21]. In US-based study, about 70% patients had elevated transaminases than ULN. Though, only 6.4% of the time was it more than five times the ULN [22]. Another study published in China found that 76.3% of 417 patients had abnormal liver [23, 24].

Despite mild transaminase elevations, liver injuries patients had more severe disease [25]. In the current study, if it was more than two times the ULN, approximately severe disease would have been present in one-third of the patients. Also, elevated ALT was less common compared to AST [26]. Because AST is initiate in tissues other than the liver, but severe disease patients might had elevated AST. Elevated AST>ALT and the presence of severe disease with transaminase elevation suggest that, in addition to the direct cytotoxic effects of SARS-CoV-2 infection, A systemic cytokine squall in liver injury may play a significant role in elevated transaminase levels.

Elevated transaminase levels were common in our study. However, according to the ACG's criteria for evaluating abnormal liver [27]. Only 2.6% of the time were transaminases more than five times the ULN. Only three patients in our study had transaminase levels that were more than ten times the ULN. One of them tested positive for dengue fever. Despite mild transaminase elevations, patients with liver injury had more severe disease [28]. In this study, if it was more than two times the ULN, approximately one-third of the patients had severe disease.

In conclusion, abnormal liver tests are common in COVID-19 patients. The majority of the patients had transaminase elevations that were mild, with alkaline phosphatase, and normal bilirubin despite mild transaminase elevation, it is linked to more severe

disease and death. An in-depth prospective study is required to validate these findings and their correlation with disease severity markers. The large number of patients in our study is its main strength. The main limitations of our study are the lack of ultrasound availability and the absence of a history of alcohol consumption.

CONCLUSION

Our study found that patients with COVID-19 had a high rate of liver test abnormalities. The majority of the patients had transaminase elevations that were borderline or mild. Abnormal liver disease patients are more susceptible to symptomatic disease, mortality, and severe COVID-19 disease.

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