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The Effect of Co-Infection of Coronavirus with Hepatitis B

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ABSTRACT

The present study was carried out during the period from October (2021) to April (2022). Blood samples were collected Among 25 covid-19 with HBV (17 male and 6 female), the percentage of males from the samples was 73.9%, with a mean age of 52 years. Ages range 20-79 years with covid-19 and viral hepatitis at Baghdad teaching hospital-Gastroenterology and liver hospital (in Baghdad) and Tikrit hospital. Detection of liver enzymes was tested to show the effect of co-infection in hepatocytes. ALT was 75.8 U/L which elevated twice than normal, while AST was 92.9U/L, ALP was 94.5U/L and TSB was 1.810mg. Addition to increasing these enzymes, IL-17 also increased.

INTRODUCTION

There is insufficient information on how COVID-19 affects people who already have chronic liver diseases like HBV or HCV (El Kassas *et al.*, 2020). On the other hand, COVID-19 co-infection with viral hepatitis shows a greater potential to cause liver damage with worse results and death. In this regard, according to (Qi *et al.*, 2020), despite receiving intensive care, a 53-year-old man with HBV-related cirrhosis, portal hypertension, and ascites passed away 48 days after the onset of the illness from irreversible multiple organ dysfunction syndromes (Qi *et al.*, 2020). According to a different study, those with HBV infection have a higher risk of dying and a higher prevalence of liver cirrhosis, total bilirubin, severe presentations, and hepatic cirrhosis (Chen *et al.*, 2020).

The most frequently reported symptoms of liver injury in COVID-19 patients are abnormal liver function and high levels of aspartate aminotransferase or alanine aminotransferase, (Zhang *et al.*, 2020) which have developed in 16.1-53.1% of SARS-CoV-2-infected patients. Liver damage is a common complication of SARS-CoV-2 infection, which can be caused by a direct viral infection of liver cells (Wang *et al.*, 2020; Huang *et al.*, 2020).

Human ACE2 Angiotensin-converting enzyme 2 (ACE2) is the host receptor by SARS-CoV-2 to infect human cells. Coronavirus binds to its specific receptor called. Despite reports that ACE2 is expressed in the lung, liver, stomach, ileum, kidney, and colon, particularly in the lung (Jin *et al.*, 2020).

SARS-CoV-2 may use co-receptors or auxiliary proteins as an ACE2 partner to facilitate virus entry. (Qi *et al.*, 2020; Lai *et al.*, 2020; Zhang *et al.*, 2020). By cleaving ACE2 and activating the SARS-CoV-2 S protein, which allows coronavirus entry into host cells, the transmembrane protease serine 2 (TMPRSS2) promotes viral uptake in the host cell (Hoffmann *et al.*, 2020). ACE2 and TMPRSS2 are present in target cells of the host, specifically alveolar epithelial type II cells (Mancia *et al.*, 2020; Zou *et al.*, 2020)

MATERIALS AND METHODS

Blood samples were collected from patients from October 2021 to April 2022 in Tikrit hospital, and Digestive system and liver Hospital in Baghdad. All patients who suspect to have COVID-19 enrolled in this study and diagnosed according to the Iraqi National Guidelines for the diagnosis of COVID-19, Common symptoms included dizziness, headache, shortness of breath, runny nose, sore throat, diarrhea, decreased appetite and jaundice (Grant *et al.*, 2020). The consent of the patients was obtained before collecting data and samples from them. The sample studied included (N=25) cases including 20 individuals from a control sample. The mean age was (52) years ranging between 20 to 79 years. To conduct medical tests, blood samples were drawn from patients as follows and an automatic hematology was used to measure, Total WBCs, monocytes, Lymphocytes Neutrophils, Eosinophils, basophils, and platelets. Others Blood samples in Gel-Tube used for Alanine transaminase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), Bilirubin, and IL-17.

RESULTS AND DISCUSSION

Among 23 patients who had covid-19 with HBV (17 male and 6 female), the percentage of males from the samples was 73.9% more than (Bekçibaşı *et al.*, 2021) which found 9 (45.0%). However, the percentage of ALT for HBV with covid-19 elevated was 66.2%, In, this present study, ALT had elevated levels in this group when compared to healthy control, mean ALT levels for HBV with SARS-COV-2 had 75.8U/L, increased twice than the upper maximum level, as show in Table (1).

SARS-CoV-2 and viral hepatitis B exhibit the evaluation level of AST, which is double that of the control. Numerous investigations found that the percentage of raised AST levels varied depending on the degree of injury, ranging from (2.5% to 61.1%) (Xu *et al.*, 2020; Zhang *et al.*, 2020; Xie *et al.*, 2020; Garrido *et al.*, 2020) which closed to the present study results that were 65% for AST but more than (Zou *et al.*, 2021) who found 29%. The levels of AST in the current study were higher than those (Wu *et al.*, 2021; Chen *et al.*, 2020) who found an increase in AST levels were 40 (25-54) and 28(19-58), less than our results. As show in Table (1).

ALP levels in co-infection with SARS-CoV-2 show a higher level compared to control, their mean value was 94.5U/L as viewed in Table (1).

Also, this group showed an increase in the level of TSB was HBV with SARS-CoV-2, its mean value was 1.810mg/dL, as show in the table(1-1), HBV co-infection with coronavirus had an elevated percentage of 39% of TSB in this group close to (Xu *et al.*, 2020; Zhang *et al.*, 2020; Xie *et al.*, 2020; Garrido *et al.*, 2020) when found the percentage of TSB was 35.3% when they reached co-infection show the same result, while (Zou *et al.*, 2021) found the percentage of TSB was 7% that decreased to result in this study. Huang (2020) found that SARS patients with HBV infection were more likely to develop severe hepatitis and a greater degree of liver damage.

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Table 1: Elevated of Liver Enzymes and IL-17 in patients with co-infection.

Patients of Co-infection (n=23)	Blood biochemistry
75.8 ±13.7 a	ALT
92.9±16.5 a	AST
94.5±11.8 a	ALP
1.810±0.4 a	TSB
184±32.7 a	IL-17

When comparing the liver function of co-infected individuals to that of healthy individuals in order to assess the damage, one of the main concerns is whether patients with pre-existing HBV infection are more susceptible to infection and have a worse prognosis for COVID-19 because COVID-19 and SARS-CoV-2 can both cause decreased liver function. However, several studies have produced inconsistent results. Confirming that HBV co-infection may encourage the development of liver injury, which is connected to adverse outcomes when compared to those without HBV infection (Chen *et al.*, 2020). Another recent study by Wu *et al.* found COVID-19 and HBV co-infected people exhibited significantly higher levels of ALT, AST, and activated partial thromboplastin time, according to a study including 70 instances of co-infection (Wu *et al.*,2021) close results to (Aldhaleei *et al.*, 2020) and close (Xu *et al.*, 2020; Zhang *et al.*, 2020; Xie *et al.*, 2020; Garrido *et al.*, 2020) that found levels of Alanine aminotransferase in co-infection variation in levels from 2.5% to 50.0%, the result in the present study was increased than(Zou *et al.*, 2021) who found the percentage of ALT was 22% numerous factors that harm the liver and increase LF, Patients who already have liver impairment from chronic liver disease may be more susceptible to liver damage from SARS-CoV-2. Biological drugs like cilizumab and baricitinib have the potential to cause liver damage due to HBV reactivation and declining liver function (Mantovani and Beatrice 2020). Nevertheless, some study indicates that a COVID-19 patient who visited the emergency room complaining of mental health difficulties had acute HBV reactivation (Aldhaleei *et al.*, 2020). Uncertainty exists regarding the etiology of COVID-19's transitory reactivation of HBV.

In line with previous studies, we show that some COVID-19 patients, with or without viral hepatitis infection, have elevated AST (Hung *et al.*, 2020) Similar findings involving SARS and MERS patients have been reported. It has been proven that SARS patients experienced liver function issues (Chan *et al.*, 2004). It is unclear if SARS-CoV or MERS-CoV has a direct cytopathic effect on the liver.

SARS-CoV-2 and HBV co-infection exacerbated liver injury, which was shown to be of the hepatocyte type rather than the cholangiocyte type, despite the disease primarily affecting the respiratory system (Lin *et al.*, 2021).

The levels of serum ALP did not vary significantly either. Consequently, these results imply that liver damage brought on by direct cytotoxicity to hepatic cholangiocytes is not the primary cause.

The liver damage brought on by COVID-19 can be explained by a number of different possible mechanisms. One method is a direct viral infection when the virus destroys bile duct cells and causes bile duct dysfunction, which causes liver damage. During viral replication, the cell sustains damage and turns dysfunctional. Another method to improve SARS-CoV-2 viral entry has been identified: the transmembrane

protease serine 2 (TMPRSS2), which may affect the S protein at the cell surface and result in SARS-CoV-2-cellular membrane fusion (Hoffmann *et al.*, 2020). Importantly, TMPRSS2 is overexpressed in HCV patients, which could cause these patients to have an accelerated SARS-CoV-2 infection (Esumi *et al.*, 2015)

Another mechanism is a systemic inflammatory response brought on by an increase in IL-6, IL-1, and TNF. This cytokine storm causes immediate liver cell injury and raises liver aminotransferase levels. most likely be the outcome of an overreacting immune system. It is vital to be aware that some medications, especially those prescribed for critically ill patients, can affect the liver while treating COVID-19 (Lei *et al.*, 2020; Sun *et al.*, 2020; Zhang *et al.*, 2020)

In addition, drug-induced liver damage is a crucial aspect that must be taken into account while hospitalized (Bertolini *et al.*, 2020; Muhovic *et al.*, 2020; Olry *et al.*, 2020) In particular, practically all of the individuals in this study have used antiviral and antibiotic drugs that potentially harm the liver, including arbidol, lopinavir/ritonavir, and interferon (Tillmann and Rockey, 2020)

The liver, on the other hand, is vital to the metabolism of drugs. It is well known that patients undergoing highly active antiretroviral therapy are more likely to develop drug-induced liver damage if they have specific viral infections, such as those caused by the human immunodeficiency virus or the hepatitis C virus (Bonacin, 2004; Boeckman *et al.*, 2020: Naidoo *et al.*, 2020), that the SARS-CoV-2 virus's offspring COVID-19 may display a similar liver-damaging mechanism. As a result, the different antiviral drugs, antibiotics, and steroids now used to treat COVID-19 patients could lead to the development of hepatotoxicity over the course of the infection (Zhang *et al.*, 2020; Bonacin, 2004)

When a patient has a cytokine storm, their health typically gets worse quickly as they go into a state of multiple organ failure; additionally, the systemic inflammation this generates could induce subsequent liver damage (Liu *et al.*, 2020).

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