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Assessment of some Biochemical Parameters among Covid-19 Patients associated with liver damage in Al-Najaf Province

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ABSTRACT
The coronavirus SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), which is responsible for the disease COVID-19 (coronavirus disease 2019), has infected over 9.5 million people and has caused more than 480,000 deaths globally, as of 24 June 2020. These are positive-sense single-strand RNA viruses with around 24 similar species from the family of coronaviridae. This family of coronaviridaeis further categorized as α, β, λ, and δ based on its distinct genetic features. However, among these, only alpha (α) and beta (β) coronavirus genera are pathogenic to mammalian and humans. Liver disease is a global health problem and is a primary cause of mortality and morbidity worldwide. Specifically, it accounts for approximately two million deaths per year worldwide. The common causes of mortality are the complications of liver cirrhosis, viral infection, and hepatocellular carcinoma (HCC).
Keywords: Covid-19, Liver dysfunction, Liver parameter.

INTRODUCTION TO THE STUDY

Liver is the body's largest organ. It sits just under your ribcage on the right side of abdomen and is about the size of a football. The liver separates nutrients and waste as they move through the digestive system. It also produces bile, a substance that carries toxins out of the body and aids in digestion. The term "liver disease" refers to any of several conditions that can affect and damage the liver such as infections, inherited conditions, obesity and misuse of alcohol. Covid-19 can rapidly progress to multiorgandysfunction or failure with high fatality rates. Theprogression from mild to severe forms of COVID-19is associated with a dysregulated immune response,responsible for uncontrolled viral replication andcellular damage leading to additional inflammationand immune-mediateddamage of tissues and organs.Many of the released inflammatory cytokines areknown to be key players of inflammation related injuryof other organs, including the liver. Furthermore, anti-SARS-CoV-2-S IgGs from patients who are severely ill with COVID-19 have been shown to induce macrophage hyperinflammatory responses. The inflammatory responses in these cases were mediated via FcγRII and FcγRIII receptor, (which are present on nonpulmonary macrophages, such as liver-resident Kupffer cells, providing another to covid-19 pathogenesis of the lung and other organs. Whether the SARS-CoV- 2 productively infects liver cells remains to be determined. Several studies observed the presence of viral RNA in the liver of severe COVID-19 cases.

REVIEW OF LITERATURE

Chau *et al*.; 2004 and Alsaad *et al*.; 2018) Liver injury as defined by elevated serum aminotransferase levels has been reported following infection with other coronaviruses, such as severe acute
respiratory syndrome and MERS. Among patients who are hospitalized with symptomatic COVID-19 disease, abnormal liver function tests (LFTs) are common, ranging from 14% to 53%. The most common observed abnormalities are hypoalbuminemia, elevated γ-glutamytransferase (γGT), mild elevation of aminotransferases, and hyperbilirubinemia(Huang., *et al* 2020 and Guan., *et al* 2020) Multiple studies have reported a correlation between COVID-19 severity and LFT abnormalities, with elevated aminotransferase levels being more frequent in intensive care unit (ICU) in patients.

(Wu *et al*.; 2020 and Wijarnpreecha *et al*.; 2020) The pattern of liver injury is typically hepatocellular rather than cholestatic. The aspartate aminotransferase (AST) levels correlate highly with alanine aminotransferase

levels throughout the course of the illness, suggesting a hepatocellular origin (Yip *et al*.; 2020) Notably, the prevalence of elevated AST was substantially. higher among patients with severe COVID-19 disease (45.5%) compared with those with mild disease (15.0%). In severe COVID-19 cases, hypoalbuminemiais common and correlates with worsepatient outcomes Although informative, these studies were limited by the fact that LFT abnormalities were not consistently reported across studies and the proportion of patients with underlying chronic liver diseases (CLD) was rarely provided. (Lenti *et al*.; 2020 and Schattenberg *et al.;* 2020) Although LFT abnormalities are frequently observed and shown to correlate with mortality, acute liver failure is extremely rare among patients with COVID-19 without underlying CLD and is more typically associated with severe pneumonia and multiorgan dysfunction.(Noor and Manoria, 2017) The prevalence of abnormal LFTs among asymptomatic patients with SARS-CoV-2 infection is unknown. The liver plays an important role in regulating immune homeostasis. Patients with CLD, particularly those with cirrhosis, may have dysregulated innate and acquired immunity and may therefore be at higher risk of acquiring SARS-CoV-2, COVID-19–related complications, and death.
(Singh and Khan, 2020) Patients with CLD may be at higher risk of developing more severe COVID-19 and higher mortality compared with those without CLD. Indeed, a large study including 2,780 patients with COVID-19 that compared the outcomes among those with and without CLD reported that patients with CLD were at ~3-fold higher risk for mortality compared with patients without CLD, and this risk was markedly higher in patients with cirrhosis (~5-fold)

OBJECTIVES OF THE STUDY

Primary objective:

To study the effect of Covid-19 on the levels of some biomarker such as liver enzyme include aminotransferase (AST), alanine aminotransferase (ALT), albumin, lactate dehydrogenase (LDH) concentration

SCOPE OF THE STUDY:

The study aimed to analyze the association between liver biomarker with liver damage in patients with covid-19.

RESEARCH METHODOLOGY

Collection of samples

A-5 ml of fresh venous blood samples were collected from COVID-19 infected patients by sterile syringes which divided into (3 ml) of blood was saved in EDTA tubes for study gene polymorphism that stored at-20°C.

Two ml of blood put in gel tubes , left for 10-15 minutes to clot at room temperature and then they were centrifuged for 5 minutes at 3000 (rpm) to obtain pure serum. the separated sera sample have been divided into small 100-200 µl numerated and kept at -20 °C until used for chemical parameter.

Biochemical marker

A. Alanine aminotransferase (ALT)

Method: UV enzymatic method Kinetic

Principle: The amino group of alanine is transferred to oxoglutarate by catalysis aminotransferase with the formation of glutamate and pyruvate. The lactate dehydrogenase reduced the pyruvate to lactate in the presence reduced nicotineamide adenine dinucleotide (NADH) (Schumann, 2002).

ALT
L-Alanine + 2-Oxoglutarate ⟶ L-Glutamate + Pyruvate

Lactate dehydrogenase

Pyruvate + NADH + H+ ~~Lactate + NAD~~ →

Table (3.15): Reagent Composition of kit ALT

Reagent	Component
R1 ALT substrate	TRIS buffer 150 mmol/L PH 7.3 L.alanin 750 mmol/L Lactate dehydrogenase >1350 U/L
R2 ALT coenzyme	NADH 1.3 mmol/L 2-oxoglutarate 75 mmol/L Biocides

B. Aspartate aminotransferase (AST)
Method: UV enzymatic method Kinetic.
Principle:

The amino group of aspartate is transferred to oxoglutarate by catalysis aminotransferase with the formation of glutamate and oxaloacetate. The malate dehydrogenase reduced the oxaloacetate to malate in the presence reduced nicotineamide adenine dinucleotide (NADH) (Schumann, 2002).

AST
Aspartate + Oxoglutarate → Glutamate + Oxaloacetate

Malate dehydrogenase
Oxaloacetate + NADH + HMalate ~~+ NAD~~ →

Table (3-17): Reagent Composition of kit AST

Reagent	Component
R1 AST substrate	TRIS buffer 121 mmol/L PH 7.8 L.aspartate 362 mmol/L malate dehydrogenase >460 U/L
R2 ALT coenzyme	NADH 1.3 mmol/L 2-oxoglutarate 75 mmol/L Biocides

RESULTS

During the period from (10 December 2021 to 1Jon 2022) 150 patients were diagnosed as COVID-19 according to the guidelines for diagnosis and management of COVID-19, In total, the median age was 50 years ranging between (25-83) years, all patients were nasopharyngeal swabs positive for covid-19 virus, in addition to 50 healthy persons as control, revealed in the following results:

Biochemical abnormalities in the liver impairment patients

Alanine Aminotransferase (ALT) parameter detection

The results showed a significant in ALT parameter means among three study groups (covid with liver dysfunction, covid without liver dysfunction, and control). The concentration of ALT in covid-19 with liver dysfunction increase to (178.15U/L), compared with covid-19 without liver dysfunction and control (29.41U/L), (28.23U/L) respectively, as shown in the table (4-5)**.**

Table (4-5): Mean and SD of ALT concentration in the patients and control groups.

ALT Parameter	Mean±SD (U/L)			p-value
	Covid ± LD NO. (26)	Covid without LD NO. (124)	Control NO. (50)	
	178.15±31.96	29.41±9.71	28.23±7.13	<0.05[S]

S= Significant (p <0.05), SD= Stander Deviation,

In addition, there were negative correlation coefficient in ALT among (Covid-19 with LD with covid-19 without LD, and control), as shown in the table 4-6).

Table (4-6): Alanine aminotransferase correlation in the patients and control groups.

ALT correlation		Covid-19 with LD	Covid-19 without LD	Control
Covid with LD	Pearson Correlation	1	.291	.216
	N	26	26	26
Covid without LD	Pearson Correlation	.291	1	-.088-
	N	26	124	50
Control	Pearson Correlation	.216	-.088-	1
	N	26	50	50

Aspartate Aminotransferase (AST) parameter detection

In the present study, a significant increase of AST in covid-19 with liver dysfunction to (206.63U/L), compared with covid-19 without liver dysfunction and control (34.06U/L), (34.06U/L) respectively, as shown in the table (4-7).

Table (4-7): Mean and SD of AST concentration in the patients and control groups.

AST Parameter	Mean±SD (U/L)			p-value
	Covid ± LD .NO (19)	Covid without LD .NO (124)	Control .NO (50)	
	206.63 ± 47.53	34.06 ± 9.78	34.06± 5.13	<0.05[S]

S= Significant (p <0.05).

In addition, there were negative correlation coefficient in AST among (Covid-19 with LD, covid-19 without LD, and control), as shown in the table (4-8).

Table (4-8): Aspartate aminotransferase correlation in the patients and control groups.

AST correlation		Covid-19 with LD	Covid-19 without LD	Control
Covid with LD	Pearson Correlation	1	-.184-	-.435-
	N	19	19	19
Covid without LD	Pearson Correlation	-.184-	1	.183
	N	19	124	50
Control	Pearson Correlation	-.435-	.183	1
	N	19	50	50

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