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# Salivary biochemical variables of Liver Function in among Individuals with COVID-19 in Thi-Qar Province

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**Abstract**

The goal of this study was to examine the changes in salivary biochemical markers such as AST, ALT, GGT, albumin, and C-RP in COVD-19 patients (n=50) to control subjects (n=50). Methods: Whole saliva samples were taken from fifty persons who were matched with sex and age and were then divided into two groups: healthy (n = 50) and COVID-19 (n = 50).Student's t-test and the Correlation-Coefficient test were used to determine statistical significance. The data is presented as a mean standard deviation. A spectrophotometric kit was used to quantify salivary AST, AST, ALP GGT, LDH, and albumin levels, while a conventional enzyme-linked immunosorbent test was used to determine CRP amounts. COVID-19 patients had significantly greater salivary levels of AST, AST, ALP GGT, LDH, and C-RP than controls. However, when compared to the control group, salivary albumin levels in COVID-19 patients were considerably lower. Conclusion: Elevated salivary ALP, AST, AST, GGT, and CRP levels in COVID-19 patients suggest salivary gland injury and could serve as a salivary marker for salivary gland involvement in COVID-19.

**Keywords:** COVID-19; Saliva; C- reactive protein; $ACE_2$

## 1. Introduction

Human saliva is a biological fluid with a variety of biological functions important for maintaining oral and general health; it is regarded as the gold standard in biochemical assays and analysis [1]. Saliva can host a variety of viruses, including COVID-19, a Coronavirus that causes severe acute respiratory syndrome (SARS- CoV-2) and has spread from China to many other countries around the world.

The liver is one of the largest organs in the body, and it performs an amazing array of vital functions in the body's maintenance, performance, and regulation of homeostasis. Its major functions include carbohydrate, protein, and fat metabolism, immunity, exogenous (drug) and endogenous (substance) detoxification, bile secretion, and vitamin storage.In hepatitis, liver tissue has a relatively high level of enzyme activity, with various enzymes altered [5,6]. COVID-19-induced liver damage could be caused by a variety of mechanisms, including the following:

1. The presence of SARS-CoV-2 in cholangiocytes could lead to liver damage due to the damage to bile duct cells. Angiotensin-converting enzyme 2 (ACE2) is the key receptor for the entry of SAR's into the cells which expressed in both liver cells and bile duct cells.[7].

2. Individuals suffering from COVID-19 were detected with high levels of TH17, CD8 T cells and interleukin-2 in samples of their peripheral blood. The excessive immune response could likely results in injury to the liver resulting in derangement of biochemical markers of liver. [8,9].

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3. Certain medications are hepatotoxic and can harm the liver while taking COVID-19 [10].

## 2. Methods:

The reverse transcription polymerase chain reaction test was used to diagnose novel coronavirus disease (COVID-19) using nasopharyngeal and oropharyngeal swabs [11].50 confirmed patients with COVID-19(22 males, 28 females) with a mean age of 38.7±12.3 years who attended to the Al-Hussein hospital in Thi-Qar province, Iraq, from November 10 to April 19, 2021. 54 healthy controls were matched for sex and age 39.3±3 years.

Stimulated saliva was collected between 9 and 11 a.m. after patients were asked to spit unstimulated saliva for 5 minutes after washing their mouths with distilled water for 5 minutes under relaxed conditions.To remove squamous cells and cell debris, saliva was centrifuged for 10 minutes at 3000 rpm in an Eppendorf centrifuge at 4°C[12].

The A25 Bio-system human ALP, AST, ALT, and GGT were determined using a spectrophotometric kit (German). The data is presented as mean standard deviation and analyzed using a paired two-tailed student's t test. P-values taken into account: P 0.005 - Significant, P 0.001 - Highly significant.

## 3. Results

In this study, the mean serum levels of ALP and GGT in COVID-19 patients were 11843 U/L and 92.723.2 U/L, respectively, while the mean in controls was 44.110.89 U/L and 285.07 U/L, respectively. When patients with COVID-19 were compared to controls, the outcome was significantly higher. The mean salivary AST and ALT levels in COVID-19 patients were significantly higher than those in the control group (85.4 22 vs 19.546.81 IU/L: 0.0001) and (97.0721.4 vs 23.417.01 IU/L: 0.0001), respectively. While serum LDH levels increased significantly (P0.009) in the COVID-19 group (89.6 7.4 IU/L) compared to the control group (5.340.22 IU/L), as shown in table1.

This study found that the mean serum albumin level in COVID-19 patients (4.24 0.29g/dl) was significantly lower than that of the control (5.340.22g/dl). While the patients with COVID-19 had a mean serum CRP level of 5.072.30 IU/L, the control group had a mean CRP level of 1.510.52 IU/ml. The difference was statistically significant in the patient group, with a P value of 0.0001, as shown in table2.

**Table 1**
**Level of liver enzymes in COVID-19 patients and the control group.**

| Parameter (U/L) | COVID-19 patients | | Control | | P-value |
|---|---|---|---|---|---|
| | No. | Mean ± SD | No. | Mean ± SD | |
| **ALP** | 50 | 118±43 | **50** | 92.7±23.2 | 0.026 |
| **GGT** | 50 | 44.1±10.89 | **50** | 28±5.07 U/L | <0.05 |
| **AST (IU/L)** | 50 | 97.07±21.4 | **50** | 23.41±7.01 | <0.000 |
| **ALT (IU/L)** | 50 | 85.4 ± 22 | **50** | 19.54±6.81 | <0.0001 |
| **LDH (IU/L)** | 50 | 89.6 ± 7.4 | **50** | 155.6 ± 41.9 | <0.05 |

Table 2
Level of albumin and CRP in COVID-19 patients and the control group.

| Parameter (U/L) | COVID-19 patients | | Control | | P-value |
|---|---|---|---|---|---|
| | No. | Mean ± SD | No. | Mean ± SD | |
| **Albumin (g/dl)** | 50 | 4.13±0.29 | 50 | 5.34±0.22 | <0.009 |
| **CRP( Units/L)** | 50 | 5.07±2.30 | 50 | 1.51±0.52 | <0.0001 |

## 4. Discussion

The presence of the virus in liver tissue may be directly responsible for liver damage in patients with coronavirus infections. The key receptor for SARS-CoV-2 entry into cells is angiotensin-converting enzyme 2 (ACE2), which is expressed in both liver cells and bile duct cells, and direct binding of SARS-CoV-2 to ACE2 receptors in cholangiocytes may result in liver damage due to bile duct cell damage. [7,13].

GGT and alkaline phosphatase (ALP) were both categorized as "cholangiocyte-related enzymes." ALP is found in a variety of tissues, but it is most abundant in the liver, bone, and kidney, whereas GGT is found in the cell membranes of many tissues, including the kidneys, bile duct, pancreas, gallbladder, spleen, heart, brain, and seminal vesicles, and is thought to be involved in oxidative stress and chronic inflammation. As a result, ALP is more sensitive than GGT in detecting bile duct injury [14-16].GGT activity increases (P = 0.05). GGT is leaked into the serum possibly as a result of normal cell turnover and cellular stresses [17], and can be a response to increased oxidative stress, facilitating increased transport of GSH precursors into cells. These findings regarding abnormal liver functions support the notion that COVID-19 is associated with liver dysfunction during infection.

Aspartate aminotransferases are predominantly mitochondrial enzymes. Although an elevated level of AST in the serum is not specific for a hepatic disorder, it is used primarily to diagnose and confirm persistent cellular injury in conjunction with other enzymes such as ALT[18,19]. The increased salivary levels of ALT and AST (P0.0001) caused by systemic hyper-inflammatory state, which is the main responsible mechanism caused by drug hepatotoxicity, cytokine storm, and/or pneumonia-associated hypoxia, could be due to increased leakage from damaged cells of soft tissues of peridontium into saliva and a reflection of metabolic changes in the inflamed gingiva [8,20].

Salivary LDH levels were significantly higher in COVID-19 patients than in controls (P: 0.05) in the current study. Because of increased LDH levels in the bloodstream and cytokine-mediated tissue damage [22]. LDH elevation reflects multiple organ injury (tissue/cell destruction) and is regarded as a common sign of tissue/cell damage. LDH can convert pyruvate to lactate and may be the key enzyme for pneumococcal pyruvate metabolism and thus pneumococcal survival in blood, suggesting viral infection or lung damage, such as SARS-CoV-2 pneumonia [22,23].LDH is not only a metabolic biomarker, but it is also a prognostic biomarker for immune surveillance in immunocompromised patients [24]. LDH causes an increase in lactate production, which boosts immune-suppressive cells like macrophages and dendritic cells (DCs) while inhibiting cytolytic cells like natural killer (NK) cells and cytotoxic T-lymphocytes (CTLs). When T cells are activated and proliferate, LDH is frequently activated [25,26].

Albumin is a globular protein with a molecular weight of 66 kDa made of 585 amino acids that is synthesized by the liver and is found in high concentrations in the intestine, muscle, skin, and all body fluids. Albumin interacts with a wide range of endogenous and exogenous molecules. It accounts for more than half of serum proteins and is an important component of interstitial fluid. Its primary function is protein binding and transport, and it is the primary negative secretory acute phase protein with antioxidant properties. This protein is thought to be a serum ultrafiltrate to the oral cavity, and it may diffuse into mucosal secretions and thus be found in saliva.Albumin binds to ligands in a reversible process in which the equilibrium between bound and unbound depends on relative concentrations and ligand. All bindable ligands, including proteins, fatty acids, and the SARS-CoV-2 virus, compete for binding sites on the albumin molecule [32]. Albumin is frequently used as a marker for the severity of oral mucositis or inflammation. Albumin extravasation as

a result of increased capillary permeability, increased catabolism, and malnutrition may result in lower albumin concentrations in the saliva [33,34].

C-reactive protein is an inflammatory marker that is typically not detected in the blood unless there is some degree of inflammation in the body[35,36]. It is produced by the monocytes of the tissue factor classified as an acute phase reactant, regulated by pro-inflammatory cytokines such as IL-6 and TNF-, and is regulated by pro-inflammatory cytokines such as IL-6 and TNF-.CRP levels in saliva were measured as a marker for systemic inflammation. CRP can contribute to inflammatory responses by activating complement proteins, which can lead to an increase in the production of thrombogenic components bound to injured cell membranes [37]. were higher in patients with COVID-19 compared to systemically healthy controls, which could be due to chronic low-grade inflammation [37,38].

## 5. Conclusions

Elevated levels of salivary AST and ALT enzymes in COVID-19 patients may be due to tissue damage in the salivary glands, which may also be responsible for reduced salivary gland function and other oral complications.

## 6. Conflicts of interest

No potential conflicts of interest are disclosed.

## 7. Acknowledgments

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