

## EFFECT OF COVID-19 ON LIVER AND KIDNEY PROFILES

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### ABSTRACT

**BACKGROUND:** The wide family of single-stranded RNA viruses known as coronaviruses (CoVs) potentially invades both humans and animals and cause respiratory, gastrointestinal, liver, and cerebral disorders. These are the largest known RNA viruses. In an analysis of the clinical manifestations in COVID-19 patients, some researchers suggested that hepatocyte infestation with the immediate cytopathic effect of SARS-CoV-2 as well as interleukins storm, lack of oxygen conditions brought on by ARDS, and drug- Individuals having severe acute respiratory-CoV 2 experiences a broad spectrum of clinical indications, including acute, intermediate, chronic, quickly progressing, and symptomatic disease. The majority of SARS-CoV-2 victims remained healthy or mildly ill, and they died at rates that were less compared to severe acute respiratory-CoV as well as Middle East respiratory syndrome-CoV induced liver injury (DILI) may be held responsible for the pathological findings of COVID-19.

**Methodology:** Data was collected according to the rule and regulations set by the ethical committee of university of Lahore. The participants for this data were selected according to the inclusion and exclusion criteria. 551 blood samples were collected from patients suffering from COVID-19. A retrospective study design was used to conduct the research. As this was retrospective study so the data and clinical information about the demographic features of study population were collected through electronic medical record system from the pathology department of Aziz Bhatti Shaheed Teaching Hospital, Gujrat. The data and information which were collected included the information of patients regarding sex, age, chronic diseases (comorbidities) and other parameters such as alanine transaminase (ALT), aspartate aminotransferase (AST), enzymes present mostly in the liver, total bilirubin (TB), ALB also called serum albumin test and other parameters. data then was analyzed by SPSS.

**Results:** Out of 551 samples 511 give the positive results for urea, creatinine, total bilirubin, ALT, ALP, globulin. 510,506, 505 out of 551 samples give positive results for the AST, TP, and ALB respectively. The mean value of these tests is 55.3425, 1.4022, 0.6620, 74.4116, 183.2114, 3.0168, 67.386, 36.7354, and 3.960 respectively.

**Conclusion(s):** In the study there is now enough data to demonstrate the involvement of organs other than lungs in the Covid-19 patients. This study shows the effect of Covid-19 on the kidney and liver profiles in certain patients. Therefore the physicians and health staff should be aware of the clinical manifestations of Covid-19 so that a timely treatment is managed thereby eliminating the complications because of Covid-19. Several studies and investigations relating to the long-term impacts of Covid-19 on the liver and kidney profiles will definitely help in increasing our knowledge.

**Keywords:** Covid-19, Angiotensin-Converting Enzyme 2 (ACE2), Liver function test (LFT's), Renal function test (RFT's)

## INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) provisionally named 2019-nCoV is the causative agent of the recent global pandemic COVID-19 with increasing fatality rate. It is depicted as a public health emergency of global concern by the World Health Organization (WHO). This contagion initially emerged in Wuhan city, Hubei Province, China on December 8, 2019, which caused pneumonia-like symptoms in a cluster of patients. Coronaviruses (CoVs) are members of the genus Coronaviridae, a group of pleomorphic RNA viruses that contain crown-shaped peplomers. SARS-CoV-2 possesses an 80% phylogenetic identity with severe acute respiratory syndrome coronavirus (SARS-CoV) and 50% similarity with the Middle East respiratory syndrome coronavirus (MERS-CoV) which caused global outbreaks in 2002–2003 and 2011 respectively. SARS-CoV-2 is now considered as a rapidly spreading pandemic virus that was initially transmitted from animals-to-humans and later transmitted through human-to-human<sup>1</sup>.

Similar to SARS-CoV, SARS-CoV-2 mainly affects the respiratory system, with fever, cough and dyspnoea being the most frequently reported symptoms<sup>2</sup>.

In severe cases, patients may develop pneumonia and associated complications, such as severe acute respiratory distress syndrome, septic shock and, eventually, death<sup>3</sup>.

SARS-CoV is believed to be a systemic infection with multiorgan involvement including the heart, kidney, pancreas and liver. Nearly half of the SARS-CoV-2 infected individuals exhibit some degree of liver impairment which becomes more evident with the increasing severity of the disease<sup>4</sup>.

In addition to this, RNA from the SARS-CoV-2 has been detected in blood and hepatic cells of the affected patients<sup>5</sup>.

There is also evidence to suggest that most of the viruses which affect respiratory system are harmful to the liver cells through the CD8+ mediated immune response<sup>6</sup>.

Hepatic involvement in COVID-19 could be related to the direct cytopathic effect of the virus with the current evidence, it is clear that elevated liver enzymes are observed predominantly in severe and critical cases of COVID-19<sup>7</sup>.

This evidence implicates the possibility of viral exposure in the liver. Both SARS-CoV-2 and SARS-CoV bind to the angiotensin-converting enzyme 2 (ACE2) receptor to enter the target cell,<sup>8</sup>.

Pathological studies in patients with SARS confirmed the presence of the virus in liver tissue<sup>9</sup>.

## **Material and methods:**

### ***Study design, duration and setting***

Retrospective study was conducted. Retrospective study needs a cohort who has experienced the disease or the effects of disease in the past. A total of almost 551 samples were collected from the study population in the pathology laboratory of Aziz Bhatti Shaheed, Hospital, Gujrat, Pakistan. Convenient and reliable sampling method was used for collecting the samples.

#### **Inclusion:**

- Patients come with positive Covid-19
- The patients suffering from COVID-19 also having the hepatic and renal injuries were included in this study population
- Age: All age groups will be included.
- Gender: Both male and female.

#### **Exclusion:**

- Exclusion Criteria include those patients who have any kind of other infection.
- Those cases with inappropriate data an incomplete were rejected and excluded from the study.

### **Ethical approval and Consent**

Ethical approval was taken from Institutional Review Board (IRB) of University of Lahore, Punjab, Pakistan. An informed was taken from the participants before collecting data. Ensured that data would be used for only research purpose. The research project was approved by research and ethics committee of University of Lahore

### **Data collection procedure and tools**

The request form was design as a data collection tool in order to collect the information from the Laboratory. The form will be comprised of data of Chemistry section of the Lab.

### **Samples collection and processing:**

- Blood samples were collected from the COVID-19 patients in the serum vials.
- Then this clotted blood samples were then centrifuged at 3400 rpm (revolution per minute) for 7 minutes in a centrifuge, in order to obtain the serum.

## **ANALYSIS**

A nucleic acid test called reverse transcriptase polymerase chain reaction test was there for the detection of corona virus RNA in the patients thus used for the confirmation of the diagnosis of COVID-19 patients.

### **Liver function tests (LFTs)**

Liver function tests (LFTs) were performed for the quantification of liver enzymes. Any type fluctuation in these tests indicates the hepatic damage. These tests typically include

#### **Aspartate aminotransferase test (AST)**

Also named as glutamic-oxaloacetic transaminase, working principle of AST is,

“In the reaction mixture this enzyme performed the catalyzation of the reversible transamination of alpha-ketoglutarate and L-aspartate to pyruvate and L-glutamate. Then, in the presence of LDH (Lactate dehydrogenase) there is reduction of pyruvate into lactate, and the NADH oxidized into NAD”.

If there is an any damage occurs to the liver, this enzyme leaks into the blood. The normal range of AST is **8 to 33U/L** <sup>10</sup>.

#### **Alkaline phosphatase (ALP),**

“Working principle of this test is, in the reaction mixture this enzyme accelerates the hydrolysis of the colorless compound which is organic phosphate ester, p-nitrophenylphosphatase to the phosphate and nitrophenol which is a yellow-colored compound. Alkaline pH of 10.3 is required for this reaction’ <sup>11</sup>.

#### **Total bilirubin (TB),**

This test was also performed to analyze the liver damage. The working principle of this test is as follows

“In the reaction mixture, the bilirubin present in the sample reacts with sulfanilic acid resulted into a purple-colored compound called azobilirubin”.

#### **Serum total protein, Serum Albumin**

“Working principle of this test is, in the reaction the albumin reacts with the reagent such as Bromocresol purple (BCP) reagent to form a complex. Then the absorbance measured at 600nm” <sup>12</sup>.

#### **Gamma-gutamyl transferase (GGT).**

The working principle of this test is in the reaction, the enzyme responsible for the transfer of gamma group from colorless compound to the recipient which is glycylglycine and hence the production of p-nitroaniline which is colored compound.

The absorbance of this test was measured on 410nm.

### **Renal function tests (RFT)**

Renal function tests (RFT) were also performed including the detection Blood Urea Nitrogen (BUN) and Serum Creatinine. Any fluctuation typically elevated level in these tests indicated the kidney damage<sup>13</sup>.

### **Statistical analysis:**

The Statistical Package for Social Sciences (SPSS) 20.0 was used to examine the data (SPSSA Inc. Chicago, USA). The categorical value was expressed in the form of frequency and percentages. The data was shown using pie charts and bar charts. To examine the data, appropriate statistical methods were used.

### **Results:**

In the current retrospective study that was conducted within four to five months of duration, in Along with LFTs the renal function tests were also performed on these collected Samples including the Blood Urea Nitrogen (BUN) and serum creatinine. These tests were performed for the analyzing the effect of Covid-19 on kidney and liver profiles. The patients that were used for the study were suffering from Covid-19 but without any previous damage of kidney and liver before Covid-19.

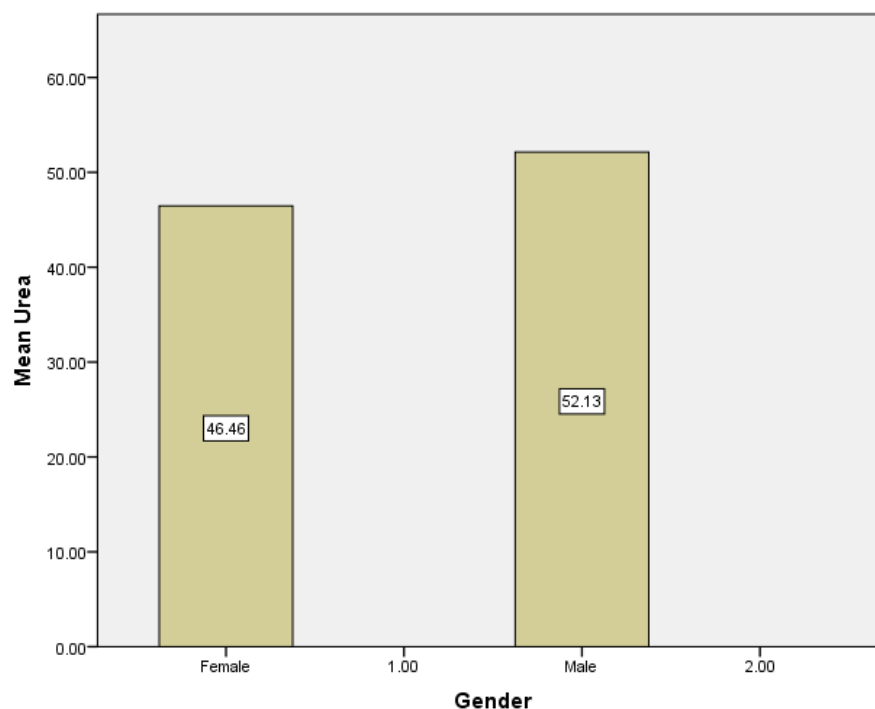
In the present study the tests proved that Covid-19 had a major effect on these profiles as shown in the table and graphs given below mean urea level in the gender wise distribution out of 600 collected Samples mean urea for female is 46.46 and for males is 52.13.

Mean creatinine is 0.96 in females and 1.28 in males. Mean total bilirubin obtained in females is 0.58 and in males 0.69. Mean ALT obtained is 75.24 and 72.99 in males and females respectively. Mean ALP is 199.70 and 187.64 in females and males accordingly. Mean TP is 6.78 and 6.77 in the females and males respectively. Mean ALB in females is 3.57 and in males slightly higher 3.64.

**Table -1**

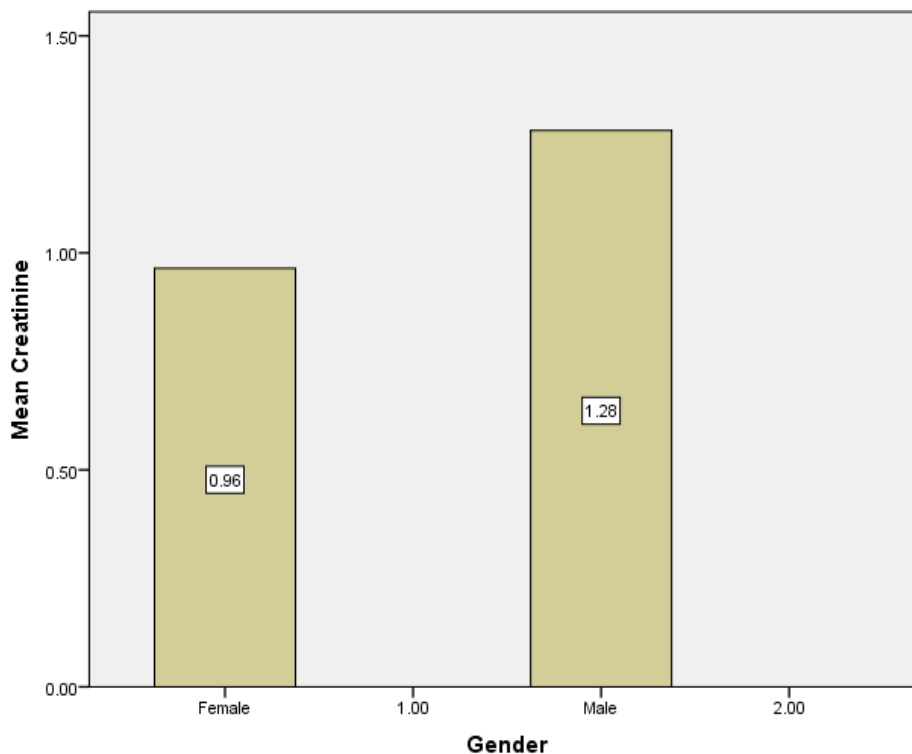
	Urea	Creatinine	Total Bilirubin	ALT	AST	ALP	TP	ALB	Glublin
Valid	511	511	511	511	510	511	506	505	511
Mean	55.3425	1.4022	.6620	74.4110	67.3863	183.2114	6.7354	3.6960	3.0168
Std. Deviation	47.95695	4.79933	.65073	87.25601	90.11112	148.59306	.77162	2.22117	2.25568
Minimum	1.00	.10	.07	5.00	11.00	43.00	2.20	.70	-35.80
Maximum	367.00	104.00	10.20	789.00	1054.00	1267.00	9.60	43.00	7.00

Table 1-. Demonstrates the biochemical parameters of liver function test and renal function test Out of 551 samples 511 give the positive results for urea, creatinine, total bilirubin, ALT, ALP, globulin. 510,506, 505 out of 551 samples give positive results for the AST, TP, ALB respectively.

**GRAPH 1**

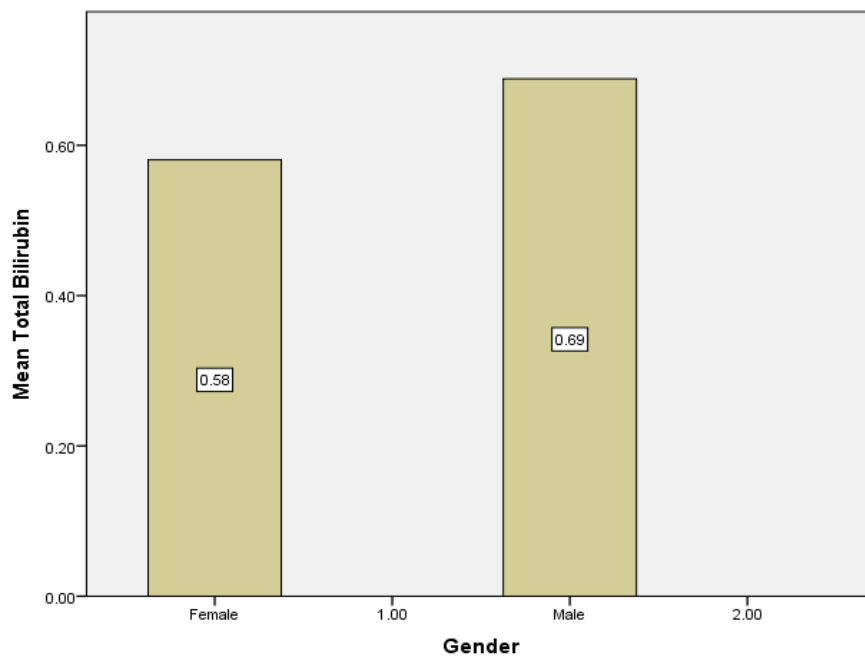
Graph shows the mean urea levels in the COVID-19 patients. Normal blood urea level is 5-20mg/dl. Out of 551 samples 511 gives the positive result. The graph shows the gender wise mean value of urea in covid-19 patients which demonstrates the damage of kidney in these patients. 46.6 mean urea level in females and 52.13 in males.

## **GRAPH 2**



Graph 2 represents the mean creatinine level in the COVID-19 patients. This shows the gender wise mean value of creatinine in females and males. Normal range of creatinine is 0.7 to 1.3mg/dl. Out of 551 511 patients were positive for creatinine test with mean urea level of 0.96 in females and 1.28 in males. Males are more affected by covid-19 in this study.

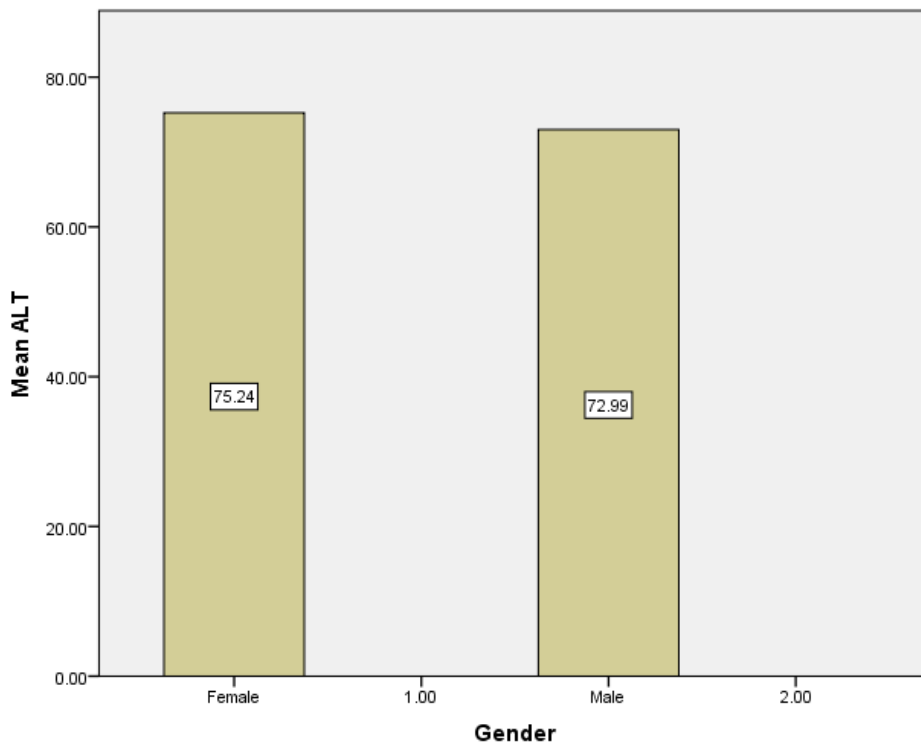
**GRAPH 3**



Graph 3 represents the mean total bilirubin level in males and females suffering from COVID-19. The normal range of total bilirubin in blood is less than 1mg/dl. In this graph the mean urea level in females is 0.58 but in males 0.69.

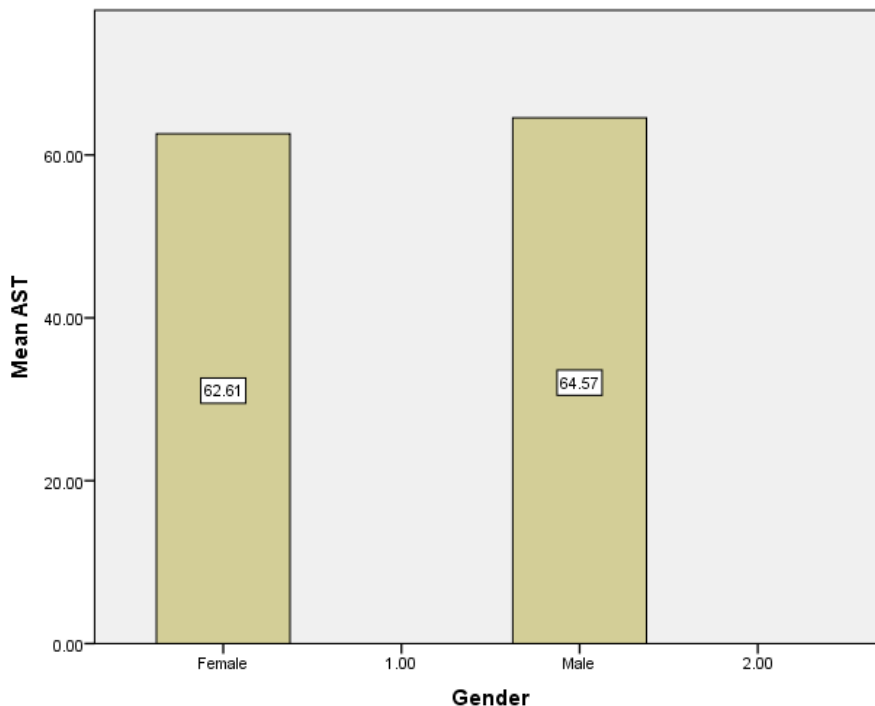


**GRAPH 4**

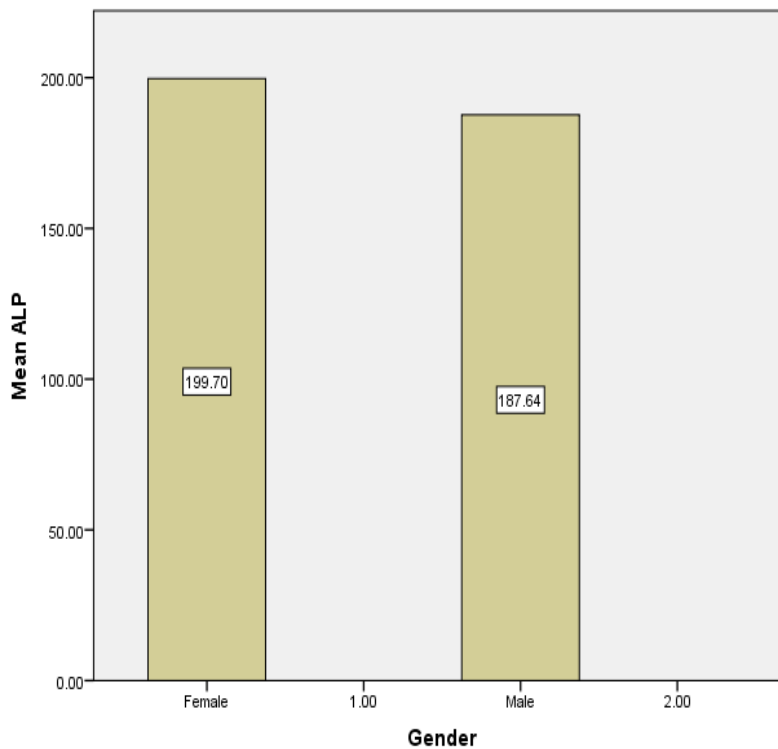


Graph 4 represents the mean ALT levels in females and males. The normal range of ALT is 4-36 U/L. this graph shows the mean ALT in females which is 75.24 very high. And in males the mean ALT level is 72.99 still high but less than that in females.

**GRAPH 5**

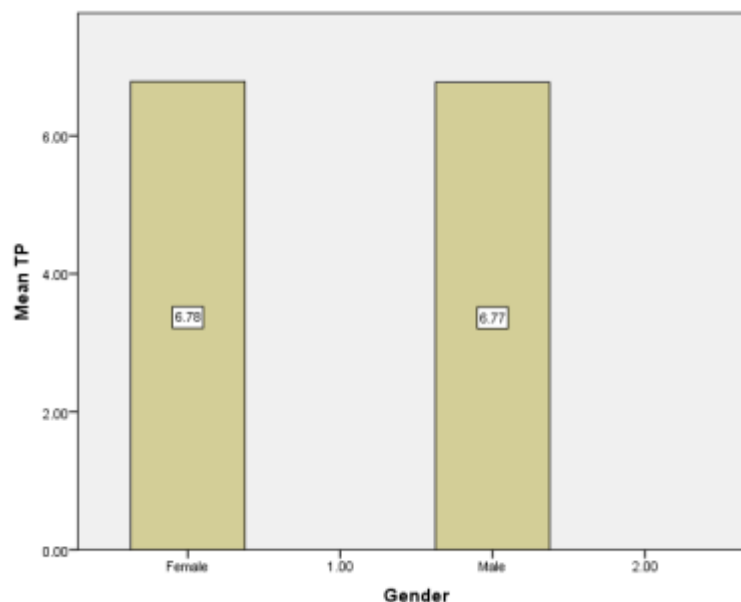


Graph 5 represents the mean AST levels in males and females suffering from COVID-19. The normal range of AST in blood is 8-33 U/L. this graph demonstrates the high mean AST in females which is 62.61 and 64.57 in males indicating the liver damage.

**GRAPH 6**

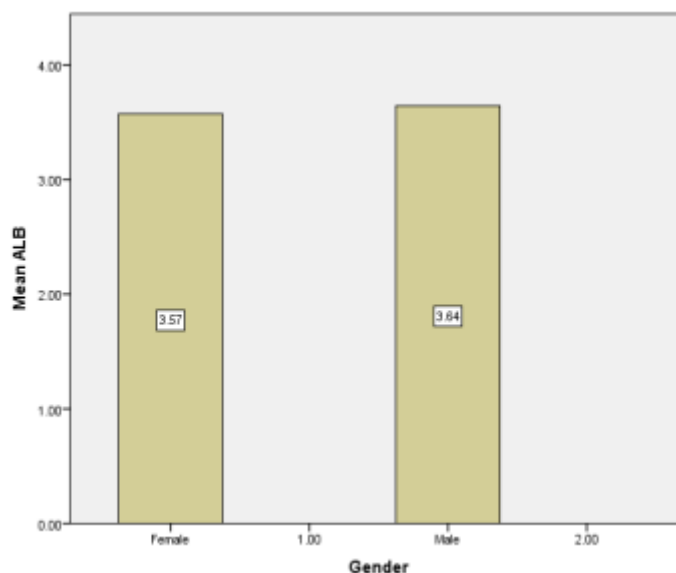
Graph 6 shows the mean ALP levels in serum of COVID-19 patients gender wise. The normal range of mean ALP in serum or blood is 44 – 147U/L. in this graph the level is very high in females which is 199.70 and also high in males 187.64 which clearly indicates the effect of covid-19 on liver profile

## GRAPH 7

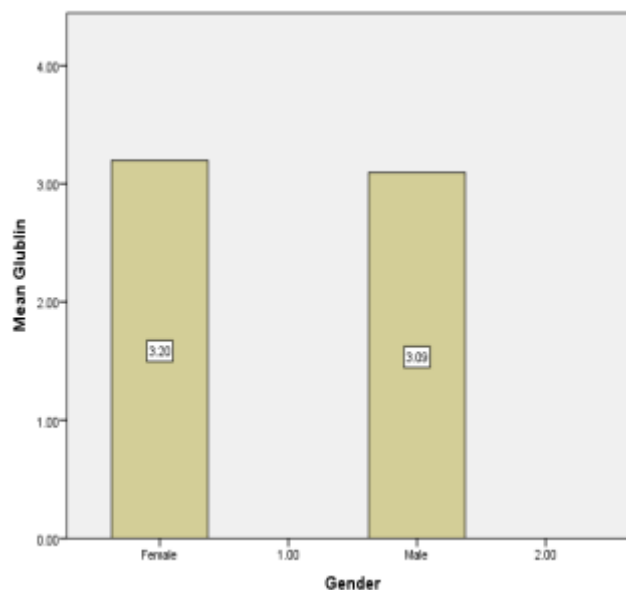


Graph 7 represents the mean TP in the COVID-19 patients' gender wise. The normal range of total protein in blood is 6-8.3 g/dl. In this graph the mean TP in females is 6.78 while in males is 6.77.

## GRAPH 8



Graph 8 shows the mean ALB levels in COVID-19 females and males. The normal range of ALB is 3.4-5.4 g/dl. This graph shows the mean ALB of 3.57 in females and 3.64 in males.

**GRAPH 9**

Graph 9 shows the mean Globulin levels in COVID-19 patients. The normal range of globulin is 2-3.5 g/dl. This graph shows the mean globulin of 3.20 in females and 3.09 in males relatively high in females.

**Discussion**

It is usually considered that there is only the lungs involvement in the patients suffering from Covid-19. Most of the studies demonstrated that lung is the only major organ affected by Covid-19 and there is no other organ involvement. Some of the previous studies demonstrated that there is involvement of kidneys as well as liver consequently affecting the liver and kidneys profiles in patients. This research basically aimed to prove the effect of Covid-19 on the kidney and liver profiles. For detecting the profiles several biochemical tests were performed. Liver function tests involve the AST, Alkaline phosphatase ALP, ALT, Total bilirubin, Total protein and serum albumin as well as globulin tests.

While the renal function tests involve the detection of urea and creatinine. The above tests were performed for analyzing the liver and the kidney damage in the patient's elevation in these parameters suggest the damage of both organs.

As the findings of this research demonstrated in table 4.1 in the chapter 4. According to this research out of 551 samples which were Covid-19 positive suggested by Polymerase chain reaction, 511 give positive results for the serum urea test with mean value of 55.34. Although the gender wise findings revealed mean urea of 46.46 in females and 52.13 in males.

Out of 551, 511 give positive test for creatinine with mean value of 1.4022 and graph 2 demonstrates the gender wise mean value of it, 0.96 in female and 1.28 in males.

511 out of 551 give positive results and 50 give negative results for total bilirubin test. The mean value of it is 0.6620. Graph 3 represents the gender wise mean value about 0.58 in females and

0.69 in males. 511 positives for alkaline transferase test 50 give negative results. Mean value of ALT is 74.4110. And graph 4 represents the mean value of 75.24 in females and 72.99 in males.

Out of 551, 510 positives for AST with a mean value of 67.3863 and graph 5 demonstrates the gender wise mean value 62.61 in females and 64.57 in males. 511 positives for ALP as well as globulin with a mean value of 183.2114 and 3.0168 respectively. The graph 6 shows the gender wise mean value of about 199.70 of ALP in females and 187.64 of ALP in male. Graph shows the mean globulin of 3.20 in females and 3.09 in males. 506 patients positive for total protein, 55 give negative results with mean value of 3.6960 with the gender wise mean value of 6.78 in females and 6.77 in males as shown in graph 7 of chapter 4. 505 patients positive for ALB with a mean of 3.6960 and gender wise distribution of mean value is 3.57 in females and 3.64. These are the findings of this research showing the effect of Covid-19 not only lungs but also on the kidney as well as the liver profiles. Previous showed the relatively similar results for the kidney and liver profiles providing the stability to these findings.

## **Conclusion:**

In the study there is now enough data to demonstrate the involvement of organs other than liver in the Covid-19 patients. This study shows the effect of Covid-19 on the kidney and liver profiles in certain patients. Therefore, the physicians and health staff should be aware of the clinical manifestations of Covid-19 so that a timely treatment is managed thereby eliminating the complications because of Covid-19. Several studies and investigations relating to the long-term impacts of Covid-19 on the liver and kidney profiles will definitely help in increasing our knowledge.

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