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# Renal function, glucose and LDH assessment of COVID-19 patients

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**Abstract**---Corona viruses are members of the order nidovirales and the corona family. Coronaviruses (CoVs) are a family of closed-cell, positive-sense, single-stranded RNA viruses with a wide range of characteristics. They produce a variety of health problems in humans and animals and affect the respiratory, digestive, liver and nervous systems. In this study, kidney function tests, LDH and glucose were evaluated in COVID-19 patients. The study included 120 cases, who were divided into three groups; a first group of 40 patients with COVID-19, and the second group of 40 recovered of COVID 19, and the third group was control of 40. The results indicated a significant increase ( $P < 0.01$ ) in the renal function parameters of Covid-19 patients compared to the recovered and control groups. The obtained results also indicated a significant increase in LDH and glucose levels ( $P < 0.01$ ) in patients compared to the recovered and control values. Among these results, it appears that the Corona virus may affect and threaten everything that cause the failure of vital organs in the body.

**Keywords**---COVID 19, Renal Function, Lactic Dehydrogenase, glucose.

## 1. Introduction

In Wuhan, China, a new member of the human coronavirus has been discovered. It has been officially named Severe Acute Respiratory Syndrome-Coronavirus-2 by the International Committee on Taxonomy of Viruses (ICTV) (SARS-CoV-2) [1]. First, cases of SARS-CoV-2 were multiplied rapidly in Wuhan and Hubei Provinces, and transmission chains spread throughout China. Many countries and territories outside China have reported imported and secondary cases, and this virus was described by the World Health Organization (WHO) as a pandemic on March 11th, 2020 [2].

Coronaviruses (CoVs) are a collection of enclosed, positive-sense, single-stranded RNA viruses with a wide range of characteristics. They cause a variety of illnesses in humans and animals. Coronaviruses are a broad family of viruses that cause diseases like SARS, MERS, and COVID-19. Mammalian and bird's viruses are the most common vectors of these viruses. So far, seven coronaviruses that have been found to be transmitted by humans respiratory, gastrointestinal, hepatic, and neurological systems [3].

Infected people spread the virus primarily by minute droplets produced by coughing or sneezing. [4], Respiratory viruses can spread through a variety of routes, including direct contact and aerosol transmission. The SARS-CoV-2 spreads mostly through droplet transmission, however one experimental investigation found that it can last up to 4 hours on copper surfaces, 24 hours on cardboard, and 2–3 days on less porous surfaces like plastic and stainless steel. These contaminated surfaces could spread the infection to others who come into contact with the same object or surface and then touch their mouth, nose, or eyes [5].

The incubation time for COVID-19 is recorded between 2 and 14 days [6]. The death rate is estimated approximately to be between 2 and 5%, however it fluctuates depending on the age and health status of the affected person [7]. It has been found that the most important factor in determining disease severity and mortality is the patient's age.

It is found that SARS-CoV-2 use the angiotensin-converting enzyme (ACE2) as a receptor on human cells. Studies have indicated that SARS-CoV-2 enters the cells by binding its spike proteins to ACE2 receptors [8]. Therefore, the number of ACE2 receptors located on the surface of the virus directly affects the degree of susceptibility of cells to infection. Studies have indicated that ACE2 plays an important role in the protective mechanisms of the lungs and can protect the lungs from severe infections caused by viral infection [9]. The first diagnostic method used to trace infected people is to detect whether they have been in contact with others who are infected [10].

The next step is to swab and collect samples of sputum, stool, and blood for COVID-19 reverse transcriptase polymerase chain reaction (RT-PCR) testing [11]. It is preferred to mention the author name, a nasal swab is more sensitive and specific than a pharyngeal swab, according to research, and the use of a lung imaging examination has been suggested as a confirmation approach. It has been

reported that RT-PCR analysis is less sensitive than computed tomography (CT) images. The results of several investigations show that, in patients with a positive CT scans for COVID-19, early pharyngeal RT-PCR assays were negative [12]. The main clinical signs of COVID-19 are fever, exhaustion, dry cough, and upper respiratory symptoms (nasal congestion and running nose), as well as gastrointestinal symptoms such as nausea, vomiting, and diarrhea, loss of sense of smell and taste [13].

By following up on Covid-19 patients, it was found that some people infected with the virus suffer from kidney problems that worsen over time, even for those who recover from the virus. Therefore, this study aims to investigate the efficiency of kidney and estimated the glucose and LDH levels for those infected with covid 19 in comparison to recovered and healthy individuals.

## **2. Materials And Methods**

### *Subjects and research methodology*

The study population was divided into three groups: patients, recovered and control (male and female, age range 20-60 years). The study included 40 patients with Covid 19 who were diagnosed after the PCR analysis showed a positive result. The number of people recovering from Covid 19 was 40 cases. The control group consisted of 40 age-matched healthy individuals for the patient group. Subjects were collected from patients who attended the consulting clinic/Baghdad Teaching Hospital/Medical City, Isolated Shifa Center Baghdad, Iraq between October and December 2020. Written informed consent was obtained from all study subjects prior to their participation and a questionnaire was filled out by patients. The covid 19 patients had a positive PCR result and were diagnosed for a prolonged period, at least (5-7) days. The patients were under treatment. The study included patients lying in isolation wards and patients in critical wards. None of the patients was a smoker, alcoholic or pregnant. Patients with other diseases such as diabetes, hypertension, hyperthyroidism, psoriasis were excluded.

### *Samples collection*

Ten ml of blood was extracted from each individual by a vein puncture with disposable syringes, 2 ml was collected in an EDTA tube, and 8 ml was collected in a gel tube. The whole blood samples were stored in a cooling fridge at 2-4°C after collection. The samples in the gel tubes were centrifuged for 10 minutes at 2000 xg. The serum was then kept at -20°C until the time of analyzing.

### *Sample Analysis*

The body mass index (BMI) of the subjects was calculated using the following formula:  $BMI = \text{weight (kg)} / \text{height (m)}^2$ . Urea and creatinine levels were measured using a spectrophotometer according to the colorimetric method following the Siemens group protocol of the available kits provided by Siemens Healthineers Erlangen, Germany. Uric acid was determined by colorimetric

method following the protocol of the available kit from Linear Chemicals, Spain. Glucose levels were determined using colorimetric method following the protocol of available kit from BIOLABO, France. LDH levels were determined using kinetic method following the protocol of available assay kit from BIOLABO, France.

### Statistical analysis

Data were analyzed using SPSS statistical software, version 23. ANOVA test was performed for independent samples between patients, recovery and control groups, and the resulting values were expressed as mean and standard deviation (SD). Statistical tests were significant at  $p < 0.05$  and highly significant at  $p < 0.01$  with 95% confidence interval. ROC CURVE was carried out for the studied parameters and the area under the curve (AUC) was determined. The sensitivity and specificity of the above-mentioned analyzes were also determined, and the cut-off value was determined.

## 3. Results and Discussion

### Age and anthropometric measurements

Age and anthropometric results for controls, recovered and patients with Covid 19 are presented in Table 1.

Table 1: Anthropometric measurements of Covid 19 patients, recovered and control groups

Parameters	Patient		Recovered		Control		p value
	Mean $\pm$ SD		Mean $\pm$ SD		Mean $\pm$ SD		
Age (year)	49.67	11.29	45.875	10.41	46.85	12.17	0.300 NS
Weight (kg)	80.60	8.80	78.32	8.45	79.45	9.07	0.513 NS
Height (cm)	168.52	9.12	165.87	9.70	167.70	8.94	0.427 NS
BMI (kg/m <sup>2</sup> )	28.55	2.63	29.22	4.43	28.47	4.43	0.650 NS

NS: Non-significant, \*: Significant at  $P \leq 0.05$

These results showed that there were non-significant differences ( $p > 0.05$ ) in the average age of the three groups studied. The calculated values for weight, height, and BMI were almost similar with non-significant differences ( $p > 0.01$ ) between patients, recovered and control groups. These results give a valuable opportunity for a case study among the studied groups, taking into account that there is no effect of age and weight on the results.

The distribution of patients to age groups showed that the highest percentage was in the group of patients aged 51-60 years, followed by age groups 41-50, 20-30 and 31-40 years, respectively, as seen in Figure 1. This finding confirmed the fact that the chances of contracting COVID-19 increase with age, which many

studies agree [14],[15], due to the immune system weakens with age. The groups participating in the research were classified by gender using a pie chart and the results were described in Figure 2.

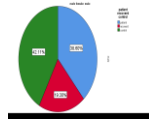


Figure 1: Pie chart shows the age distribution in covid 19 patients.

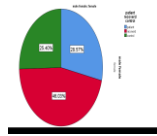


Figure 2: Pie chart shows the classification of groups participating in the research by gender

The results in figure 2 showed that the largest percentage of people infected with Covid-19 were males, amounting to 38.60%, compared to the percentage of females, which amounted to 28.57%. This finding consistent with several studies that reported that male is more likely to be infected with Covid 19 than female. The figure also shows that the percentage of women recovering from Covid-19 was 40.63%, which is the largest percentage compared to the males recovery from Covid-19, which amounted to 19.30%, and these results agree with the results obtained previously [16][17]. The effect of sex on patterns of immune response during viral infections has been extensively studied in both preclinical and clinical research, which suggested that sex differences in viral infection incidence, pathogenesis, and response maybe linked to strong female humoral and cell-mediated immune responses to viral antigens [18]. Higher innate immune system activity in women, mediated by Toll-like receptors, retinoic acid-inducible gene I-

like receptors, and nucleotide oligomerization domain-like receptors, may lead to faster and higher recognition of viral components, and consequently higher production of type 1 interferon (IFN) and inflammatory cytokines (IL-1, TNFs) [19].

### Renal Function

The renal function was assessed for patients with Covid 19 by measuring blood urea, creatinine and uric acid, then the results compared with the recovered and control groups, as shown in table 2. The results showed that blood urea, creatinine and Uric acid levels were significantly higher ( $p < 0.001$ ) than the recovered and control groups. While the results showed that the recorded values were approximately similar for recovered and control groups.

Table 2: Renal function tests levels for the Covid 19 patients, recovered and control groups

Spelling	Patient		Recovered		Control		p-value
	Mean	SD	Mean	SD	Mean	SD	
Urea (mg/dl)	61.82	22.923	30.70	6.37	31.55	5.82	0.001*
Creatinine (mg/dl)	1.17	0.68	0.80	0.15	0.82	0.16	0.001*
Uric acid (mg/dl)	5.252	2.364	3.85	0.79	3.64	0.93	0.001*

Several studies reported results in agreement with the results of the present work, which revealed an increase in urea and creatinine levels that may be due to impaired renal function and renal failure [20][21]. So, it can be said that Covid-19 practically affects kidney function, which leads to unfavorable results. It was found that in hospitalized Covid-19 patients, renal impairment (hematuria, proteinuria, and renal impairment) was common [22]. Signs of renal impairment were associated with an increased risk of death in hospital after controlling for covariates. In fact, according to these signs, clinicians should be more attentive to kidney impairment in hospitalized Covid-19 patients.

Table 3: Glu and LDH values for COVID-19 patient, recovered and control groups

Parameters	Patient		Recovered		Control		P-value
	Mean	SD	Mean	SD	Mean	SD	
Glucose Mg/dl	183.05	79.31	95.32	13.42	94.87	13.65	0.001*
LDH U/L	531.35	241.11	197.525	26.57	193.52	25.314	0.001*

Significant ( $p < 0.001^*$ )

The glucose level of Covid-19 patients was evaluated and then the results were compared with the recovered group and the control group as shown in Table 3. The results revealed the presence of a significant ( $p < 0.01$ ) increase in glucose

level for patients compared to the recovered and control groups, as shown in Figure 3.

The results of the blood sugar analysis obtained were high among the patients, especially in the IUC unit in the Medical City Hospital / Al-Shifa Center compared to the recovered group and the control group. This case necessitated the use of insulin injections to reduce blood sugar level in patients infected with coronavirus. The increase in glucose level may be due to several reasons including the patient's family history and susceptibility to diabetes, as well as the patient's psychological state and oxidative stress resulting from shortness of breath. Moreover, the treatment protocol used, which includes hydrocortisol injections, may affect the activity of the hormone insulin, leading to an imbalance in the blood sugar system. Previous studies agreed to a significant increase in blood sugar values in COVID-19 patients. In fact, increasing evidence indicates that coronavirus may lead to diabetes mellitus which is consistent with the results obtained in this study[23],[24],[25].



Figure 3: Glucose levels for Covid 19 patients, recovered and control groups

The LDH values appeared to be higher for Covid 19 patients compared to the recovered and control groups, as shown in Table 3. The data obtained of LDH showed a significant increase in serum concentration of patients compared with the recovered and healthy control group ( $p > 0.01$ ), as represented in Figure 4.

Several studies agreed with the findings of this research, as they supported an increase in LDH values in Covid-19 patients compared to healthy and recovered [26][27]. Lactate dehydrogenase (LDH) is an enzyme that converts lactate into pyruvate in the cells of most tissues of the body, and its activity increases during tissue breakdown. As a result, high serum LDH can be found in a variety of clinical conditions, including hemolysis, cancer, severe infections, sepsis, liver disease, hematological malignancies. There is now plenty of evidence that serum LDH levels can be used as a non-specific biomarker of cell death in a variety of diseases including COVID-19 [28][29]. In COVID-19 pneumonia, serum LDH has

been validated for its potential usefulness as a marker for determining clinical severity and monitoring treatment response[30].



Figure 4: LDH levels for Covid 19 patients, recovered and control groups.

Table 4: Correlations between variables in the Covid 19 patients group.

<b>Correlations<sup>a</sup></b>					
	urea	creatinin	uric acid	glucose	LDH
urea	1	.629**	.385*	-.063	.301
creatinin	.629**	1	.435**	-.047	.277
uric acid	.385*	.435**	1	-.103	.058
glucose	-.063	-.047	-.103	1	.115
LDH	.301	.277	.058	.115	1

\*\* . Correlation is significant at the 0.01 level (2-tailed).

\* . Correlation is significant at the 0.05 level (2-tailed).

The association between all the variables included in this study of Covid-19 patients was examined using Pearson's correlation analysis, and the results were represented in Table 4. The results revealed a positive relationship between uric acid levels and creatinine levels with urea level. The analysis also showed a positive correlation between creatinine with uric acid level in COVID-19 patients, as shown in Table 4.



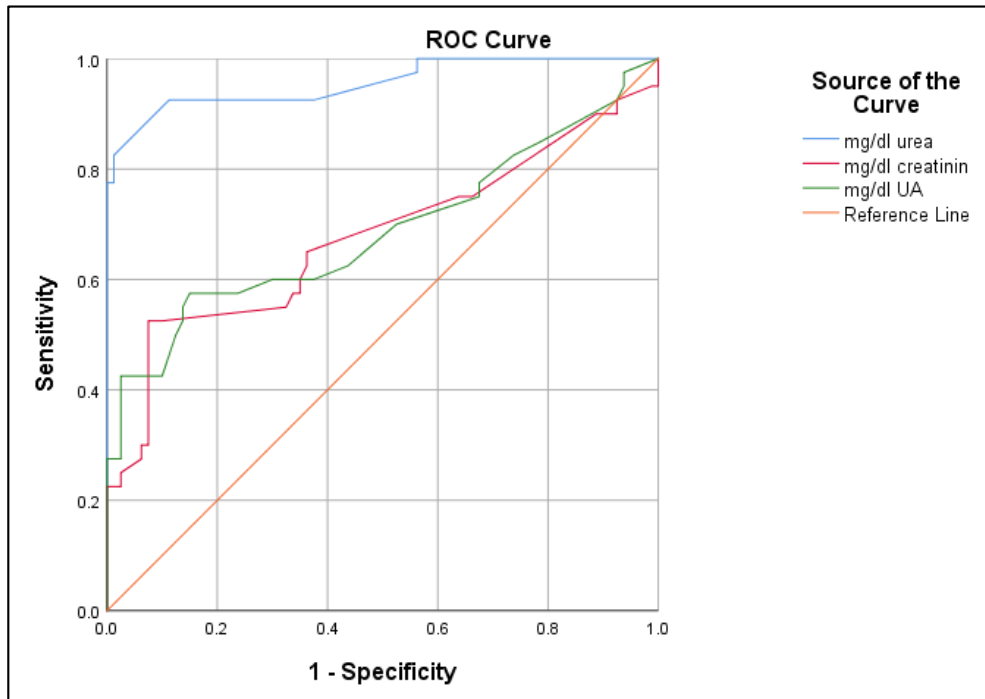


Figure 5: ROC curve for Urea, Creatinine and uric acid of Covid 19 patients.

The ROC Curve study was carried out to explore if Urea, Creatinine and uric acid could be utilized to diagnose Covid-19. The area under the curve (AUC) for Urea was found to be 0.956=excellent. Specificity: 98, sensitivity: 82, and the cutoff value 40.5 mg/dl. In light of this, all results higher than 40.5mg/dl within the patient population, and results less than 40.5 mg/dl are classified within the healthy population.

ROC curve analysis of creatinine and uric acid revealed that the AUC value for both was weak and useless. It was 0.676 for uric acid and 0.688 for creatinine, as shown in Figure 5. It can be suggested from these results that the urea test can be used as a reliable tool for diagnosing and monitoring the disease.

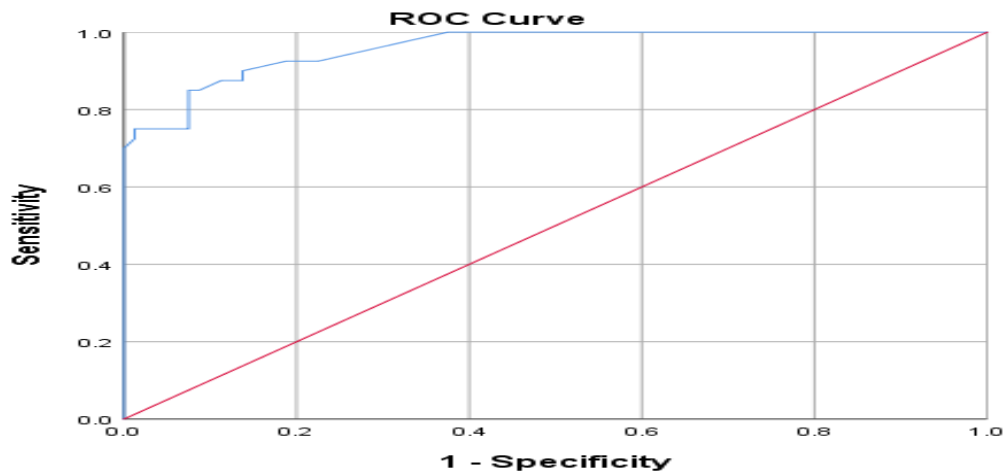


Figure 6: ROC curve for Glucose of Covid 19 patients.

The ROC curve for Glucose showed that the area under the curve (AUC) was found to be 0.960 = excellent. Specificity: 72, sensitivity: 95 and the cutoff value 100.5 mg/dl. In light of this, all results higher than 100.5 mg/dl within the patient population, and results less than 100.5 mg/dl are classified within the healthy population. It can be suggested from these results that the glucose test can be used as a reliable test for monitoring the disease.

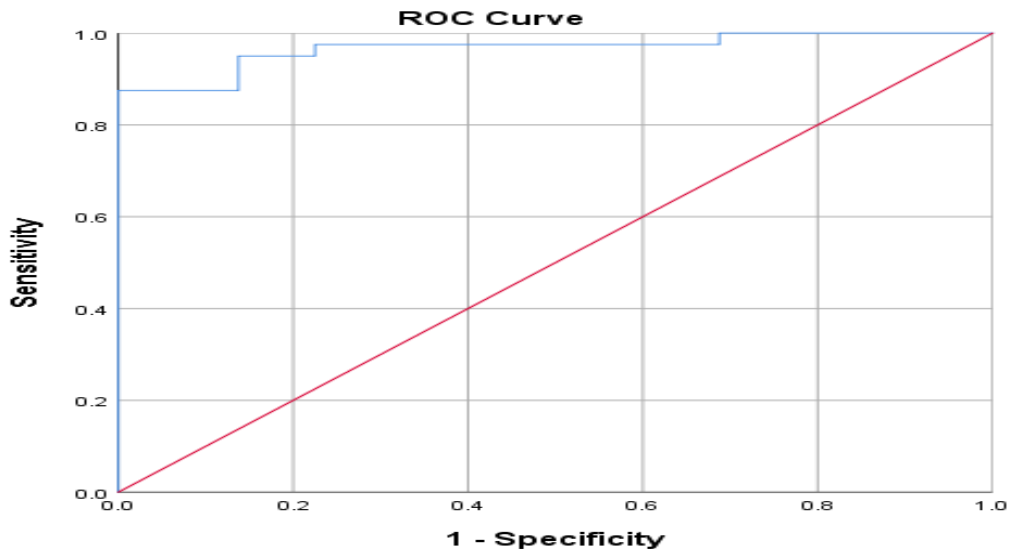


Figure 7: ROC curve for LDH of Covid 19 patients.

The ROC Curve of LDH for COVID-19 revealed that the area under the curve (AUC) was found to be 0.967 = excellent. Specificity: 73, sensitivity: 97, and the cutoff value 198.5 U/I. This result suggested that the LDH test can be used as a reliable test for monitoring Covid 19 disease.

#### 4. Conclusion

This study evaluates some important vital signs of Covid-19 patients. The results of this study showed an increase in indicators of renal function. Increases in LDH and glucose levels have also been observed in Covid-19 patients. On this basis, through this study, it is possible to suggest that monitoring of kidney function, glucose, LDH and the effect of treatment on these variables is very useful for Covid 19 patients. In fact, the effects of Covid-19 treatment should be taken into account and studied in detail. Therefore, more research is needed to determine the effect of the treatment used for Covid-19 patients and to follow up on the effect of disease severity on kidney function, glucose level, and LDH values.

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