Translational Research Urology

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Original Article

Laboratory Diagnostic Markers of Renal Patients with COVID-19

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HIGHLIGHTS

- In renal patients with COVID-19, the relationship of SpO2 with disease outcome variables, blood group O, intubation, K, INR, PT, MCHC, sore throat, care in ICU, and respiratory rate is known to be statistically significant.
- FBS, renal markers, and inflammatory markers were higher than the normal range in renal patients with COVID-19.
- The mean of liver diagnostic markers including SGOT, SGPT, and LDH were observed above the normal range in renal patients with COVID-19.

ARTICLE INFO

Receive Date: 16 May 2023
Accept Date: 31 July 2023
Avaliable online: 17 September 2023
DOI: 10.22034/TRU.2023.407331.1153

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ABSTRACT

Introduction
This study was planned and implemented with the aim of investigating the laboratory diagnostic markers of renal patients with COVID-19.
Methods
In this analytical cross-sectional study, by referring to the Department of medical records and health information system (HIS) and reviewing the files of kidney patients with covid-19 admitted from March 20, 2020, to March 19, 2021, in Taleghani Educational Hospital as the center of covid-19 disease in Abadan city, the information of patients were received.
Results
In this research, 125 patients were studied, of which 77 were men (61.6%) and 48 (38.4%) were female. The results showed that among the laboratory and clinical markers, fasting blood sugar (FBS), potassium (K), blood urea nitrogen (BUN), creatinine, serum glutamic oxaloacetic transaminase (SGOT), Serum glutamate pyruvate transaminase (SGPT), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), lactate dehydrogenase (LDH) and respiratory rate (RR) were higher than the normal range and oxygen saturation (SpO2) was lower than the normal range. Also, a significant relationship was found between SpO2 index and the outcome of the disease, blood type O, intubation, K, International normalized ratio (INR), prothrombin time (PT), mean corpuscular hemoglobin concentration (MCHC), sore throat, care in the intensive care unit (ICU) and respiratory rate.
Conclusions
Results showed that FBS, renal markers, inflammatory markers and liver markers were higher than the standard range in renal patients with COVID-19, and between the reduction of SpO2 and some clinical and laboratory diagnostic markers was a significant relationship.

Keywords: Kidney Disease; COVID-19; SpO2

Introduction

An acute respiratory illness of unknown origin was started in Wuhan, Hubei Province, China in December 2019. The World Health Organization (WHO) renamed the disease caused by SARS-CoV-2 to coronavirus disease 2019 (COVID-19) on February 11, 2020. The disease spread

rapidly throughout the world (1-3). Among the symptoms of patients with COVID-19 were shortness of breath, fever, anorexia, and muscle pain, impaired sense of taste, cough, and fatigue (4). In addition to the pulmonary system, as the main organ involved in this disease, other organs such as the kidney, digestive, and nervous systems are also involved (5). New investigations have acknowledged that kidney involvement is also prevalent among patients with COVID-19 (6). After infecting the lungs, this virus enters the blood and may damage kidney cells (3).

Chronic kidney disease occurs more among indigenous, minority, and socioeconomically disadvantaged populations and progresses more rapidly (7). Chronic kidney patients and those undergoing dialysis are at a higher risk of death from COVID-19 disease (8).

The risk of acute kidney injury in SARS was estimated to be 6.7%, which was associated with 91.7% mortality (9). Kidney disorders because of the coronavirus disease 2019 (COVID-19), including acute kidney damage, due to acute tubular necrosis (ATN) caused by sepsis, dehydration, cytokine storm syndrome, rhabdomyolysis, and hypoxia. In addition, the direct invasion of the virus into tubular interstitial or glomerular cells is also possible. The direct cytopathic impact of virus on different kidney cells has been determined in previous studies (10). The importance of the relationship between the pandemic disease of COVID-19 and kidney disease prompts us to carefully analyze the clinical and paraclinical relationship between the two diseases. Based on this, this investigation has been organized to examine laboratory markers in renal patients with COVID-19.

Methods

The current research is a cross-sectional analytical research that by referring to the medical records of Ayatollah Taleghani Educational Hospital in Abadan City of Iran, from March 20, 2020, to March 19, 2021, the clinical and laboratory information on 125 hospitalized renal patients with COVID-19 was received through the HIS. The laboratory information included liver factors (SGOT (AST), SGPT (ALT), (alkaline phosphatase (ALK), direct bilirubin, total bilirubin, lactate dehydrogenase (LDH)); hematologic Factors (White Blood Cell (WBC), Red Blood Cells (RBC), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin Concentration (MCHC)); coagulation factors (Platelets, PTT, PT, and INR); renal factors (Creatinine (Cr), Blood Urea Nitrogen (BUN), serum potassium (K) and serum sodium (Na); inflammatory markers (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Information was categorized according to date of admission, sex, age, and type of disease, duplicate data was removed, and the information was recorded in Excel software. This research was confirmed by the Ethics Committee of Abadan University of Medical Sciences (IR.ABADANUMS.REC.1399.161).

Inclusion criteria

Renal patients with COVID-19 with nasopharyngeal swabs positive for SARS-CoV-2 in RT-PCR were hospitalized at Ayatollah Taleghani Hospital, for whom laboratory and clinical data of them were available in the HIS. If the laboratory and clinical data of the mentioned patients were incomplete or unavailable, these patients were excluded from the study.

Statistical Analysis

SPSS software was used for data analysis in this research. Frequency and percentage in qualitative variables and mean and standard deviation in quantitative variables were used to describe the data. Multiple linear regressions were used to check the correlation and relationship of variables with SpO2 index. A P-value less than 0.05 was significant.

Results

Demographic and clinical findings

In the present study, 125 patients were studied, of which 77 were male (61.6%) and 48 (38.4%) were women. The mean age of the studied patients was 59.43±17.05. The majority of these patients were chronic kidney patients 89 (71.20%) and the rest were other kidney diseases including acute renal failure, urolithiasis, acute nephritic syndrome, glomerular diseases, disorders resulting from impaired renal tubular function, renal tubulo-interstitial diseases, calculus of lower urinary tract and other disorders of urinary system. The frequency and percentage of comorbidities are as follows: diabetes 55 (44%), heart disease 34 (27.2%), and lung disease 3 (2.4%) were reported in these patients. In the studied population, AB, B, A, and O blood types were 6.4%, 28.8%, 19.2%, and 45.6%, respectively. Among these patients, 64% recovered and 36% died. The most common symptoms are shortness of breath (76.8%), fever (49.6%), cough (30.4%), and sore throat (11.2%). The mean RR (21.31±2.98) in these patients was higher than standard. Also, the mean SpO2 of the patients (93.01% ±5.06) was lower than the standard range Table 1.

Laboratory markers in renal patients with COVID-19

The results of this research indicated that in renal patients with covid-19, the mean FBS of 174.98±117.80 was higher than the standard. The mean of BUN 55.46±27.50 and creatinine 4.14±3.13 in patients was found to be higher than the standard range. The mean of liver diagnostic markers including SGOT 47.73±43.47, SGPT 38.62±38.03, and LDH 631.82±251.56 were observed

Table 1. Demographic, laboratory and clinical characteristic of patients, (N = 125)

Variable	Mean or N	SD or %
Age, year		
≤50 years5	35	28.0%
1–70 years5	55	44.0%
≥71 years	35	28.0%
Sex		
Female	48	38.4%
Male	77	61.6%
Outcome		
Recovery	80	64.0%
Deceased	45	36.0%
Diabetes Yes	55	44.0%
Renal disease Yes	125	100.0%
Seizure Yes	0	0.0%
Heart disease Yes	34	27.2%
Lung disease Yes	3	2.4%
Blood type		
A	24	19.2%
B	36	28.8%
AB	8	6.4%
O	57	45.6%
FBS	174.98	117.80
BUN	55.46	27.50
Cr	4.14	3.13
Na	136.86	4.42
K	4.50	0.60
ALK	229.18	79.37
LDH	631.82	251.56
Total bilirubin	0.76	0.40
Direct bilirubin	0.26	0.24
SGOT	47.73	43.47
SGPT	38.62	38.03
PT	13.82	3.06
PTT	37.09	10.00
INR	1.23	0.47
ESR	55.38	28.81
CRP		
Negative	34	27.2%
CRP +	36	28.8%
CRP ++	33	26.4%
CRP +++	22	17.6%
WBC	10.49	7.05
RBC	4.34	0.94
MCV	83.50	7.26
MCH	27.17	2.85
MCHC	31.6	1.70
PLT	243.97	98.88
RR	21.31	2.98
SpO2	93.01	5.06
SBP	126.67	17.75
Fever Yes	62	49.6%
Cough Yes	87	30.4%
Shot ness of breath Yes	96	76.8%
Sore sroat Yes	14	11.2%
Intub Yes	29	23.2%
ICU care Yes	29	23.2%
ICU duration (day)	1.30	2.82

SD: Standard deviation; N: Number; FBS: Fasting blood sugar; Cr: Creatinine; BUN: Blood urea nitrogen; K: Potassium; Na: Sodium; LDH: Lactate dehydrogenase; ALP: Alkaline phosphatase; SGPT: Serum glutamate pyruvate transaminase; SGOT: Serum glutamic oxaloacetic transaminase; PTT: Partial thromboplastin time; PT: Prothrombin time; INR: International normalized ratio; CRP: C-reactive protein; ESR: Erythrocyte sedimentation; RBC: Red blood cell; WBC: White blood cell; MCH: Mean corpuscular hemoglobin; MCV: Mean corpuscular volume; MCHC: Mean corpuscular hemoglobin concentration; RR: Respiratory rate; SBP: Systolic blood pressure; SpO2: Oxygen saturation.

above the normal range. Coagulation markers such as PTT 37.09±10, and PT 13.82±3.06 in patients were higher than the normal range Table 1. The investigated inflammatory markers such as CRP1+, CRP2+, and CRP3+ were also reported in 36 (28.8%), 33 (26.4%), and 22 (17.6%) and the mean of ESR 55.38±28.8 in renal patients with COVID-19 Table 1.

SpO2 relationship with laboratory and clinical findings of patients

The results of the investigation of the relationship between SpO2 and the variables examined in this research using linear regression are presented in Table 2. The findings obtained from the linear regression analysis indicated that the level of SpO2 in renal patients with COVID-19 has a significant relationship with the outcome of their death so according to the estimated regression coefficient, SpO2 in patients who died; is 1.85 units less than in patients who have recovered (P-value=0.049). Also, with increasing age, the mean of SpO2 decreases by 0.036 units, and the mean of SpO2 in men was 0.29 units less than that of women.

In general, among other investigated factors, the relationship of SpO2 patients with disease outcome variables, blood group O, intubation, K, INR, PT, MCHC, sore throat, care in ICU, and respiratory rate is known to be statistically significant (P-value<0.05). In this way and according to the estimated regression coefficients:

For each unit increase of SpO2, the mean K decreases by 0.022 units, which has a significant relationship (P-value=0.043). The mean SpO2 in patients who were intubated upon entering the emergency room is 2.659 units lower than in patients who were not intubated at

Table 2. Association between SpO2 and laboratory diagnostic factors in the linear regression model

Variable	Unstandardized		Standardized	t	P-value	95.0% CI for B	
	B	Std. Error	Beta			Lower	Upper
Age, year	-.036	.027	-.120	-1.340	.183	-.088	.017
Sex (male)	-.291	.934	-.028	-.312	.756	-2.141	1.558
Outcome (died)	-1.853	.932	-.176	-1.988	.049	-3.698	-.008
Diabetes (yes)	-.274	.915	-.027	-.299	.765	-2.086	1.538
Heart problem (yes)	.676	1.020	.060	.663	.509	-1.343	2.694
Blood type (A)	-	-	-	-	-	-	-
Blood type (B)	1.314	1.341	.118	.980	.329	-1.342	3.970
Blood type (AB)	3.272	2.043	.159	1.602	.112	-.773	7.317
Blood type (O)	2.943	1.228	.291	2.397	.018	.512	5.373
Lung problem (yes)	-4.107	2.947	-.125	-1.394	.166	-9.940	1.727
FBS	-1.365	2.095	-.059	-.652	.516	-5.512	2.781
BUN	-.094	.490	-.017	-.192	.848	-1.064	.876
Cr	.040	.056	.065	.722	.472	-.070	.150
Na	-.126	.078	-.144	-1.616	.109	-.280	.028
K	-.022	.011	-.181	-2.041	.043	-.043	-.001
ALK	-.617	1.413	-.039	-.437	.663	-3.413	2.180
LDH	-1.510	4.479	-.030	-.337	.737	-10.377	7.356
Total bilirubin	.009	.007	.114	1.277	.204	-.005	.023
Direct bilirubin	.005	.004	.103	1.148	.253	-.003	.013
SGOT	-1.393	.764	-.162	-1.823	.071	-2.906	.120
SGPT	-.836	.673	-.111	-1.241	.217	-2.168	.497
PT	.129	.053	.213	2.419	.017	.023	.234
PTT	.187	.177	.094	1.052	.295	-.165	.538
INR	.018	.008	.190	2.150	.034	.001	.034
ESR	.763	.473	.144	1.616	.109	-.172	1.699
CRP (Negative)	-	-	-	-	-	-	-
CRP (+)	.662	1.213	.059	.546	.586	-1.739	3.063
CRP (++)	1.427	1.239	.125	1.151	.252	-1.026	3.880
CRP (+++)	2.003	1.388	.151	1.443	.152	-.744	4.750
WBC	-.057	.125	-.041	-.453	.652	-.305	.192
RBC	-.018	.017	-.098	-1.087	.279	-.051	.015
MCV	.136	.129	.094	1.052	.295	-.119	.390
MCH	.090	.050	.160	1.795	.075	-.009	.189
MCHC	.061	.030	.183	2.059	.042	.002	.120
PLT	.044	1.761	.002	.025	.980	-3.443	3.530
RR	-.252	.048	-.427	-5.240	.000	-.347	-.157
SBP	.260	.315	.074	.824	.412	-.364	.884
Fever (yes)	.176	.909	.017	.194	.847	-1.623	1.976
Cough (yes)	-.140	.988	-.013	-.141	.888	-2.096	1.816
Shot ness of breath (yes)	-.977	1.073	-.082	-.911	.364	-3.102	1.147
Sore throat (yes)	-3.227	1.412	-.202	-2.285	.024	-6.021	-.432
Intub (yes)	-2.659	1.050	-.223	-2.533	.013	-4.738	-.581
ICU care (yes)	-2.659	1.050	-.223	-2.533	.013	-4.738	-.581
ICU duration (day)	-.097	.049	-.175	-1.970	.051	-.195	.000

CI: confidence interval

the beginning of hospitalization, which has a significant relationship (P-value=0.013). Mean SpO2 in patients who were under care in ICU was 2.659 units less than those who were hospitalized outside the ICU, which has a significant relationship (P-value=0.013). With each unit increase in SpO2, the mean RR decreases by 0.252 units, which has a significant relationship (P-value<0.001). The mean SpO2 in patients who had a sore throat was 3.227 units lower than in patients who had no sore throat, which has a significant relationship (P-value=0.024). For each unit increase of SpO2, the mean MCHC, INR, and PT increased by 0.061, 0.018, and 0.129 ((P-value=0.042), (P-value=0.034) and (P-value=0.017)) respectively. The mean SpO2 in patients who had blood group O is 2.943 units higher than in patients who had other blood groups, which has a significant relationship (P-value=0.018).

Discussion

In the current research, 125 renal patients with COVID-19 were studied. Most of these patients were between the ages of 51 and 70 (55%). Diabetes was reported as the most common disease associated with these patients and was observed in 44% of patients. A significant relationship was found among laboratory and clinical markers between SpO2 index and disease outcome, blood group O, intubation, K, INR, PT, MCHC, sore throat, care in ICU, and respiratory rate. The findings obtained from the linear regression analysis showed; the level of SpO2 in renal patients with COVID-19 has a significant relationship with the outcome of their death. The mean BUN and creatinine in patients were higher than the normal range. The mean of liver markers was higher than the normal range in patients. The mean FBS, PT, PTT, LDH, ESR, and RR were also higher than standard in these patients and the mean SpO2 was lower than the normal range.

In a retrospective study conducted by Akhavizadegan and colleagues in 2020 in Iran; 522 elderly patients hospitalized with COVID-19 were examined; Out of this number, about 77% (422 people) of hospitalized elderly people were saved from this disease and 23% of them died. The average age of the participants was 72 years and about 54% (281 people) of them were men. 23 of these people had kidney disease; 16 people recovered and 7 people died, and in general, the amount of oxygen at the beginning of the hospitalization of the patients who died was significantly lower than the amount of oxygen of the patients; who had survived (11). In a retrospective research done by Pie et al., in 2020 in Wuhan, China; 333 patients with COVID-19 were hospitalized. Patients with kidney involvement had higher mortality than those without (12). The current investigation's mean SpO2 was lower than standard range in renal patients with covid-19. Also, low SpO2 increased the risk of death of patients.

In a cohort research led by Cheng et al., in Wuhan, China in 2020, 701 patients with COVID-19 were hospitalized, including 367 males and 334 females, with a mean age of 63 years in terms of kidney problems. Patients with renal disease were at significant risk of in-hospital death, and elevated serum creatinine, elevated BUN, and leukocyte count were independent predictors of in-hospital death. Therefore, the findings of this study show that the prevalence of hospitalized kidney disease in patients with COVID-19 is high and is associated with in-hospital mortality (13). In the present study, BUN and creatinine were significantly increased in renal patients with COVID-19. Also, low SpO2 increases the risk of patient death, but in this research, the mean of WBC was in the standard range.

In the study by Li et al., conducted in China in 2020, 59 hospitalized patients with COVID-19 were examined. Of these, 28 patients had severe disease and three patients died and increase in creatinine level was seen in 19% of patients and an increase in BUN in 27% of patients (14). In the research conducted by Su et al., conducted in China in 2020, in autopsies of 26 patients with COVID-19, 9 patients showed symptoms of kidney involvement, which included an increase in serum creatinine or newly started proteinuria (15). In a study conducted by Rouhani Zadeh and colleagues in the population of Mazandaran province in 2021; the chance of getting a COVID-19 infection in people with blood group O is significantly lower by 30% compared to other blood groups (16). In the present research, the mean of SpO2 in patients with blood type O was significantly more than in patients who had other blood groups; but the frequency of these patients in the present study is higher in blood type O.

In a cohort investigation conducted by Amin et al., in 2020; Out of 192,182 patients with covid-19, 12% of patients had hyperkalemia. Its prevalence is higher in men, and blacks, with a history of chronic kidney disease, and diabetes mellitus than in people who did not have hyperkalemia. The mortality rate in patients with hyperkalemia was significantly higher than in patients without hyperkalemia. Also, the probability of hospitalization was higher in patients with hyperkalemia (17). In the current study, the mean potassium is higher than the normal level and with each unit increase in potassium, the mean SpO2 decreases by 0.022 units, which has a significant relationship. Also, low SpO2 increased the risk of death in patients.

In a retrospective study conducted by Pawar et al., in 2021 in India; a total of 30 chronic kidney patients with covid 19 were studied; As a result of this study, the mortality rate was 53.3%, and IL-6 and high LDH were significantly related to mortality, and lymphopenia was associated with fatal consequences in 50% of cases (18). In the present study, 36% of renal patients with COVID -19 died. The mean of LDH and ESR were higher than normal but no significant relationship with SpO2 level

was observed and the number of leukocytes was observed in the normal range.

In a retrospective study conducted by Hakami et al., in 2021 in Saudi Arabia, 20 patients (19.8%) died out of 101 hospitalized COVID-19 patients with ESRD. Patients over 65 years of age had a significant mortality risk. The most common clinical symptoms observed in these patients included fever, shortness of breath, and cough, and the most common comorbidities included blood pressure, diabetes, and heart disease, respectively. It was also observed that 17% of the studied patients were admitted to the intensive care unit and needed mechanical ventilation. Respiratory failure (19%) was one of the most common complications leading to death (19). In the present study, Hypertension (20%), heart disease (27.2%), lung disease (2.4%), and diabetes (44%) were reported in these patients; and shortness of breath (76.8%) was the most common clinical symptom, and the mean of LDH, AST, and ALT in our study was observed to be higher than normal. In the current study, a significant relationship was found between hospitalization in the ICU and intubation and RR, with SpO2.

In the cohort study of Bruce Bode et al., in 2020, it was found that uncontrolled diabetes or hyperglycemia occurs frequently among hospitalized patients with COVID-19. Also, the covid-19 patients with diabetes had a longer length of hospitalization and their mortality was more significant and higher than patients without diabetes (20). In the present study, 44% of the patients had diabetes and the mean FBS was higher than the normal range.

In a retrospective study conducted by Yao et al., in 2020 in Wuhan, China; 202 patients with COVID-19 were hospitalized. In the results of this study, most patients (152 patients; 75.2%) had hypoxemia (Sao2<90%) before intubation, and death occurred in 24 hours in 21 patients (10.4%) (21). In the present study, the mean SpO2 in patients who were intubated is 2.659 units lower than the patients who were not intubated during hospitalization, which has a significant relationship. Also, low SpO2 increased the risk of death of patients.

In the cohort study of Bruce Bode et al., in 2020, it was found that uncontrolled diabetes or hyperglycemia occurs frequently among hospitalized patients with COVID-19. Also, the COVID-19 patients with diabetes had a longer length of hospitalization and their mortality was more significant and higher than patients without diabetes (20). In the present study, 44% of the patients had diabetes and the mean FBS was higher than the normal range.

In a retrospective study done by Yao et al., in 2020 in Wuhan, China; 202 patients with COVID-19 were hospitalized. In the results of this paper, most patients (152 patients; 75.2%) had hypoxemia (Sao2<90%) before intubation, and death occurred in 24 hours in 21 patients (10.4%) (21). In the current paper, the mean SpO2 in patients who were intubated is 2.659 units lower than the patients who were not intubated during hospitalization, which has a significant relationship. Also, low SpO2 increased the risk of death of patients.

Considering the retrospective nature of the design and the absence of a control group in the current study, it is suggested to implement larger control case designs with the aim of comparing laboratory, liver, kidney, etc. indicators in patients with and without kidney disease affected by COVID-19 and it should be implemented to determine independent risk factors affecting the death of this group of patients while comparing these indicators.

Conclusions

The results showed that in renal patients with COVID-19, the laboratory and clinical markers such as potassium, BUN, Cr, SGOT, SGPT, ESR, CRP, LDH, and respiratory rate were higher than the normal range and SpO2 was lower than the normal range. Also, a significant relationship was found between the SpO2 index and the outcome of the disease, blood type O, intubation, K, INR, PT, MCHC, sore throat, care in the intensive care unit, and respiratory rate; Therefore, it is very important to pay attention to these markers in the diagnosis and treatment of renal patients with COVID-19.

Authors' contributions

Conceptualization: ER, Formal analysis: NK, Investigation: ER, ME, HK, MB, NK, Methodology: ER, ME, HK, NK, SM, MB, KhK, Project administration: ER, Validation: MB, NK, KhK, SM, Writing – original draft: ER, ME, Writing – review & editing: ER, MB, NK.

Acknowledgments

Special thanks to the Ethics Committee of Abadan University of Medical Sciences and the Clinical Research Development Unit of Taleghani Educational Hospital, Abadan University of Medical Sciences, Abadan, Iran.

Conflict of interest

All authors declare that there is no conflict of interest.

Funding

There was no funding.

Ethics statement

This study was approved by the Ethics Committee of Abadan University of Medical Sciences (IR.ABADANUMS.REC.1399.161).

Data availability

Data will be provided on request.

Abbreviations

ALP	Alkaline phosphatase
BUN	Blood urea nitrogen

Cr	Creatinine
CRP	C-reactive protein
ESR	Erythrocyte sedimentation
FBS	Fasting blood sugar
INR	International normalized ratio
LDH	Lactate dehydrogenase
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
PT	Prothrombin time
PTT	Partial thromboplastin time
RBC	Red blood cell
RR	Respiratory rate
SBP	Systolic blood pressure
SGOT	Serum glutamic oxaloacetic transaminase
SGPT	Serum glutamate pyruvate transaminase
SpO2	Oxygen saturation
WBC	White blood cell

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How to cite this article

Eftekhar M, Kamyari N, Ban M, Karimi H, Kanani KH, Mobarak S, Radmanesh E. Laboratory Diagnostic Markers of Renal Patients with COVID-19. Transl. res. urol., 2023 Sep;5(3):128-135.
DOI:10.22034/TRU.2023.407331.1153
URL:https://www.transresurology.com/article_176578.html