Electronic Journal of General Medicine
2023, 20(6), em547
e-ISSN: 2516-3507
https://www.ejgm.co.uk/

MODESTUM

Original Article

OPEN ACCESS

Investigating kidney function changes in young adults with COVID-19: Serum creatinine level, glomerular filtration rate, and biochemical profile analysis

Nikita Matyushin [1], Dmitriy Ermakov [2*], Inna Vasileva [3], Roza Vakolyuk [4], Anastasiya Spaska [5]

[1] Department of Nursing, I. M. Sechenov First Moscow State Medical University, Moscow, RUSSIA
[2] Department of Pharmacy, I. M. Sechenov First Moscow State Medical University, Moscow, RUSSIA
[3] Department of Polyclinic Therapy, Institute of Clinical Medicine named after N. V. Sklifosovsky, I. M. Sechenov First Moscow State Medical University, Moscow, RUSSIA
[4] Department of 2nd Hospital Therapy, I. M. Sechenov First Moscow State Medical University, Moscow, RUSSIA
[5] College of Medicine, Ajman University, Ajman, UAE
***Corresponding Author:** dmitriyermakov23@rambler.ru

Citation: Matyushin N, Ermakov D, Vasileva I, Vakolyuk R, Spaska A. Investigating kidney function changes in young adults with COVID-19: Serum creatinine level, glomerular filtration rate, and biochemical profile analysis. Electron J Gen Med. 2023;20(6):em547. https://doi.org/10.29333/ejgm/13750

ARTICLE INFO

Received: 19 Jun. 2023

Accepted: 15 Aug. 2023

ABSTRACT

The study's objective was to comprehensively assess kidney function alterations in patients with COVID-19. The study was carried out in Moscow (Russia) in 2021. 100 patients of 19-30 years old (51 females and 49 males) took part in the survey. The study collected participant data on basal urine, serum creatinine, and estimated glomerular filtration rate from medical histories before COVID-19 infection. COVID-19 diagnosis (delta strain) was confirmed by polymerase chain reaction test. Serum creatinine was measured, considering age and race. Micro-albuminuria levels from daily urine samples were established. Laboratory blood tests included quantitative indices of blood-forming elements, hemoglobin levels, and biochemical parameters. Based on the results, the study observed a slight increase in serum creatinine levels after COVID-19 infection, with concentrations of 78.4±6.4 mmol/L before infection and 87.5±7.7 mmol/L after the disease ($p \geq 0.05$). The microalbuminuria-creatinine ratio also showed an increase. The glomerular filtration rate in renal glomeruli declined from 93.3±10.1 mL/min/1.73 m^2 before infection to 78.9±8.7 mL/min/1.73 m^2 after the disease ($p \geq 0.05$). These findings suggest a trend towards decreased kidney function in young patients with moderate COVID-19 severity. However, normoalbuminuric compared to creatinine was significantly higher than normal after COVID-19. Urine tests indicated a trend of decreased renal glomerular filtration rate. Clinical symptoms included high temperature, weakness, cough, and, in some cases, liquid stools. Laboratory findings revealed significant deviations in hematocrit, neutrophil, and eosinophil concentrations. Parallel tests focusing on cystatin C and beta-2 macroglobulin are recommended to assess kidney function and identify potential dysfunction.

Keywords: COVID-19, functional kidney disorders, procalcitonin, beta-2-microglobulins, cystatin C

INTRODUCTION

Coronavirus infection has a widespread impact on vital organs, including the lungs, heart, and kidneys [1]. COVID-19 exhibits varying degrees of severity, ranging from mild to critical [1-4]. The majority of cases (about 80%) present with mild or moderate symptoms and recover at home [4]. Moderate cases may require hospitalization and medical supervision due to worsened lung function. Severe COVID-19 cases demand intensive care and respiratory support, while critical cases involve acute respiratory failure, organ failure, and shock, requiring immediate medical intervention.

COVID-19 can lead to renal damage, particularly in patients with chronic kidney disease (CKD) and cardiovascular abnormalities [3]. The risk of severe outcomes is higher in older patients, especially those with CKD, diabetic and hypertensive nephropathy, renal transplant recipients, and those on immunosuppressants [5-6]. Elevated proteinuria is associated with a severe course of COVID-19 and an increased risk of kidney failure [7]. Impaired renal function is more common in severe cases with lower blood oxygen levels [7-8].

Deaths among dialysis patients have increased during the pandemic [9-10]. CKD is a common comorbidity in elderly patients, associated with higher mortality rates [11-14]. COVID-19 can lead to new-onset mild or severe nephropathy, often accompanied by proteinuria and hematuria [15]. The virus's toxic effects may cause segmental glomerulosclerosis and renal tubule necrosis, leading to proteinuria and end-stage renal disease [16-19]. Patients with specific gene variants are at higher risk of developing glomerulosclerosis.

COVID-19 patients necessitate meticulous surveillance of their renal function, and the presentation of acute kidney injury symptomatology may exhibit variability, as indicated in references [17, 20, 21]. Urinalysis and serum creatinine measurements play a crucial role in diagnosing and managing renal disease in COVID-19 patients, especially in severe cases

Table 1. Age characteristics of patients from COVID-19 group & reference group

Variable	COVID-**19 group**	**Reference group**
Male		
Number	49	47
Age	23.9±2.8	24.1±2.4
Female		
Number	51	53
Age	23.1±2.2	23.5±2.7

[1]. Timely and intensive treatment may resolve these pathologies, but high mortality rates have been associated with proteinuria and hematuria [7].

In conclusion, COVID-19 impacts multiple organs, including the kidneys, and varies in severity [2]. Proper assessment and management of kidney function are essential for improving clinical outcomes and reducing mortality rates in COVID-19 patients. Primary objective of study was to comprehensively assess kidney function alterations in patients with COVID-19. Specifically, the aim was to examine serum creatinine levels, investigate glomerular filtration rate, and analyze the laboratory test results and biochemical profiles of the patients.

MATERIALS AND METHODS

Sample

This study is a baseline one since it aims to detect changes in the biochemical parameters of blood in patients with coronavirus. The study was conducted from January to October 2021 in two polyclinics of Moscow, Russia, based on patients hospitalized and diagnosed with COVID-19. The patients were 19-30 years of age (average age=23.4 and standard deviation=2.5 years). For this study, individuals aged between 19 and 30 years, exhibiting a moderate form of COVID-19, were recruited from the existing population of hospitalized patients diagnosed with this condition. Within the scope of this research, the diagnosis of COVID-19 was confirmed using polymerase chain reaction (PCR) testing. All patients included in this study were young, as the age group chosen was specifically between 19 and 30 years and exhibited a moderate form of COVID-19. This approach was undertaken to investigate specific alterations in biochemical blood parameters and renal function within this particular age group affected by the moderate form of the disease. The sample comprised 100 patients (**Table 1**).

All patients exhibited an average severity of illness. According to the anamnesis documents, all patients had no pre-COVID-19 kidney and urinary tract pathologies or disorders. The reference group included the same number of practically healthy respondents (**Table 1**). These two groups are comparable due to identical gender and age composition.

Below are the risk factors associated with the development of CKD in patients diagnosed with SARS-CoV-2 infection:

1. Advanced age
2. Comorbidities (e.g., diabetes mellitus, arterial hypertension, and cardiovascular diseases)
3. Elevated levels of C-reactive protein (CRP) indicate the presence of inflammation in the body
4. Increased levels of lactate dehydrogenase, which may signify tissue and organ damage
5. The requirement for intensive care and mechanical ventilation
6. Usage of nonsteroidal anti-inflammatory drugs, which may elevate the risk of kidney dysfunction in certain patients

However, it is noteworthy that risk factors may vary for each patient and depend on the infection severity and the presence of other diseases.

Research Design

All patients were under the same conditions, given the same treatment, and observed identical daily diet conditions, and the diet was also identical. The following are the methods of therapy used. Oxygen therapy–in case of a decrease in blood oxygen saturation, patients were prescribed oxygen to the respiratory system to maintain sufficient oxygen levels in the body. Medications–various medications were prescribed to treat COVID-19 symptoms, including glucose-corticosteroids and anticoagulants. The severity of COVID-19 was determined using various indicators, including symptoms, blood oxygen saturation, general health, and medical data such as blood protein levels and white blood cell counts. Several of the prevalent indications of severe COVID-19 include fever, cough, acute difficulty breathing, chest pain, organ dysfunction, and loss of consciousness. Treatment of severe cases of COVID-19 typically takes place in a hospital under the supervision of medical personnel. The following symptoms were observed:

1. Mild symptoms: Moderate fever, cough, sore throat, rhinitis, headache, and fatigue
2. Respiratory complications: Pneumonia (lung inflammation), bronchitis, and tracheitis
3. Neurological complications: Loss of smell and taste, vertigo, and sleep disturbance
4. Cardiological complications: Cardiac arrhythmias
5. Complications from the digestive system: Diarrhea, nausea, vomiting, and abdominal pain

During the disease, various complications manifested, including thrombosis, hyperglycemia, nephropathy, and immune dysregulation.

Following the screening, patients were interviewed to explain the purpose of the work and the methods used. Based on the interview, the patients willingly signed a study participation agreement. The contract guaranteed that the information obtained would be anonymous and confidential. The study was conducted in a manner consistent with international ethical and moral standards.

The inclusion and exclusion criteria for this study were meticulously defined to ensure the homogeneity of participant selection. The study enrolled patients who had no pre-existing kidney issues before COVID-19 infection (confirmed through medical history), fell within a specific age range of young adults, exhibited a moderate severity of COVID-19, and provided their informed written consent to participate. Patients not meeting one or more of these criteria were excluded from the study.

It is important to note that the study was confined to a specific age group of young adult individuals from all Caucasian ethnicities, as biochemical parameters may significantly differ across various age groups and ethnic backgrounds. The inclusion criteria for the study encompassed the following conditions:

1. Confirmed diagnosis of COVID-19
2. Moderate severity of COVID-19
3. Alignment with the specified age group
4. Absence of severe comorbidities such as diabetes, cardiovascular issues, and renal impairments
5. Provision of written informed consent for participation in the research

By applying rigorous inclusion and exclusion criteria, the study aimed to ensure the validity and substantiation of its findings pertaining to kidney function in young patients with a moderate course of COVID-19.

Research Methods: Assessment of Kidney Function in Patients with COVID-19 Using Laboratory & Biochemical Analyses

Participants' data on basal urine, serum creatinine, and estimated glomerular filtration rate collected before the COVID-19 infection were extrapolated from their medical histories. The basis for this study was the diagnosis of COVID-19 (delta strain), confirmed by PCR test. The creatinine level was measured by an enzymatic method using a specialized biochemical analyzer (daytona model from Rendox manufacturer, country of origin Great Britain). In addition, consideration was given to the filtration rate parameter in the renal tubules. It was done using the EPI formula, as follows:

$$Renal\ glomerular\ filtration\ rate = a\ (blood\ creatinine\ (mg/dL)/b)c \times (0.993)\ age. \quad (1)$$

Eq. (1) is CKD-EPI formula. We have used CKD-EPI 2012 (a modified formula [22]).

The calculation was based on race (all patients in this study were white) and age. The first of these parameters is included in variable a, while the second is in variable b. Serum creatinine was standardized by isotope dilution-mass spectrometry.

The micro-albuminuria level based on daily urine samples has also been established. An enzymatic assay method was used, using the same biochemical analyzer.

Normoalbuminuric to creatinine ratio (urine albumin creatinine ratio) was calculated using the formula:

$$ratio = albumin\ concentration\ level\ (in\ milligrams\ PUP)/ creatinine\ concentration\ level\ (in\ grams\ PUP), \quad (2)$$

where PUP means per urine portion.

The following parameters were considered in the laboratory blood tests: quantitative indices of blood-forming elements (platelets, erythrocytes, and leukocytes, in $\times 10^{12}$/l for erythrocytes and $\times 10^{9}$/l for the rest), hemoglobin level index (in g/l), and erythrocyte index. Biochemical blood tests were also completed, including glucose levels, CRP, folic acid, and D-dimer levels.

The comparison between the groups employed to the biochemical parameters of blood and urine. It was carried out within the group of patients with COVID-19 during hospitalization and after their discharge.

Statistical Analysis

Statistical analysis was performed using the statistical package for the aocial aciences (SPSS) version 10. The data was also completed and organized in Microsoft Excel 2016.

For each parameter, the arithmetic mean was calculated, and a comparison was made between the obtained indices and the reference values of the control group, which consisted of patients of the same age. To assess differences between groups, the atudent's t-test for independent samples was utilized. Specifically, the values within the group of COVID-19 patients were compared before and after hospitalization. The significance level for all analyses was set at $p \leq 0.05$. The data was presented in the form of mean values and the standard error of the mean (SEM). The power index of the study was determined to be 80%, and the differences between the groups were considered reliable when $p \leq 0.05$. It should be noted that a sample size of 100 to 200 participants was deemed sufficient for these statistical parameters.

RESULTS

Examination of Serum Creatinine Level & A Study of Glomerular Filtration Rate

The average duration of the disease was seven-10 days. However, in some (21 people) patients it was more than 10 days due to the slow progression and gradual worsening of COVID-19 symptoms. It was found that there was a slight increase in the level of creatinine in the group of patients. Furthermore, the microalbuminuria-creatinine ratio was increased. Parameters of glomerular filtration rate in renal glomeruli were found to be declining.

For the creatinine, the concentration was 78.4±6.4 mmol/L before the patients got infected with COVID-19 and 87.5±7.7 mmol/L after the disease passed ($p \geq 0.05$). Changes in normoalbuminuric and creatinine were also insignificant, amounting to 22.1±2.8 mg/L before the disease and 33.7±4.3 mg/L after ($p \geq 0.05$).

Despite the insignificance of the differences obtained, the level of normoalbuminuric compared to creatinine following COVID-19 was above normal ($p \leq 0.05$). This group index was above normal in 28% of patients. For urine tests, the ratio of normoalbuminuric to creatinine before COVID-19 disease was 28.0±2.9 mg/g creatinine and 42.9±5.1 mg/g creatinine after ($p \geq 0.05$).

The decrease in renal glomerular filtration rate was implicit and amounted to 93.3±10.1 mL/min/1.73 m^2 before infection and 78.9±8.7 mL/min/1.73 m^2 after the disease ($p \geq 0.05$).

Study of Laboratory Test Results & Biochemical Profile of Patients

The data obtained allowed for establishing a trend toward the decreased functional status of the kidneys in young patients with moderate severity of COVID-19. At the same time, laboratory and biochemical analyses of patients' urine were performed before discharge, which enabled the development of the following patterns (**Table 2**).

In terms of clinical signs, all patients had similar symptoms: high temperature (39 °C), muscle weakness, and cough with virtually no expectoration. In 50% of cases, liquid stools were observed. Peripheral edema was not seen, and the mean respiration rate was 25/min. Saturated values averaged 91% at the time of discharge. Blood pressure readings were 120 over 80 mm Hg. All patients had the same clinical diagnosis (U07.2. COVID-19).

Table 2. Indicators of laboratory blood tests of patients after recovery

Indicator name	Quantitative indicators after discharge	Normal values (reference group)	Significance of differences between obtained & reverence values
EC	5.29	4.2-5.6	p≥0.05
Gb	162.0	130.0-173.0	p≥0.05
H	51.0	38.0-48.0	p≤0.05
P	198.0	15.0-375.0	p≥0.05
L	8.515	4.0-10.0	p≥0.05
Peripheral blood values (erythrocyte indices)			
MCV	97.0	80.0-100.0	p≥0.05
MCH	31.0	27.0-35.0	p≥0.05
MCHC	33.0	32.0-36.0	p≥0.05
RDW	13.0	11.0-14.0	p≥0.05
Peripheral blood values (indices for leukocytes)			
N%	68.58	46.0-70.0	p≥0.05
NEU	5.831	2.05-5.80	p≤0.05
E%	0.1011	1.0-5.0	p≤0.05
EOS	0.0089	0.20-0.30	p≤0.05
B%	0.9599	0-1.0	p≥0.05
BASO	0.021	0-0.070	p≥0.05
L%	22.81	20.0-38.0	p≥0.05
LYM	1.943	1.1-3.0	p≥0.05
M%	7.61	4.0-10.0	p≥0.05
MONO#	0.6442	0.10-0.60	p≤0.05
BSR	11.0	2.0-15.0	p≥0.05

Note. EC: Erythrocyte count (in $\times 10^{12}$/l); Gb: Amount of hemoglobin (in g/l); H: Hematocrit fraction (in %); P: Platelet counts (in $\times 10^{9}$/l); L: Leukocyte counts (in $\times 10^{9}$/l); MCV: Mean erythrocyte volume values (femtoliters [fl]); MCH: Average hemoglobin in erythrocyte (pg); MCHC: Average Hb concentration index in erythrocyte (g/dL); RDW: Distribution range of red blood cells (in %); N%: Proportion of neutrophils (%); NEU: Neutrophil concentration (in $\times 10^{9}$/l); E%: Share of eosinophils (%); EOS: Eosinophils concentration (in %); B%: Presence of basophils (%); BASO: Basophil concentration (%); L%: Share of lymphocytes (%); LYM: Lymphocyte concentration (%); M%: Share of monocytes (%); MONO#: Monocyte concentration (%); & BSR: Blood sedimentation rate (mm/h)

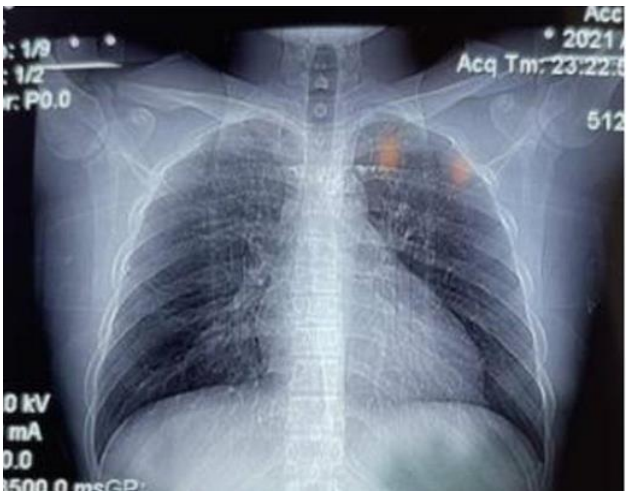

Figure 1. X-ray of patient's thoracic area (age 24) (reprinted with permission of the patient)

All cases involved polysemantic pneumonia characterized by severe treatment (**Figure 1**, **Figure 2**, and **Figure 3**).

Respiratory failure corresponding to the first degree was recorded. As for the kidneys, preclinical disease of these organs was found in all cases.

It was established that most parameters did not differ significantly from the baseline values at the discharge time. At the same time, significantly higher or lower values relative to the reference values were found for the following parameters:

1. Hematocrit fraction (above normal)
2. Neutrophil concentration (slightly above normal)
3. Fraction and concentration of eosinophils (below normal).

Significant differences were also identified in biochemical parameters of the blood (**Table 3**). Significant differences were

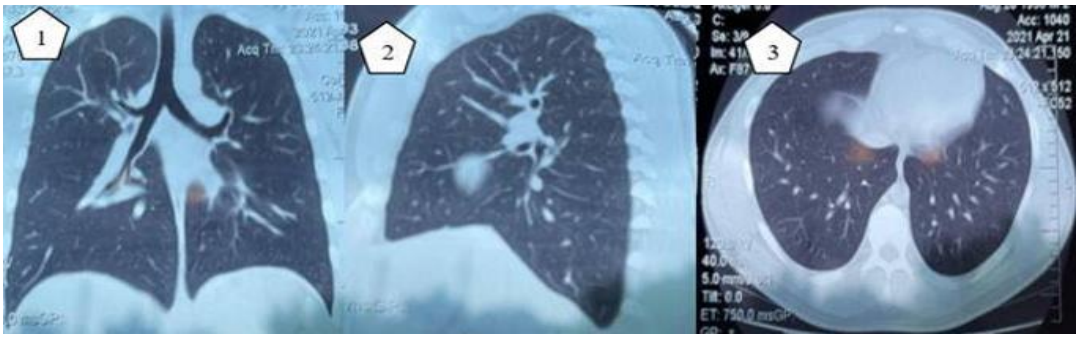

Figure 2. Lung CT scan taken in the same patient in sagittal plane (1), axial plane (2), & frontal plane (3) (reprinted with permission of the patient)

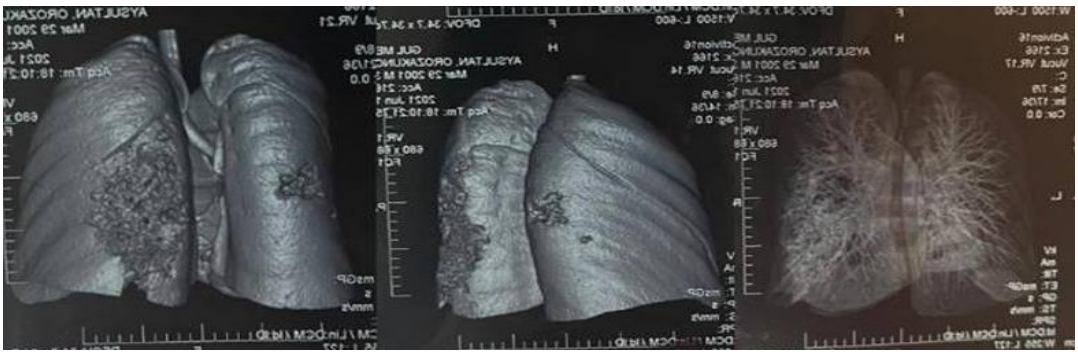

Figure 3. Results of a computed tomography (3D) scan in a patient (age 21) (reprinted with permission of the patient)

Table 3. Results of biochemical blood & urine tests

Indicator name	Quantitative indicators after discharge	Normal values (reference group)	Reliability of differences between normal & obtained indicators
G	5.75	3.80-5.80	p≥0.05
C-r	11.8	Up to 5.0	p≤0.05
F_A	4.8	3.0-20.0	p≥0.05
A_{AE}	15.5	0-20.0	p≥0.05
A_{AmE}	28.9	0-20.0	p≤0.05
I_{gE}	31.4	Up to 87.0	p≥0.05
D	1.590	0-0.550	p≤0.05
P	0.159	0-0.100	p≤0.05
Cytokine-related indicators			
I-10	13.989	Up to 30.0	p≥0.05
I-6	8.489	Up to 10.0	p≥0.05
T_{NAF}	0.944	Up to 6.0	p≥0.05
G_{EC}	11.9	10.0-700.0	p≥0.05
Indicators indicating functional state of kidneys indicators indicating functional state of kidneys			
C_r	103.7	60.0-115.0	p≥0.05
C_{ys}	1.65	0.30-0.80	p≤0.05
H_{Cys}	14.45	5.45-16.20	p≥0.05
B_{-2-B}	2.610	0.970-2.630	p≥0.05
B_{-2-U}	0.662	0.099-0.320	p≤0.05
C_{FR}	89.1		
E_{FR}	45.9		
C_{rC}	118.0		

Note. Presence of antibodies to COVID-19, class G immunoglobulins: ratio of optical density of patient sample to a threshold value of 0.10; if ratio is greater than 1.1, result is positive; if less than 0.8, result is negative; result is questionable in case of values between 0.8 & 1.1; presence of antibodies to COVID-19, M-class immunoglobulins: same criteria, ratio 0.13; G: Glucose levels (mmol/L); C-r: C-reactive protein level (mg/L); FA: Folic acid levels (ng/ml); AAE: Alanine aminotransferase enzyme levels (U/L); AamE: Aspartate aminotransferase enzyme levels (U/L); IgE: Level of immunoglobulin type E (IU/ml); D: D-dimer levels (mg FEU/L); P: Procalcitonin levels (ng/ml); I-10: Interleukin-10 level (pg/ml); I-6: Interleukin-6 levels (pg/ml); TNAF: Tumor necrosis-associated factor (alpha type [pg/ml]); GEC: Factor associated with growth of endothelial cells in vessels (pg/ml); Cr: Creatinine content (mmol/L); Cys: Cystatin content (mg/L); HCys: Homocysteine content (mmol/L); B-2-B: Beta-2 macroglobulin content in blood test (mg/L); B-2-U: Beta-2 macroglobulin content in urinalysis (mg/L); CFR: Calculated filtration rate in glomeruli of renal tubules for creatinine (ml/min/1.73m^2); EFR: Estimated filtration rate in glomeruli of renal tubules for cystatin C (ml/min/1.73m^2); & CrC: Creatinine clearance values calculated according to Cockcroft-Gault formula (ml/min/1.73m^2)

found for several indicators, both increasing and decreasing, as a result of biochemical analysis (**Table 2**). These are, as follows:

1. CRP level (more than two times higher than normal)
2. Aspartate aminotransferase level, higher than normal
3. D-dimer level, three times higher than normal
4. Procalcitonin level, half higher than normal
5. Cystatin content was also two times higher than normal
6. Beta-2 microglobulin content was also two times above the upper limit of normal.

Among all the investigated parameters, the most significant was the blood creatinine level. Changes in this parameter were statistically significant and held considerable importance in assessing the renal function of young patients with a moderate form of COVID-19. This underscores the impact of the disease on kidney function and emphasizes the significance of monitoring this parameter during the infection. The following parameters facilitate the assessment of the degree of kidney involvement in patients with COVID-19.

Blood Analyses

Creatinine level

Measuring the creatinine level in the blood enables the evaluation of renal function. An elevated creatinine level may indicate a decline in glomerular filtration in the kidneys.

C-reactive protein

Increased levels of CRP indicate inflammatory processes that could impact kidney function.

Urinalysis

Microalbuminuria

This parameter is associated with the level of albumin (protein) in the urine. An elevated level of microalbuminuria may indicate early damage to renal structures and serves as an indicator of kidney involvement.

Microalbumin-to-creatinine ratio

This parameter is employed to adjust the microalbumin level in urine, considering the varying urine concentration.

DISCUSSION

This study was limited to patients aged from 19 to 30 years since its purpose was to examine the functional status of the kidneys in this age group. The selection of patients was random in this study. The discharge criterion was the patient's stable condition. The determination of patient discharge was not exclusively reliant on the oxygen saturation level, albeit in certain cases it reached 91%. When assessing the condition of a patient with COVID-19, doctors consider numerous other factors, such as symptoms, medical records, age, and the presence of concomitant diseases. Hospital discharge may be considered feasible when the patient's condition attains stability, and they can sustain further treatment within the confines of their home environment. However, this decision is individual for each patient and depends on many factors, including the level of oxygen saturation. The connection between kidney failure and COVID-19 is an actively researched problem in medical science. Some studies show that COVID-19 can lead to various disorders of kidney function, including kidney failure. A study confirmed that patients with COVID-19 may have elevated creatinine levels in the blood, which is a manifestation of impaired kidney function. It was also found that patients with severe COVID-19 had a higher incidence of renal failure than patients with a milder course of disease [1].

Other studies also indicate a link between kidney failure and COVID-19. For instance, one study showed that patients with COVID-19 who needed mechanical ventilation had a higher incidence of acute renal failure [11]. Another study also found that patients with COVID-19 who developed renal failure had a higher mortality rate than patients without impaired renal function [7]. Thus, kidney failure can be a serious complication of COVID-19 and requires closer medical supervision and treatment. Based on the material of 100 patients diagnosed with covid-19 of moderate severity, our study showed that most biochemical parameters of blood and urine (its uniform composition, blood composition, and urine test results) had no significant differences at the time of discharge compared to the reference group. At the same time, we have proposed two markers (beta-2-microglobulin [β2M]

and cystatin C), which may detect incipient kidney damage against the background of COVID-19. In this work, the concentration of certain compounds was considered excessive or rather deficient. For example, cystatin is a prevalent protein synthesized in every body cell with nuclei. This protein is synthesized at the same speed. In transport and metabolic processes, this protein is filtered by the cell membranes of the renal glomeruli and subsequently metabolized in the renal tubules. Over the past few years, cystatin has been considered a reliable marker for assessing the extent to which kidneys function. In particular, upon examining 101 patients who underwent COVID-19, it was established that cystatin could have predictive value. In patients with severe disease, elevated COVID-19 concentrations have been observed in serum samples [23]. Colleagues from Russia found that cystatin C can serve as a reliable indicator for immediate differentiation of the group at risk for acute renal lesion progression. The study was conducted in a sample of children acutely diagnosed with intestinal infections. Infections were moderate in severity [24, 25]. Another study assessed the association between cystatin C levels at the time of COVID-19 infection and the patient's age [26]. It has been found that high levels of cystatin C during COVID-19 are associated with kidneys actively participating in the process of disease development. With an increased concentration of cystatin C in the blood, it can be assumed that the renal glomerular structure was destroyed, which is often observed during COVID-19 disease. Negative factors contributing to glomerular destruction during COVID-19 include infection itself, hypoxia, and toxicity of renal glomerular endothelial cells [27].

Moreover, the pharmacological charge on the body plays an important role [28]. The influence of these factors in combination may cause the microcirculatory processes of blood flow to be disrupted and, consequently, the filtering volume in the renal tubules to slow down. Interestingly, this stage of the pathology process is characterized by a normal level of creatinine in the bloodstream [29, 30]. That is consistent with the data in this study. Despite patients' young age and average creatine concentrations, all patients exhibited elevated cystatin C content. Another compound found in high amounts is β2M. This protein, with a low molecular weight (11800 Da), is located on the surface of cells, where cell nuclei are present. Beta 2 macroglobulin is a light chain to the histocompatibility antigen (HLA antigen). The protein concentration in the blood reflects the process of lymphocyte proliferation and cellular renewal. In adults, beta-2 micro globulins are synthesized at a steady rate. But this protein is extracted into the kidneys through filtration and reabsorption [31]. This latter process occurs in the lumen of the kidney tubules. This protein can therefore be regarded as a marker reflecting the degree of damage to the proximal renal tubules.

A trace shedding of this protein in the urine is considered normal. The half-life of beta-2 macroglobulin is within 90 minutes in the blood plasma. As renal insufficiency progresses, there is a steady rise in the level of this protein, which may indicate that renal clearance is also declining. When kidney tubular damage occurs, the excretion of beta-2 microglobulin in urine increases significantly. Damage may be caused by disease, drug poisoning, and exposure to toxic substances. For COVID-19, when no renal damage has been observed previously, the situation can evolve under two scenarios. One is mild kidney dysfunction, and the other is acute kidney disease. Some authors point out that kidney dysfunction after a coronavirus infection can occur in many patients [32]. This can be caused by the ACE-2 receptor, which the virus invades. This receptor type is common in many cells comprising the kidneys–podocytes, epithelium, and cells forming the proximal tubules. That is why the kidneys are a priority target of COVID-19 infection.

Furthermore, following infection, a urinary syndrome can develop [30]. This syndrome manifests primarily through elevated levels of beta-2 microglobulin in the urine. Kidney tubules and glomeruli are also damaged due to hypoxia and hyper coagulant processes [7]. This research has also found increased protein levels in both the blood and urine.

A more in-depth study of changes in the concentration of anti-inflammatory proteins (cytokines and chemokines) in young adults is required. COVID-19 may not appear on peripheral blood tests among young adults. Parallel kidney function tests must be performed if pulmonary lesions are observed, primarily for cystatin C and beta-2 microglobulin. If high levels of these proteins are found in urine and blood samples, a diagnosis of kidney dysfunction is very likely.

Cystatin C and β2M are markers of renal functional disorders, and their levels can increase in various kidney diseases, including COVID-19. Research has demonstrated that COVID-19 patients, particularly those afflicted with renal functional impairments, may exhibit elevated levels of cystatin C and β2M. Such heightened concentrations of cystatin C and β2M are indicative of a potential decrease in glomerular filtration rate and other forms of renal dysfunction [33, 34]. Furthermore, certain investigations have uncovered a positive correlation between the levels of cystatin C and β2M and the severity of COVID-19.

Specifically, patients with more severe manifestations of the disease tend to manifest higher levels of cystatin C and β2M in comparison to those presenting with milder forms of the illness. Consequently, the observed elevation in cystatin C and β2M levels may be associated with renal functional disorders in COVID-19 patients. These data can be used to assess the severity of the disease. However, this conclusion requires additional research to confirm the connection.

Cystatin C and β2-microglobulin are biomarkers related to kidney function. During COVID-19 infection, kidney function may deteriorate, leading to an increase in the levels of cystatin C and β2-microglobulin in the blood. According to researchers, an increase in the level of cystatin C and β2-microglobulin after COVID-19 infection is due to pathophysiological mechanisms, such as hypoxia (oxygen starvation) and inflammation. Hypoxia is a common complication of COVID-19. It can cause tissue damage, including kidney damage. This damage can deteriorate kidney function and increase the level of cystatin C and β2-microglobulin in the blood. Inflammation is another important pathophysiological mechanism that accompanies COVID-19 infection. Inflammation can inflict tissue damage and deterioration of kidney function, which can also increase levels of cystatin C and β2-microglobulin in the blood. In addition, an increase in the levels of cystatin C and β2-microglobulin may be associated with other factors, such as age, concomitant diseases, and the presence of other COVID-19 complications.

Limitations

This study also has limitations. These include the use of CKD-EPI formula. Indeed, the equation may yield inaccurate results under certain conditions.

1. Non-specificity of creatinine markers: CKD-EPI equation uses the level of creatinine in blood plasma to calculate the glomerular filtration rate. However, creatinine levels may be influenced by other factors such as age, gender, muscle mass, diet, etc. This feature may generate inaccuracies in the calculation of GFR and the classification of CRF.
2. Creatinine variability: Creatinine levels may vary over time, thereby producing errors in the assessment of changes in kidney function. For example, creatinine levels may temporarily increase when taking certain medications or during dehydration.
3. CKD-EPI equation fails to incorporate various factors such as albumin, glucose, and other relevant variables into its calculations. Nevertheless, they may affect kidney function.
4. Inaccuracies in determining GFR at the initial stage: At the initial stage of CRF, when GFR is not reduced, the results of CKD-EPI equation may be imprecise. Therefore, CKD-EPI equation requires a combination with other methods for assessing kidney function. Additionally, it is crucial to consider all possible factors that may affect creatinine levels.

The limitations of this study included a relatively small sample size and the absence of certain data such as symptoms, body mass index, weight, temperature, and other parameters, which could have provided a more comprehensive picture of the patients' condition.

Future directions of research could entail expanding the sample size to enhance statistical power and improve the overall generalizability of the findings. Additionally, it would be beneficial to consider the possibility of gathering supplementary data on symptoms and clinical characteristics of the patients, enabling a more comprehensive exploration of the interrelationships between COVID-19 and kidney function. Hence, in the future, it is necessary to use a combination of methods for assessing kidney function, including the determination of the urea level in blood plasma; the levels of protein and albumin in urine; the assessment of the glomerular filtration rate and the blood volume that passes through the kidneys per unit of time.

CONCLUSIONS

The study found that patients with moderate COVID-19 are highly likely to have renal lesions. Most parameters studied (blood components, blood composition, urinalysis) did not detect renal lesions. Hematocrit levels were higher than normal, while eosinophil concentrations were below the required standard. The biochemical analysis provided more in-depth results than the general analysis. At discharge, the majority of patients had elevated concentrations of certain compounds. CRP levels were more than twice as high as reference values, and aspartate aminotransferase levels exceeded the standard. D-dimer levels were three times higher than normal. Procalcitonin levels were about half of normal values, while cystatin C levels were twice as high as the standard. β2M levels were, on average, twice as high as normal. Among these parameters, increased levels of cystatin C and β2M were the most reliable markers, indicating potential renal lesions during COVID-19. In this investigation encompassing a cohort of 100 COVID-19 patients, noteworthy dissimilarities in various biochemical markers were discerned, notwithstanding the relatively modest sample size. These findings constitute a substantial rationale for future inquiries in this domain.

Author contributions: NM: software & resources; **DE:** formal analysis & data curation; **NM & DE:** conceptualization & writing–original draft preparation; **IV:** methodology & investigation; **RV:** supervision & funding acquisition; **AS:** visualization & project administration; **IV, RV, & AS:** validation & writing–review & editing. All authors have agreed with the results and conclusions.

Funding: No funding source is reported for this study.

Acknowledgements: The authors would like to thank the anonymous reviewers whose valuable feedback significantly contributed to enhancement of this study's quality.

Ethical statement: The authors stated that the study was approved by the Ethical Committee of I. M. Sechenov First Moscow State Medical University on 19 September 2023 (Protocol No. 443). This study was conducted in a manner consistent with international ethical & moral standards. Informed consents were obtained from the participants.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

REFERENCES

1. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020;97(5):829-38. https://doi.org/10.1016/j.kint.2020.03.005 PMid:32247631 PMCid:PMC7110296
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. https://doi.org/10.1016/S0140-6736(20)30183-5 PMid:31986264
3. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270-3. https://doi.org/10.1038/s41586-020-2012-7 PMid:32015507 PMCid:PMC7095418
4. Li W, Moore MJ, Vasilieva N, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature. 2003;426:450-4. https://doi.org/10.1038/nature02145 PMid:14647384 PMCid:PMC7095016
5. Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med. 2020;14(2):185-92. https://doi.org/10.1007/s11684-020-0754-0 PMid:32170560 PMCid:PMC7088738
6. Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARS-CoV-2. Gastroenterology. 2020;158(6):1831-33.e3. https://doi.org/10.1053/j.gastro.2020.02.055 PMid:32142773 PMCid:PMC7130181
7. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. Int Urol Nephrol. 2020;52(6):1193-4. https://doi.org/10.1007/s11255-020-02451-9 PMid:32222883 PMCid:PMC7103107
8. Wang X, Fang X, Cai Z, et al. Comorbid chronic diseases and acute organ injuries are strongly correlated with disease severity and mortality among COVID-19 patients: A systemic review and meta-analysis. Research (Wash D C). 2020;2020:2402961. https://doi.org/10.34133/2020/2402961 PMid:32377638 PMCid:PMC7187729

9. Guan GW, Gao L, Wang JW, et al. Exploring the mechanism of liver enzyme abnormalities in patients with novel coronavirus-infected pneumonia. Zhonghua Gan Zang Bing Za Zhi. 2020;28(2):100-6. https://doi.org/10.3760/cma.j.issn.1007-3418.2020.02.002
10. Oyelade T, Alqahtani J, Canciani G. Prognosis of COVID-19 in patients with liver and kidney diseases: An early systematic review and meta-analysis. Trop Med Infect Dis. 2020;5(2):80. https://doi.org/10.3390/tropicalmed5020080 PMid:32429038 PMCid:PMC7345004
11. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9. https://doi.org/10.1001/jama.2020.1585 PMid:32031570 PMCid:PMC7042881
12. Shahid Z, Kalayanamitra R, McClafferty B, et al. COVID-19 and older adults: What we know. J Am Geriatr Soc. 2020;68(5):926-9. https://doi.org/10.1111/jgs.16472 PMid:32255507 PMCid:PMC7262251
13. International Society of Nephrology. COVID-19. Available at: https://www.theisn.org/covid-19 (Accessed: 2 May 2023).
14. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA. 2020;323(20):2052-9. https://doi.org/10.1001/jama.2020.6775 PMid:32320003 PMCid:PMC7177629
15. Fanelli V, Fiorentino M, Cantaluppi V, et al. Acute kidney injury in SARS-CoV-2 infected patients. Crit Care. 2020;24(1):155. https://doi.org/10.1186/s13054-020-02872-z PMid:32299479 PMCid:PMC7161433
16. Rabb H. Kidney diseases in the time of COVID-19: Major challenges to patient care. J Clin Invest. 2020;130(6):2749-51. https://doi.org/10.1172/JCI138871 PMid:32250968 PMCid:PMC7259985
17. Nasr SH, Kopp JB. COVID-19-associated collapsing glomerulopathy: An emerging entity. Kidney Int Rep. 2020;5(6):759-61. https://doi.org/10.1016/j.ekir.2020.04.030 PMid:32368701 PMCid:PMC7196556
18. Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci. 2020;63(3):364-74. https://doi.org/10.1007/s11427-020-1643-8 PMid:32048163 PMCid:PMC7088566
19. Van den Akker JP, Egal M, Groeneveld AB. Invasive mechanical ventilation as a risk factor for acute kidney injury in the critically ill: A systematic review and meta-analysis. Crit Care. 2013;17(3):R98. https://doi.org/10.1186/cc12743 PMid:23710662 PMCid:PMC3706893
20. Li Y, Yang S, Peng D, et al. Predictive value of serum cystatin C for risk of mortality in severe and critically ill patients with COVID-19. World J Clin Cases. 2020;8(20):4726-34. https://doi.org/10.12998/wjcc.v8.i20.4726 PMid:33195640 PMCid:PMC7642558
21. Chugunova OL, Grebenkina EY, Usenko DV, et al. Significance of cystatin C and various techniques for calculating glomerular filtration rate in assessing renal function abnormalities in children with acute intestinal infections. Almanac Clin Med. 2021;49(3):196-206. https://doi.org/10.18786/2072-0505-2021-49-018
22. Stevens LA, Padala S, Levey AS. Advances in glomerular filtration rate-estimating equations. Curr Opin Nephrol Hypertens. 2010;19:298-307. https://doi.org/10.1097/MNH.0b013e32833893e2 PMid:20393287 PMCid:PMC3192437
23. Li Z, Wu M, Yao J, et al. Caution on kidney dysfunctions of COVID-19 patients. medRxiv; 2020;1:1-25. https://doi.org/10.1101/2020.02.08.20021212
24. Zhumabayev R, Zhumabayeva G, Kapanova G, Tulepbekova N, Akhmetzhan A, Grjibovski A. Quality of life in children with cochlear implants in Kazakhstan. BMC Pediatr. 2022;22(1):194. https://doi.org/10.1186/s12887-022-03254-w PMid:35410192 PMCid:PMC8996533
25. Sidorko TN, Sarybaeva GK, Kapanova GZh, Zhusupov BS. Questionnaire survey as a method to improve organisation of nutrition in a school café. Voprosy Detskoi Dietologii. 2018;16(2):66-9. https://doi.org/10.20953/1727-5784-2018-2-66-69
26. Xiang HX, Fei J, Xiang Y, et al. Renal dysfunction and prognosis of COVID-19 patients: A hospital-based retrospective cohort study. BMC Infect Dis. 2021;21(1):158. https://doi.org/10.1186/s12879-021-05861-x PMid:33557785 PMCid:PMC7868870
27. Ronco C, Reis T, Husain-Syed F. Management of acute kidney injury in patients with COVID-19. Lancet Respir Med. 2020;8(7):738-42. https://doi.org/10.1016/S2213-2600(20)30229-0 PMid:32416769
28. Chueh TI, Zheng CM, Hou YC, Lu KC. Novel evidence of acute kidney injury in COVID-19. J Clin Med. 2020;9(11):3547. https://doi.org/10.3390/jcm9113547 PMid:33153216 PMCid:PMC7692179
29. Yelchibayeva A, Ryskulova AG, Baimuratova M, Kapanova G, Sharipova G, Maksutova A. Analysis of financial and economic aspects of company functioning and their influence on the tourist cluster. J Environ Manage Tour. 2021;12(8):2157-67.
30. Werion A, Belkhir L, Perrot M, Schmit G, Aydin S, Chen Z, et al. SARS-CoV-2 causes a specific dysfunction of the kidney proximal tubule. Kidney Int. 2020;98(5):1296-307. https://doi.org/10.1016/j.kint.2020.07.019 PMid:32791255 PMCid:PMC7416689
31. Wang L, Li X, Chen H, et al. Coronavirus disease 19 infection does not result in acute kidney injury: An analysis of 116 hospitalized patients from Wuhan, China. Am J Nephrol. 2020;51(5):343-8. https://doi.org/10.1159/000507471 PMid:32229732 PMCid:PMC7179524
32. De Oliveira MMD, do Couto Dias E, da Silva PL, de Magalhães-Neto AM, Gonçalves LCO. COVID-19 and kidney disease: The role of nurses. World J Pharm Pharm Sci. 2021;10(08):2540-59.
33. Khang AR, Lee MJ, Yi D, Kang YH. The ratio of estimated glomerular filtration rate based on cystatin c and creatinine reflecting cardiovascular risk in diabetic patients. Diabetes Metab J. 2023;47(3):415-25. https://doi.org/10.4093/dmj.2022.0177 PMid:36872062 PMCid:PMC10244204
34. Zhou J, Li Y, Kong C, Li Y, Liang Y. Assessment of the effects of SARS-Cov-2 infection on multiple organs using laboratory indices. Al-Kindy Coll Med J. 2021;17(2):73-8. https://doi.org/10.47723/kcmj.v17i2.429