The relationship between CT value and clinical outcomes in renal patients with COVID-19

Sadra Ashrafi1,2,3 · Pouya Pourahmad Kisomi3 · Saman Maroufizadeh4 · Mohammad Reza Jabbari5 · Mohsen Nafar6,7 · Shiva Samavat8 · Mahmoud Parvin9 · Nooshin Dalili1,2,10

Received: 11 February 2022 / Accepted: 28 July 2022 / Published online: 19 September 2022 © The Author(s), under exclusive licence to Springer Nature B.V. 2022

Abstract

Purpose Concomitant kidney diseases raise the mortality rate due to the SARS-CoV-2 virus as an independent factor. Although a qualitative PCR test’s result is sufficient for diagnosis, Cycle threshold value may present relevant information to the physicians in providing faster treatment in patients with chronic conditions, including kidney diseases, to prevent morbidity and subsequent mortality. Thus, the present study was conducted to determine the relationship between the Cycle threshold value and clinical outcomes in renal patients with the coronavirus 2019.

Methods This retrospective study was conducted on renal patients with the coronavirus 2019 infection admitted to Labbafinejad Hospital in Tehran, the capital of Iran, within a period of one year, from late February 2020 to February 2021. Data were collected per the prepared checklist. Cycle threshold values were measured by performing PCR on nasopharynx and oropharynx swab samples of patients.

Results According to the adjusted analysis, having high viral load increased the odds of in-hospital mortality (aOR = 11.65, 95% CI 3.93–34.54), ICU admission (aOR = 5.49, 95% CI 2.16–13.97), and invasive ventilation (aOR = 7.18, 95% CI 2.61–19.74). Having high viral load also increased the odds of O2 therapy (aOR = 3.08, 95% CI 0.79–12.01), although the difference was not statistically significant (P = 0.105).

Conclusion Cycle threshold value was a significant predictor of mortality in renal patients. Nevertheless, further studies are required on how to render optimal use of the Cycle threshold value, given that the quality of the test sample and the different groups of patients under study affect the effectiveness of this marker in predicting disease severity.

Keywords Cycle threshold · Mortality · Clinical outcome · COVID-19 · Renal patients

Introduction

The coronavirus 2019 (COVID-19) pandemic has imposed a heavy burden on healthcare systems worldwide. The adverse impacts of this disease can be easily observed within various aspects of the populations’ health and socio-economic status worldwide [1, 2]. The disease is caused by an infection with SARS-CoV-2, which is an RNA virus that causes initial symptoms of pneumonia and acute respiratory syndrome [3]. Symptoms of the disease may range from an asymptomatic infection with loss of smell and taste to severe respiratory failure. Yet, the respiratory system is not the sole target of the virus [3, 4]. Extensive evidence indicates that COVID-19 with chronic conditions has a significant impact on mortality rates. Chronic lung, heart, liver, and kidney diseases, diabetes, and obesity have contributed to the mortality rates noted for COVID-19 [3, 5]. Accordingly, the role of chronic kidney disease (CKD) is particularly striking among other chronic...
conditions. Patients with CKD indicate a higher rate of all infections due to changes in their immune systems’ function and the chronic and systemic inflammation that dominates their bodies. As a result, these individuals have higher odds of a more severe infection with the SARS-CoV-2 virus [3]. The incidence of COVID-19 infection is three times higher in CKD patients than in non-CKD patients.

Furthermore, CKD patients are 12 times more likely to be admitted to the ICU of a hospital following COVID-19 infection than patients without an underlying medical condition. This rate is higher than the rate for patients with diabetes and cardiovascular conditions. The mortality rate of COVID-19 in hemodialysis patients is 15–25%, even under no pulmonary involvement [3]. Ample evidence exists about the adverse impacts of coronavirus on patients’ kidneys. SARS-CoV-2 is found in the urine samples of renal patients, and further pathological evidence confirms the impact of COVID-19 on the kidneys in the form of glandular and tubular damage. Indeed, the kidneys are one of the several organs that are highly attacked by this virus [4, 6]. Besides, concomitant kidney diseases raise the mortality rate due to the SARS-CoV-2 virus as an independent factor. This rate extends may be maximum in dialysis patients. Accordingly, dialysis patients are up to four times more prone to succumb to the coronavirus. Also, dialysis patients are more likely to experience complications of the disease and display the worst prognosis along with kidney transplant recipients. In addition, COVID-19 patients are more likely to face acute kidney damage as a complication of coronavirus infections if their condition worsens. Although the exact mechanism underlying these injuries is unknown, other factors affecting them require further examination [2, 4, 6–12].

An accurate and rapid diagnostic approach is necessary as the SARS-CoV-2 virus undermines the healthcare systems. In this regard, real-time reverse transcriptase-polymerase chain reaction (RT-PCR) is preferred, given its speed and accuracy. There are various semi-quantitative indexes associated with PCR (e.g., Cycle threshold). These indices appear to be able to assist us in predicting prognosis and infectivity in patients with COVID-19. In addition, the indices are associated with different aspects of disease severity. Some of these aspects include mortality, disease severity, disease progression, biochemical and hematological markers, and infectivity. Extensive studies have examined the link between Cycle threshold value (CT value) and each of these cases, leading to various outcomes. Although a qualitative PCR test’s result is sufficient for diagnosis, CT value may present relevant information to the physicians in providing faster treatment in patients with chronic conditions, including kidney diseases, to prevent morbidity and subsequent mortality [13, 14]. Thus, the present study was conducted to determine the link between CT value and clinical outcomes in renal patients with COVID-19.

Methods

Study population and setting

This retrospective study was conducted to examine the relationship between Cycle threshold (CT) values and clinical outcomes in renal patients with COVID-19 infection admitted to Labbafinejad Hospital in Tehran, the capital of Iran. The data were taken from the Hospital Information System (HIS) unit of the Labbafinejad Hospital. Medical records of all renal patients with a positive COVID-19 PCR test were included in the study while patients with incomplete medical records were excluded.

The study population consists of renal patients with COVID-19 admitted to Labbafinejad Hospital within a period of 1 year, from late February 2020 to February 2021. Sampling was performed by the census method. 225 cases pertaining to renal patients with positive COVID-19 PCR tests were reviewed. Of these, 168 cases with all the information based on the checklist were included in the study. Data collection was conducted after the approval and receipt of a letter of introduction from the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR. SBMU.UNRC.REC.1400.019), which was presented to the concerned authorities.

Viral load assessment

In the present study, two nasopharynx and oropharynx swab samples of patients in a VTM (Viral transport medium) culture medium were collected by an experienced individual during the initial stage. The RNA was extracted by the Gene-Affili® RibospinTM vRD RNA extraction kit, following the kit’s protocols. Next, PCR was performed using the Sansure® SARS-CoV-2 Multiplex Nucleic Acid Diagnostic Kit (PCR-Fluorescence Probing). By this kit, ORF 1ab, N and E genes were used to calculate and measure the CT value. If the disease was observed as positive in any gene, the gene’s corresponding CT value was also reported. In case the disease was positive for more than one gene, the average CT value was reported.

Data collection

Data were collected per the prepared checklist. This tool includes demographic information (age, sex, and BMI), underlying conditions (hypertension, diabetes, chronic respiratory diseases, obesity, and cardiovascular disease), patient’s condition in terms of renal diseases (CKD not on dialysis, CKD on dialysis, Kidney Transplant Recipients), physiological indices (PSO₂, DBP, SBP, mean arterial pressure, respiratory rate, heart rate), lung CT scan findings, and
CT value. Furthermore, based on their CT value, the patients were categorized into two classes: low viral load (CT > 20) and high viral load (CT ≤ 20). Estimated glomerular filtration rate (eGFR) was calculated by CKD-EPI equations. By eGFR, the patients were divided into six grade, based on the KDIGO CKD stages. All variables were collected at the time of admission. Clinical outcomes in the present study were as follows: ICU admission, O2 Therapy, Invasive ventilation, and In-hospital mortality. All of the mentioned data were collected from the patient file in HIS (hospital information system).

**Statistical analysis**

Data analysis was carried out using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA) and graphs were depicted using GraphPad Prism, Version 8.0.1 (GraphPad Prism Software Inc., San Diego, CA, USA). Continuous variables are presented as median (interquartile range (IQR)) and compared using Mann–Whitney test. Categorical variables are presented as numbers (percentages) and compared using chi-square test.

Multiple logistic regression analysis was also applied to examine the relationships of clinical and demographic characteristics with outcome variables. The odds ratio (OR) and 95% confidence interval (CI) were calculated. All statistical tests were two-sided and level of significance was set at 0.05.

**Results**

The present study examined the potential relationship between the CT value and the occurrence of clinical outcomes (in-hospital mortality, invasive ventilation, O2 Therapy, ICU admission) among renal patients infected by COVID-19 admitted to Labbafinejad hospital in Tehran, the capital of Iran. Comparing the data in terms of mortality shows that of the 168 examined patients, 127 survived and 41 deceased. In these two groups (Deceased and Survived), the median CT value and its categories (CT ≤ 20 and CT > 20), median age (P = 0.009), diabetes (P = 0.04), number of comorbidities (P = 0.004), PSO2 (P = 0.005), and CT chest (P < 0.001) showed a significant statistical relationship. Moreover, the eGFR (P = 0.003) and CKD stages (P = 0.002) were significantly different between these two groups. The eGFR was lower in deceased group and they also have higher CKD stages or worse kidney function (Table 1).

The results further show that 49 patients were admitted to the ICU. There was a significant statistical relationship between admittance to ICU and median CT value (P = 0.001) and its categories (CT ≤ 20 and CT > 20) (P = 0.01), number of comorbidities (P = 0.006), PSO2 (P = 0.02), and CT chest (P < 0.001), the eGFR (P = 0.014) and CKD stages (P = 0.016) (Table 2).

Furthermore, the results show that invasive ventilation was used in 35 patients. A statistically significant relationship was observed between the use of invasive ventilation and CT value’s mean (P = 0.005), its classification ((CT > 20) and (CT ≤ 20)), number of comorbidities (P = 0.01), PSO2 (P = 0.01), and CT chest (P < 0.001), the eGFR (P = 0.003) and CKD stages (P = 0.002) (Table 3).

Moreover, the results show that among 133 patients using O2 therapy, there is a statistically significant statistical relationship between O2 therapy and median CT value (P < 0.02), the number of clinical symptoms (P < 0.001), number of comorbidities (P = 0.04), PSO2 (P = 0.005), and CT chest (P < 0.001) (Table 4).

Figure 1 indicates the relationship between high viral load and increased clinical outcomes (in-hospital mortality, ICU admission, invasive ventilation, and O2 therapy). Also, Fig. 2 (i.e., the impact of the type of renal disease on clinical outcomes) indicates that kidney transplant patients and similar dialysis patients recorded more mortality, ICU admission, invasive ventilation, and O2 therapy than the non-dialysis groups. As presented in Fig. 3, there was no significant correlation between eGFR and CT value (r = 0.114, P = 0.142).

Based on adjusted analysis, the odds of death increased with rising age. As compared to patients aged ≤ 60 years, those aged > 60 years were 2.91 (95% CI 1.08–7.83) times more likely to die from COVID-19. Compared with CKD not on dialysis group, patients with kidney transplant were at significantly increased risk of death (OR = 2.99, 95% CI 1.05–8.49). Patients with 1 and ≥ 2 comorbidities had significantly increased odds of death (OR = 6.39, 95% CI 1.21-33.73 and OR = 6.06, 95% CI 1.22–30.16, respectively) as compared with patients with no comorbidities. Other variables were not significantly associated with death (Table 5).

Regarding ICU admission, patients with CKD on dialysis and patients with kidney transplant were at increased risk of ICU admission (OR = 1.75, 95% CI 0.62–4.92, OR = 2.11, 95% CI 0.83–5.34) as compared with CKD not on dialysis group, although these increases were not statistically significant (P = 0.290 and P = 0.115, respectively). Patients with 1 and ≥ 2 comorbidities had significantly increased odds of ICU admission (OR = 8.36, 95% CI 1.71–40.82 and OR = 7.51, 95% CI 1.58–35.73, respectively) as compared with patients with no comorbidities. For every one-unit increase in GFR, the odds of mortality and invasive ventilation decreased by 3% (OR = 0.97, 95% CI 0.95–0.99 and OR = 0.97, 95% CI 0.94–0.99, respectively) (Table 5).

As presented in Table 6, patients with high viral load significantly had higher in-hospital mortality, ICU admission and invasive ventilation as compared with patients with low viral load. O2 therapy in patients with high viral load was higher than patients with low viral load, although this
Table 1  Characteristics of patients with pre-existing chronic kidney disease and COVID-19 by in-hospital mortality

|                        | In-hospital mortality |  |
|------------------------|-----------------------|---|
|                        | Survived (n = 127)    | Deceased (n = 41) | \( P \) |
| **Demographics**       |                       |               |      |
| Age (years)            | 57.0 (42.0–66.0)      | 64.0 (53.5–72.5) | 0.009 |
| Age group (years)      |                       |               | 0.019 |
| \( \leq 60 \)          | 67 (52.8)             | 13 (31.7)     |      |
| \( > 60 \)             | 60 (47.2)             | 28 (68.3)     |      |
| Male sex               | 86 (67.7)             | 30 (73.2)     | 0.511 |
| Active smoking         | 7 (5.5)               | 4 (9.8)       | 0.339 |
| No. of symptoms        | 3.0 (2.0–5.0)         | 4.0 (2.5–5.0) | 0.208 |
| **Chronic kidney disease** |                       |               | 0.393 |
| CKD not on dialysis    | 49 (38.6)             | 11 (26.8)     |      |
| CKD on dialysis        | 23 (18.1)             | 9 (22.0)      |      |
| Kidney transplant recipients | 55 (43.3)        | 21 (51.2)     |      |
| eGFR                   | 34.0 (14.0–58.0)      | 18.0 (8.5–34.5) | 0.003 |
| **CKD-EPI stage**      |                       |               | 0.002 |
| Stage 1                | 5 (3.9)               | 2 (4.9)       |      |
| Stage 2                | 23 (18.1)             | 0 (0)         |      |
| Stage 3a               | 24 (18.9)             | 3 (7.3)       |      |
| Stage 3b               | 14 (11.0)             | 7 (17.1)      |      |
| Stage 4                | 26 (20.5)             | 10 (24.4)     |      |
| Stage 5                | 35 (27.6)             | 19 (46.3)     |      |
| **Comorbidities**      |                       |               |      |
| Hypertension           | 79 (62.2)             | 30 (73.2)     | 0.201 |
| Diabetes               | 54 (42.5)             | 25 (61.0)     | 0.040 |
| Chronic respiratory diseases | 6 (4.7)             | 6 (14.6)      | 0.032 |
| Cardiovascular disease | 31 (24.4)             | 16 (39.0)     | 0.070 |
| Obesity                | 24 (18.9)             | 11 (26.8)     | 0.277 |
| No. of comorbidities   | 1.0 (0–2.0)           | 2.0 (1.0–3.0) | 0.004 |
| **Physiological parameters** |                   |               |      |
| SBP                    | 123.0 (113.0–140.0)   | 130.0 (113.0–152.5) | 0.361 |
| DBP                    | 79.0 (70.0–80.0)      | 76.0 (71.0–85.0) | 0.809 |
| Mean arterial pressure | 93.3 (86.0–101.0)     | 95.3 (88.2–103.0) | 0.289 |
| Respiratory rate       | 18.0 (18.0–20.0)      | 18.0 (17.0–21.0) | 0.858 |
| Heart rate             | 85.0 (79.0–95.0)      | 88.0 (80.0–94.0) | 0.387 |
| PSo2                   | 93.0 (89.0–95.0)      | 90.0 (80.0–94.5) | 0.005 |
| **CT Chest**           |                       |               | <0.001|
| Normal                 | 33 (26.0)             | 5 (12.2)      |      |
| Mild                   | 53 (41.7)             | 1 (2.4)       |      |
| Moderate               | 34 (26.8)             | 10 (24.4)     |      |
| Severe                 | 7 (5.5)               | 25 (61.0)     |      |
| Ct value               | 28.0 (24.0–31.0)      | 23.0 (18.0–29.0) | 0.001 |
| Ct value category      |                       |               | <0.001|
| Low viral load (Ct > 20) | 114 (89.8)           | 23 (56.1)     |      |
| High viral load (Ct ≤ 20) | 13 (10.2)            | 18 (43.9)     |      |

Values are given as number (percentage) for categorical variables and as median (interquartile range) for continuous variables.

CKD chronic kidney disease; eGFR estimated glomerular filtration rate
Table 2  Characteristics of patients with pre-existing chronic kidney disease and COVID-19 by ICU admission

| Demographics | ICU admission |  | P   |
|--------------|--------------|-----------------|-----|
|              | Ward (n = 119) | ICU (n = 49)    |     |
| Age (years)  | 61.0 (46.0–67.0) | 63.0 (49.5–70.0) | 0.184 |
| Age group (years) | 0.428       |                 |     |
| ≤60          | 59 (49.6) | 21 (42.9) |     |
| >60          | 60 (50.4) | 28 (57.1) |     |
| Male sex     | 78 (65.5) | 38 (77.6) | 0.126 |
| Active smoking | 9 (7.6)       | 2 (4.1) | 0.512 |
| No. of symptoms | 3.0 (2.0–5.0) | 4.0 (2.0–5.0) | 0.680 |
| Chronic kidney disease | 0.156       |                 |     |
| CKD not on dialysis | 47 (39.5) | 13 (26.5) |     |
| CKD on dialysis | 19 (16.0) | 13 (26.5) |     |
| Kidney transplant recipients | 53 (44.5) | 23 (46.9) |     |
| eGFR         | 33.0 (14.0–56.0) | 18.0 (8.0–38.5) | 0.014 |
| CKD-EPI stage | 0.016       |                 |     |
| Stage 1      | 6 (5.0) | 1 (2.0) |     |
| Stage 2      | 18 (15.1) | 5 (10.2) |     |
| Stage 3a     | 22 (18.5) | 5 (10.2) |     |
| Stage 3b     | 16 (13.4) | 5 (10.2) |     |
| Stage 4      | 25 (21.0) | 11 (22.4) |     |
| Stage 5      | 32 (26.9) | 22 (44.9) |     |
| Comorbidities | 0.135       |                 |     |
| Hypertension | 73 (61.3) | 36 (73.5) |     |
| Diabetes     | 51 (42.9) | 28 (57.1) | 0.092 |
| Chronic respiratory diseases | 6 (5.0) | 6 (12.2) | 0.110 |
| Cardiovascular disease | 29 (24.4) | 18 (36.7) | 0.105 |
| Obesity      | 21 (17.6) | 14 (28.6) | 0.113 |
| No. of comorbidities | 1.0 (0–2.0) | 2.0 (1.0–3.0) | 0.006 |
| Physiological parameters | 0.199       |                 |     |
| SBP          | 123.0 (115.0–140.0) | 128.0 (112.0–150.0) |     |
| DBP          | 80.0 (70.0–81.0) | 76.0 (70.5–85.0) | 0.729 |
| Mean arterial pressure | 93.3 (85.0–101.0) | 95.33 (88.2–103.2) | 0.189 |
| Respiratory rate | 18.0 (18.0–20.0) | 18.0 (17.0–21.5) | 0.644 |
| Heart rate   | 83.0 (79.0–95.0) | 88.0 (80.0–93.0) | 0.203 |
| PSo2         | 93.0 (89.0–96.0) | 91.0 (87.5–94.0) | 0.022 |
| CT chest     | < 0.001 |                 |     |
| Normal       | 34 (28.6) | 4 (8.2) |     |
| Mild         | 51 (42.9) | 3 (6.1) |     |
| Moderate     | 27 (22.7) | 17 (34.7) |     |
| Severe       | 7 (5.9) | 25 (51.0) |     |
| Ct value     | 27.0 (23.0–31.0) | 26.0 (18.0–29.0) | 0.011 |
| Ct value category | < 0.001 |                 |     |
| Low viral load (Ct > 20) | 106 (89.1) | 31 (63.3) |     |
| High viral load (Ct ≤ 20) | 13 (10.9) | 18 (36.7) |     |

Values are given as number (percentage) for categorical variables and as median (interquartile range) for continuous variables.

CKD chronic kidney disease, ICU intensive care unit; eGFR estimated glomerular filtration rate.
Table 3  Characteristics of patients with pre-existing chronic kidney disease and COVID-19 by invasive ventilation

|                           | Invasive ventilation |   |   |
|---------------------------|----------------------|---|---|
|                           | No (n = 133)         | Yes (n = 35) |   |
| **Demographics**          |                      |   |   |
| Age (years)               | 61.0 (45.5–67.0)     | 63.0 (49.0–72.0) | 0.156 |
| Age group (years)         |                      |   |   |
| ≤ 60                     | 66 (49.6)            | 14 (40.0)  | 0.310 |
| > 60                     | 67 (50.4)            | 21 (60.0)  |   |
| Male sex                  | 92 (69.2)            | 24 (68.6)  | 0.945 |
| Active smoking            | 10 (7.5)             | 1 (2.9)    | 0.462 |
| No. of symptoms           | 3.0 (2.0–5.0)        | 4.0 (2.0–5.0) | 0.238 |
| **Chronic kidney disease**|                      |   |   |
| CKD not on dialysis       | 50 (37.6)            | 10 (28.6)  | 0.584 |
| CKD on dialysis           | 24 (18.0)            | 8 (22.9)   |   |
| Kidney transplant recipients | 59 (44.4)          | 17 (48.6)  |   |
| eGFR                      | 34.0 (14.0–56.0)     | 14.0 (8.0–33.0) | 0.003 |
| **CKD-EPI stage**         |                      |   |   |
| Stage 1                   | 5 (3.8)              | 2 (5.7)    | 0.018 |
| Stage 2                   | 23 (17.3)            | 0 (0)      |   |
| Stage 3a                  | 24 (18.0)            | 3 (8.6)    |   |
| Stage 3b                  | 17 (12.8)            | 4 (11.4)   |   |
| Stage 4                   | 29 (21.8)            | 7 (20.0)   |   |
| Stage 5                   | 35 (26.3)            | 19 (54.3)  |   |
| **Comorbidities**         |                      |   |   |
| Hypertension              | 85 (63.9)            | 24 (68.6)  | 0.693 |
| Diabetes                  | 58 (43.6)            | 21 (60.0)  | 0.084 |
| Chronic respiratory diseases | 6 (4.5)             | 6 (17.1)   | 0.019 |
| Cardiovascular disease    | 34 (25.6)            | 13 (37.1)  | 0.175 |
| Obesity                   | 25 (18.8)            | 10 (28.6)  | 0.205 |
| No. of comorbidities      | 2.0 (1.0–3.0)        | 2.0 (1.0–3.0) | 0.018 |
| **Physiological parameters** |                      |   |   |
| SBP                       | 124.0 (114.0–140.0)  | 130.0 (113.0–156.0) | 0.350 |
| DBP                       | 79.0 (70.0–80.0)     | 76.0 (70.0–85.0) | 0.668 |
| Mean arterial pressure    | 93.3 (86.2–101.2)    | 96.7 (88.3–104.0) | 0.251 |
| Respiratory rate          | 18.0 (18.0–20.0)     | 18.0 (17.0–21.0) | 0.395 |
| Heart rate                | 84.0 (79.0–91.0)     | 88.0 (80.0–98.0) | 0.126 |
| PSo2                      | 93.0 (89.0–95.0)     | 90.0 (85.0–94.0) | 0.014 |
| CT chest                  |                      |   |   |
| Normal                    | 36 (27.1)            | 2 (5.7)    | <0.001 |
| Mild                      | 52 (39.1)            | 2 (5.7)    |   |
| Moderate                  | 36 (27.1)            | 8 (22.9)   |   |
| Severe                    | 9 (6.8)              | 23 (65.7)  |   |
| Ct value                  | 27.0 (23.5–0.0)      | 23.0 (18.0–30.0) | 0.005 |
| Ct value category         |                      |   |   |
| Low viral load (Ct > 20)  | 117 (88.0)           | 20 (57.1)  | <0.001 |
| High viral load (Ct ≤ 20) | 16 (12.0)            | 15 (42.9)  |   |

Values are given as number (percentage) for categorical variables and as median (interquartile range) for continuous variables.

CKD chronic kidney disease; eGFR estimated glomerular filtration rate
| Characteristics of patients with pre-existing chronic kidney disease and COVID-19 by O₂ therapy | O₂ therapy | P |
|---|---|---|
| Demographics | No (n=35) | Yes (n=133) |
| Age (years) | 55.0 (40.0–71.0) | 61.0 (47.0–67.0) | 0.614 |
| Age group (years) |  |  | 0.612 |
| ≤60 | 18 (51.4) | 62 (46.6) |  |  |
| >60 | 17 (48.6) | 71 (53.4) |  |  |
| Male sex | 21 (60.0) | 95 (71.4) | 0.193 |
| Active smoking | 1 (2.9) | 10 (7.5) | 0.321 |
| No. of symptoms | 2.0 (2.0–3.0) | 4.0 (3.0–4.0) | < 0.001 |
| Chronic kidney disease |  |  | 0.545 |
| CKD not on dialysis | 15 (42.9) | 45 (33.8) |  |  |
| CKD on dialysis | 5 (14.3) | 27 (20.3) |  |  |
| Kidney transplant recipients | 15 (42.9) | 61 (45.9) |  |  |
| eGFR | 26.0 (16.0–58.0) | 25.0 (11.0–52.0) | 0.442 |
| CKD-EPI stage |  |  | 0.516 |
| Stage 1 | 4 (11.4) | 3 (2.3) |  |  |
| Stage 2 | 4 (11.4) | 19 (14.3) |  |  |
| Stage 3a | 2 (5.7) | 25 (18.8) |  |  |
| Stage 3b | 5 (14.3) | 16 (12.0) |  |  |
| Stage 4 | 13 (37.1) | 23 (17.3) |  |  |
| Stage 5 | 7 (20.0) | 47 (35.3) |  |  |
| Comorbidities |  |  |  |
| Hypertension | 20 (57.1) | 89 (66.9) | 0.281 |
| Diabetes | 13 (37.1) | 66 (49.6) | 0.188 |
| Chronic respiratory diseases | 0 (0) | 12 (9.0) | 0.074 |
| Cardiovascular disease | 6 (17.1) | 41 (30.8) | 0.109 |
| Obesity | 7 (20.0) | 28 (21.1) | 0.891 |
| No. of comorbidities | 1.0 (0–3.0) | 2.0 (1.0–3.0) | 0.042 |
| Physiological parameters |  |  |  |
| SBP | 127.0 (115.0–150.0) | 125.0 (113.0–140.0) | 0.388 |
| DBP | 78.0 (70.0–90.0) | 79.0 (70.0–83.0) | 0.926 |
| Mean arterial pressure | 93.3 (84.0–106.7) | 93.3 (86.7–101.2) | 0.879 |
| Respiratory rate | 18.0 (18.0–20.0) | 18.0 (18.0–20.0) | 0.283 |
| Heart rate | 84.0 (80.0–95.0) | 85.0 (79.5–94.5) | 0.697 |
| PSo2 | 95.0 (92.0–96.0) | 92.0 (88.0–95.0) | 0.005 |
| CT chest |  |  | < 0.001 |
| Normal | 13 (37.1) | 25 (18.8) |  |  |
| Mild | 19 (54.3) | 35 (26.3) |  |  |
| Moderate | 2 (5.7) | 42 (31.6) |  |  |
| Severe | 1 (2.9) | 31 (23.3) |  |  |
| Ct value | 30.0 (22.0–35.0) | 27.0 (22.0–30.0) | 0.022 |
| Ct value category |  |  | 0.090 |
| Low viral load (Ct > 20) | 32 (91.4) | 105 (78.9) |  |  |
| High viral load (Ct ≤ 20) | 3 (8.6) | 28 (21.1) |  |  |

Values are given as number (percentage) for categorical variables and as median (interquartile range) for continuous variables.

CKD chronic kidney disease; eGFR estimated glomerular filtration rate.
difference was not statistically significant (90.3% vs 76.6%, $P=0.105$). After adjusting for the variables, having high viral load increased the odds of in-hospital mortality (aOR = 11.65, 95% CI 3.93–34.54), ICU admission (aOR = 5.49, 95% CI 2.16–13.97), and invasive ventilation (aOR = 7.18, 95% CI 2.61–19.74). Having high viral load also increased the odds of O2 therapy (aOR = 3.08, 95% CI 0.79–12.01), although the difference was not statistically significant ($P=0.105$) (Table 6).

Discussion
Severe acute respiratory syndrome (SARS-CoV-2), known as COVID-19, has been the most formidable healthcare issue for physicians worldwide to date. In the coronavirus pandemic, managing the conditions of patients with either chronic kidney diseases or acute kidney injuries and kidney transplant patients undergoing immunosuppressive therapy proves a clinical challenge for nephrologists,
particularly in patients with severe COVID-19. Under such circumstances, efficient management is necessary to mitigate side effects and drug interactions due to renal failure [15, 16], given the absence of specific anti-COVID-19 treatment programs. Efficient management of these patients demands markers that are both effortlessly measurable and can help predict the condition of these patients. In this respect, CT value has been proposed as an approximate measure of the initial viral load in SARS-CoV-2 [17]. Despite limited studies on using the CT value as a predictor of disease severity in renal patients, the result of the present study indicated that kidney patients with high viral loads displayed higher in-hospital mortality (10.14 times) than patients with low viral loads.

Rajyalakshmi et al. concluded that low CT value is associated with increased ICU hospitalization, mortality, and length of stay in the ICU. Elsewhere, Rajyalakshmi et al. maintained that the CT value could be regarded as one of the prognostic variables beside some other biomarkers [18]. Similarly, Magleby et al. demonstrated that the SARS-CoV-2 viral load in hospitalized patients was associated with the risk of intubation and in-hospital mortality as an independent variable [19]. The link between CT levels and duration of symptoms with mortality in COVID-19 patients was further confirmed in another study by Miller et al. [20]. Regarding the cause of higher mortality in renal patients with low CT values (i.e., high viral loads) observed in the above studies and the present one, it is noteworthy that the immune system’s function is reduced due to uremia in these patients. In addition, the mortality rate and critical conditions are higher in patients with kidney transplantations due to using immunosuppressive agents to prevent transplant rejection [21].

In contrast, researchers such as Karahasan Yagci et al. concluded that viral load was not a significant factor in hospitalization and mortality [22]. The difference in these results may be attributed to the differences in study...
Table 5 Multivariate logistic regression models of factors associated with clinical outcomes

| Outcome                  | In-hospital mortality | ICU admission | Invasive ventilation | O2 Therapy |
|--------------------------|-----------------------|---------------|----------------------|------------|
|                          | OR (95% CI)           | P             | OR (95% CI)          | P          |
| Age (years)              |                       |               |                      |            |
| ≤ 60                     | 1                     | 1             | 1                    | 1          |
| > 60                     | 2.91 (1.08–7.83)      | 0.034         | 1.25 (0.53–2.94)     | 0.602      |
|                          |                       |               | 1.45 (0.54–3.85)     | 0.459      |
|                          |                       |               | 0.86 (0.30–2.43)     | 0.774      |
| Sex                      |                       |               |                      |            |
| Male                     | 1.11 (0.46–2.65)      | 0.823         | 1.91 (0.84–4.34)     | 0.124      |
| Female                   | 1                     | 1             | 0.90 (0.38–2.17)     | 0.820      |
|                          |                       |               | 1.92 (0.81–4.58)     | 0.141      |
| Smoking                  |                       |               |                      |            |
| No                       | 1                     | 1             | 1                    | 1          |
| Yes                      | 1.26 (0.26–6.03)      | 0.776         | 0.34 (0.06–1.89)     | 0.219      |
|                          |                       |               | 0.24 (0.03–2.22)     | 0.207      |
| Kidney transplant        |                       |               |                      |            |
| CKD not on dialysis      | 1                     | 1             | 1                    | 1          |
| CKD on dialysis          | 0.94 (0.30–2.95)      | 0.911         | 1.75 (0.62–4.92)     | 0.290      |
| Kidney transplant        | 2.99 (1.05–8.49)      | 0.040         | 2.11 (0.83–5.34)     | 0.115      |
|                          | 1.92 (0.67–5.50)      | 0.223         | 1.08 (0.39–2.99)     | 0.876      |
| eGFR                     | 0.97 (0.95–0.99)      | 0.003         | 0.98 (0.97–1.00)     | 0.068      |
|                          | 0.97 (0.94–0.99)      | 0.004         | 0.99 (0.97–1.01)     | 0.263      |
| No. of Comorbidity       |                       |               |                      |            |
| 0 (none)                 |                       |               |                      |            |
| 1                        | 6.39 (1.21–33.73)     | 0.029         | 8.36 (1.71–40.82)    | 0.009      |
|                          | 4.47 (0.84–23.95)     | 0.080         | 1.83 (0.62–5.41)     | 0.273      |
| ≥ 2                      | 6.06 (1.22–30.16)     | 0.028         | 7.51 (1.58–35.73)    | 0.011      |
|                          | 5.56 (1.10–29.07)     | 0.038         | 3.34 (1.10–10.10)    | 0.033      |
| No. of symptoms          | 1.23 (0.96–1.58)      | 0.095         | 1.05 (0.84–1.31)     | 0.652      |
|                          | 1.27 (0.98–1.64)      | 0.067         | 1.61 (1.23–2.10)     | < 0.001    |

OR odds ratio; CI confidence interval; CKD chronic kidney disease; ICU intensive care unit; eGFR estimated glomerular filtration rate

Table 6 Model-adjusted and unadjusted analysis risk of clinical outcomes

| Outcome                  | Prevalence, n (%) | Unadjusted analysis | Adjusted analysis |
|--------------------------|-------------------|---------------------|-------------------|
|                          | OR (95% CI)       | P                   | OR (95% CI)       | P            |
| In-hospital mortality    |                   |                     |                   |              |
| Ct value                 | 0.89 (0.84–0.95)  | < 0.001             | 0.88 (0.82–0.95)  | 0.002        |
| CT value category        |                   |                     |                   |              |
| Low viral load (Ct > 20) | 1                 | 1                   | 1                 | 1            |
| High viral load (Ct ≤ 20)| 6.86 (2.96–15.94) | < 0.001             | 11.65 (3.93–34.54)| < 0.001      |
| ICU admission            |                   |                     |                   |              |
| Ct value                 | 0.92 (0.86–0.98)  | 0.006               | 0.92 (0.86–0.98)  | 0.012        |
| CT value category        |                   |                     |                   |              |
| Low viral load (Ct > 20) | 31 (22.6%)        | 1                   | 1                 | 1            |
| High viral load (Ct ≤ 20)| 4.73 (2.09–10.73) | < 0.001             | 5.49 (2.16–13.97) | < 0.001      |
| Invasive ventilation     |                   |                     |                   |              |
| Ct value                 | 0.90 (0.84–0.97)  | 0.003               | 0.90 (0.83–0.97)  | 0.006        |
| CT value category        |                   |                     |                   |              |
| Low viral load (Ct > 20) | 20 (14.6%)        | 1                   | 1                 | 1            |
| High viral load (Ct ≤ 20)| 5.48 (2.35–12.82) | < 0.001             | 7.18 (2.61–19.74) | < 0.001      |
| O2 therapy               |                   |                     |                   |              |
| Ct value                 | 0.92 (0.85–0.98)  | 0.014               | 0.94 (0.87–1.01)  | 0.087        |
| CT value category        |                   |                     |                   |              |
| Low viral load (Ct > 20) | 105 (76.6%)       | 1                   | 1                 | 1            |
| High viral load (Ct ≤ 20)| 28 (90.3%)        | 2.84 (0.81–9.97)    | 0.102             | 3.08 (0.79–12.01) | 0.105        |

OR odds ratio; CI confidence interval; ICU intensive care unit
populations. In Karahasan Yagci et al.’s study, both hospitalized patients and outpatients were examined, but the present study merely examined hospitalized patients.

Findings signify that the ICU hospitalization of the high viral load renal patients (CT ≤ 20) was higher (5.7 times) than the ICU hospitalization of the low viral load renal patients (CT > 20). Additionally, invasive ventilation in patients with high viral load was 6.69 times higher than in the other group. According to Rajyalakshmi et al. a low CT was associated with increased ICU hospitalization and prolonged the patient’s stay. Rajyalakshmi et al. also reported a negative link between the length of stay in ICU and the CT value [18]. In another study, Wenyuchen concluded that increasing the viral load is a key factor leading to higher immune response and disease progression. Lung damage and respiratory dysfunctions, which develop after the disease, need invasive ventilation [23]. In contrast, Atique et al. did not observe statistically significant differences in disease severity between different CT value groups [24]. The difference in the results might be attributed to the way the CT value is divided. In the above study, CT value is divided into three categories, while the present study opts for two categories.

O2 treatment was higher in patients with high viral loads than in patients with low viral loads, and this difference was not deemed statistically significant (90.3% versus 76.6%). Abdulrahman et al. concluded that viral load had no significant association with oxygen demand during hospitalization [25]. Accordingly, the discrepancy between viral load and oxygen demand is because most hospitalized patients undergo intermittent or permanent oxygen therapy following COVID-19 infection.

The CKD Stages and eGFR was significantly different between survived and deceased groups. The eGFR was higher in the survived group. Moreover, more patients in the deceased group had CKD stages four and five. Generally, the survived group had better kidney function. The COVID-19 was also more severe in the patients with lower kidney function. Therefore, the eGFR was lower in the patients needed invasive oxygen therapy or admission to ICU and they had more severe CKD stages. In a study conducted by Gibertoni et al., the incidence and mortality of COVID-19 was higher in non-dialysis chronic kidney disease than patients without comorbid diseases. Furthermore, the mortality rate was higher in CKD-EPI stage 4 [26]. Ozturk et al. achieved the same result in a retrospective study on CKD patients. They concluded that CKD stage 3–5 patients had highest mortality rate after COVID-19 infection among the CKD patients [27].

Examining the impact of other variables on clinical outcomes revealed that the probability of death increases with age. Renal patients over 60 years were 2.93 times more likely to succumb to COVID-19 than those below 60 years. Oto et al. observed that factors such as ischemic heart diseases and inadequate transplant function were among the leading causes of higher mortality following COVID-19 in individuals over the age of 60 [28]. In another study, on a predominantly African-American population, increasing age was linked to worsening prognosis in chronic renal patients with COVID-19 infection [29].

In the present study, kidney transplant patients were significantly (2.74 times) more likely to succumb to COVID-19 than chronic kidney patients who were not on dialysis. In a systematic review by Alfishawy, COVID-19 was linked to higher mortality in transplant recipients, including kidney transplant recipients. Accordingly, this high mortality rate is attributed to immunosuppressive drug intakes [30]. In another study concerning kidney transplant patients with COVID-19, the mortality rate in these patients was higher than in hemodialysis patients [31].

The present study revealed that the presence of comorbid disease(s) in kidney patients significantly increases the probability of death (by 6.34 times) compared to patients without any comorbid disease. Symptoms of COVID-19 range from asymptomatic infection to severe pneumonia with respiratory failure and even death. More severe cases with higher mortality have been reported in elderly patients and individuals with chronic conditions such as hypertension, diabetes, or cardiovascular diseases. Hence, patients with chronic kidney diseases (CKD) are more likely to suffer from various infections and cardiovascular diseases than the general population. The significantly altered and suppressed immune system in CKD patients may predispose these individuals to infectious complications. In addition, it is of note that CKD patients have a chronic systemic inflammation that may also increase morbidity and mortality [3].

Patients on dialysis and kidney transplant were more likely to be admitted to the ICU than non-dialysis patients, although with a non-significant difference. In dialysis patients, symptoms develop more severely than in non-dialysis patients, and laboratory parameters indicators of inflammation such as lymphocyte and neutrophil count, and creatine kinase are observed higher. Hence, the severity of COVID-19 diseases and the need for ICU hospitalization will be higher in patients under dialysis [4].

Accordingly, the probability of admission to the ICU, the use of invasive ventilation, and oxygen therapy had significantly increased in patients with one, two, or more comorbid conditions than in those without any comorbidity. The presence of any of the comorbidities alone can be associated with increased mortality and morbidity following COVID-19 infection. Therefore, this issue is exacerbated in the presence of multiple comorbidities [32, 33].
Conclusion

Kidney transplant patients and similarly dialysis patients had higher mortality, ICU admission, invasive ventilation, and oxygen therapy following COVID-19 than the non-dialysis group. As a result, early prediction of the severity of COVID-19 in renal patients via laboratory markers may help manage treatment to prevent mortality and morbidity. In the present study, CT value was a significant predictor of mortality in renal patients. Nevertheless, further studies are required on how to render optimal use of the CT value, given that the quality of the test sample and the different groups of patients under study affect the effectiveness of this marker in predicting disease severity.

Acknowledgements We thank all patients for participating in this study and the authorities of the Shahid Beheshti University of Medical Sciences, Labbafinejad Hospital and Chronic Kidney Diseases Research Center for cooperation in data collection and supporting this study.

Author contributions Study concept and design: SA, ND, MN, and SM. Acquisition, analysis, or interpretation of data: SA and SM. Drafting of the manuscript: SA, PPK, and SM. Critical revision of the manuscript for important intellectual content: SA, PPK, SM, and ND. Statistical analysis: SM. Obtained funding: not applicable. Administrative, technical, or material support: MRJ, SS, MP, and MN. Study supervision: SA and ND.

Funding This study did not receive any specific grant from any agency in the public, commercial, or not-for-profit sector.

Availability of data and materials The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declared that they have no conflict of interests.

Ethics approval and consent to participate The Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran, approved this study (IR.SBMU. UNRC.REC.1400.019), and waived the need for informed consent. All methods in the present study were performed in accordance with the relevant guidelines and regulations.

Consent for publication Not applicable.

References

1. Benedetti C, Waldman M, Zaza G, Riella LV, Cravedi P (2020) COVID-19 and the kidneys: an update. Front Med 7:423
2. Mohamed NE, Benn EKT, Astha V, Okhawere KE, Korn TG, Nkendirim W et al (2021) Association between chronic kidney disease and COVID-19-related mortality in New York. World J Urol 39(8):2987–2993
3. D’Marco L, Puchades MJ, Romero-Parras M, Gimenez-Civera E, Soler MJ, Ortiz A et al (2020) Coronavirus disease 2019 in chronic kidney disease. Clin Kidney J 13(3):297–306
4. Yang D, Xiao Y, Chen J, Chen Y, Luo P, Liu Q et al (2020) COVID-19 and chronic renal disease: clinical characteristics and prognosis. QJM Mon J Assoc Phys 113(11):799–805
5. Haybar H, Kazemnia K, Rahim F (2020) Underlying chronic disease and COVID-19 infection: a state-of-the-art review. Jundishapur J Chronic Dis Care 9(2):e103452
6. Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, Zhao S et al (2021) AKI in hospitalized patients with COVID-19. J Am Soc Nephrol 32(1):151–160
7. Collado S, Arenas MD, Barbosa F, Cao H, Montero MM, Villar-Garcia J et al (2020) COVID-19 in grade 4–5 chronic kidney disease patients. Kidney Blood Press Res 45(5):768–774
8. Ganswevoort RT, Hilbrands LB (2020) CKD is a key risk factor for COVID-19 mortality. Nat Rev Nephrol 16(12):705–706
9. Henry BM, Lippi G (2020) Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. Int Urol Nephrol 52(6):1193–1194
10. Kant S, Menze SP, Hanouneh M, Fine DM, Crews DC, Brennan DC et al (2020) The COVID-19 nephrology compendium: AKI, CKD, ESKD and transplantation. BMC Nephrol 21(1):449
11. Oyelade T, Alqahtani J, Canciani G (2020) Prognosis of COVID-19 in patients with liver and kidney diseases: an early systematic review and meta-analysis. Trop Med Infect Dis 5(2):80
12. Pakhchanian H, Raiker R, Mukherjee A, Khan A, Singh S, Chatrjee A (2021) Outcomes of COVID-19 in CKD patients: a multicenter electronic medical record cohort study. Clin J Am Soc Nephrol CJASN 16(5):785–786
13. Rao SN, Manissero D, Steele VR, Pareja J (2020) A systematic review of the clinical utility of cycle threshold values in the context of COVID-19. Infect Dis Ther 9(3):573–586
14. Sule WF, Oluwayelu DO (2020) Real-time RT-PCR for COVID-19 diagnosis: challenges and prospects. Pan Afr Med J 35(Suppl 2):121
15. Roberto P, Francesco L, Emanuela C, Giorgia G, Pasquale N, Sara D (2020) Current treatment of COVID-19 in renal patients: hope or hype? Intern Emerg Med 15(8):1389–1398
16. Martino F, Amici G, Grandesso S, Mortellaro RF, Cicero AL, Novara G (2021) Analysis of the clinical and epidemiological meaning of screening test for SARS-CoV-2: considerations in the chronic kidney disease patients during the COVID-19 pandemic. J Clin Med 10(5):1139
17. Choudhuri J, Carter J, Nelson R, Skalina K, Osterbur-Bradney M, Johnston A et al (2021) SARS-CoV-2 PCR cycle threshold at hospital admission associated with patient mortality. PLoS ONE 15(12):e0244777
18. Rajyalakshmi B, Samavedam S, Reddy PR, Aluru N (2021) Prognostic value of “cycle threshold” in confirmed COVID-19 patients. Indian J Crit Care Med 25(3):322
19. Magleby R, Westblade LF, Trzebucki A, Simon MS, Rajan M, Park J et al (2020) Impact of SARS-CoV-2 viral load on risk of intubation and mortality among hospitalized patients with coronavirus disease 2019. Clin Infect Dis 73(11):e4197–e4205
20. Miller EH, Zucker J, Castor D, Annavajhala MK, Sepulveda JL, Green DA et al (2021) Pretest symptom duration and cycle threshold values for severe acute respiratory syndrome coronavirus 2 reverse-transcription polymerase chain reaction predict coronavirus disease 2019 mortality. Open Forum Infect Dis 8(2):ofab003
21. Nopsopon T, Kittrakulrat J, Takkavatakarn K, Eiamsitrakoon T, Chakkapan P, Chowers J et al (2020) COVID-19 and chronic kidney disease: a systematic review and meta-analysis. J Nephrol CJASN 16(5):785–786
22. Karahasen Yagi C, Sarinoglu RC, Bilgin H, Yanilmaz O, Sayin E, Deniz G et al (2020) Relationship of the cycle threshold values of SARS-CoV-2 polymerase chain reaction and total severity score of computerized tomography in patients with COVID 19. Int J Infect Dis 101:1878–3511
23. Chen W, Xiao Q, Fang Z, Lv X, Yao M, Deng M (2021) Correlation analysis between the viral load and the progression of COVID-19. Comput Math Methods Med 2021:9926249
24. Atique M, Ghafoor A, Javed R, Fatima N, Yousaf A, Zahra S (2021) Correlation of viral load with the clinical and biochemical profiles of COVID-19 patients. Cureus 13(7):e16655-e
25. Abdulrahman A, Mallah SI, Alqahtani M (2021) COVID-19 viral load not associated with disease severity: findings from a retrospective cohort study. BMC Infect Dis 21(1):688
26. Gibertoni D, Reno C, Rucci P, Fantini MP, Buscaroli A, Mosconi G et al (2021) COVID-19 incidence and mortality in non-dialysis chronic kidney disease patients. PLoS ONE 16(7):e0254525
27. Ozturk S, Turgutalp K, Arici M, Odabas AR, Altiparmak MR, Aydin Z et al (2020) Mortality analysis of COVID-19 infection in chronic kidney disease, haemodialysis and renal transplant patients compared with patients without kidney disease: a nationwide analysis from Turkey. Nephrol Dial Transpl 35(12):2083–2095
28. Oto OA, Ozturk S, Turgutalp K, Arici M, Alpay N, Merhametsiz O et al (2021) Predicting the outcome of COVID-19 infection in kidney transplant recipients. BMC Nephrol 22(1):100
29. Navarrete J, Tong D, Cobb J, Rahbari-Oskou F, Hosein D, Caberto S et al (2021) Epidemiology of COVID-19 infection in hospitalized end-stage kidney disease patients in a predominantly African-American Population. Am J Nephrol 52:1–9
30. Alfishawy M, Elbendary A, Mohamed M, Nassar M (2020) COVID-19 mortality in transplant recipients. Int J Organ Transplant Med 11(4):145–162
31. Goffin E, Candelier A, Vart P, Noordzij M, Arnol M, Covic A et al (2021) COVID-19-related mortality in kidney transplant and haemodialysis patients: a comparative, prospective registry-based study. Nephrol Dial Transpl. https://doi.org/10.1093/ndt/gfab145.004
32. Ssentongo P, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM (2020) Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: a systematic review and meta-analysis. PLoS ONE 15(8):e0238215
33. Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B (2021) Association of sex, age, and comorbidities with mortality in COVID-19 patients: a systematic review and meta-analysis. Intervirology 64(1):36–47

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Authors and Affiliations

Sadra Ashrafi1,2,3 · Pouya Pourrahmad Kisomi3 · Saman Maroufizadeh4 · Mohammad Reza Jabbari5 · Mohsen Nafar6,7 · Shiva Samavat8 · Mahmoud Parvin9 · Nooshin Dalili1,2,10

Sadra Ashrafi
sadra.ashrafi@gmail.com
Pouya Pourrahmad Kisomi
bvbppk@gmail.com
Saman Maroufizadeh
saman.maroufizadeh@gmail.com
Mohammad Reza Jabbari
a_jabbariy@yahoo.com
Mohsen Nafar
m.nafar.md@gmail.com
Shiva Samavat
sssamavat@gmail.com
Mahmoud Parvin
mahuinparvin@yahoo.com
Nooshin Dalili
n.dalili2@sbmu.ac.ir

1 Chronic Kidney Disease Research Center, Department of Nephrology, Shahid Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2 Urology and Nephrology Research Center, Shahid Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3 Student Research Committee, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4 Department of Biostatistics, School of Nursing and Midwifery, Guilan University of Medical Sciences, Rasht, Iran
5 Department of Virology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
6 MD, Prof. of Nephrology, Division of Nephrology, Department of Internal Medicine, Shahid Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
7 Chronic Kidney Disease Research Center (CKDRC), Department of Nephrology, Labbafinejad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
8 Chronic Kidney Disease Research Center (CKDRC), Shahid Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences (SBMU), Tehran, Iran
9 Department of Pathology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
10 Department of Internal Medicine, Shahid Labbafinejad Medical Center, Department of Nephrology, Shahid Labbafinejad Hospital, Shahid Beheshti University of Medical Sciences, Boustan 9, Pasdaran Ave, Tehran, Iran