OPINION

from
Assoc. Prof. Dr. Kiril Svetoslavov Nenov, MD .

The dissertation for the award of a scientific degree
"Doctor"
By Kiril Zhivkov Zhelyazkov

TOPIC: COVID-19 IN PATIENTS WITH END STAGE RENAL FAILURE - COMPLICATIONS, RISK FACTORS AND MORTALITY

Scientific supervisor: Assoc. Prof. Dr. Alexander Stoyanov Stoyanov , MD .

On 16.12.2025, by order of the rector of the Medical University "Prof. Dr. Paraskev Stoyanov" - city of Varna No. R-109-516, I was elected as a Member of the Scientific Jury, voted by the Faculty Council of MEDICINE (protocol of the Faculty Council No. 1/22.12.2025) for the acquisition of the ONS "Doctor" in the field of higher education:

7.0 Health and Sports
7.1 Medicine and specialty "Nephrology"

After discussion , the dissertation is sent for defense to the Department Council of the Second Department of Internal Medicine of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

BIOGRAPHICAL DATA of Dr. Kiril Zhivkov Zhelyazkov

The doctoral candidate graduated from the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna in 2016. From December 2016 he started working as a doctor in the Nephrology Clinic of the University Hospital "St. Marina" - Varna. In August 2018 he began specializing in nephrology, and in December 2022 he acquired a specialty in nephrology. In February 2019 he was appointed as an honorary assistant to the Department of Nephrology, Hemodialysis and Toxicology, and from September 2019 he was appointed as a full-time assistant. He teaches 5th year students of Medicine. He speaks English - level C1 and German - B1.

Analysis of the dissertation:

The dissertation contains 110 standard pages and is illustrated with 15 tables and 16 figures.

The literature review includes 206 literature sources (6 in Cyrillic and 200 in Latin). The scientific works are mainly from the last 3 years. The literature review examines in detail chronic renal failure, hemodialysis treatment, COVID-19 infection and the relationship between them.

After a thorough and critical analysis of the literature data and highlighting the unresolved issues on the topic, **the GOAL** of the dissertation work was determined :

To analyze the impact of the COVID-19 pandemic on chronic hemodialysis patients. To assess the complications caused by the disease , the risk factors that contribute to a more severe course and higher mortality.

The chosen topic is relevant and socially significant. The relevancy stems from the increasing number of patients on renal replacement therapy and the global conditions contributing to more frequent epidemics and the pandemic caused by newly emerging viral infections. In addition, to date, no studies have been conducted on the impact of COVID-19 on this population of patients in Bulgaria. Research on the complications, risk factors and mortality during the COVID-19 pandemic in Bulgaria in high-risk groups (patients on renal replacement therapy on chronic hemodialysis) is of key importance for completing the picture that led to Bulgaria being the country in the European Union with the highest mortality rate.

To achieve the goal of the dissertation, 5 main **tasks** were formulated and implemented:

- To study survival and causes of death in chronic hemodialysis patients with COVID-19..
- To analyze the demographic characteristics (age , gender) and accompanying diseases (diabetes , hypertension , cardiovascular diseases) in the monitored dialysis cohort .
- To investigate the relationship between SARS-CoV-2 infection and vaccination status as predictors of hemodialysis effectiveness and clinical outcome.
- To establish the relationship between the quality of hemodialysis (measured by URR and Kt /V) and clinical outcomes, including length of hospitalization, severity of the course, and 6-month survival.
- To determine whether there is a change in the efficiency of the dialysis procedure before and after COVID-19 infection, by comparing URR and Kt /V in patients.

A total of 190 patients were studied – 82 men and 108 women. Patients were divided into groups depending on their COVID -19 infection status, vaccination status, comorbidities in the patients and mortality. Several studies were performed in the dissertation work, the largest cohort included 190 patients with a mean age of 62.7 years (range 32–88). In this group, 101 patients were diagnosed with at least one confirmed SARS-CoV-2 infection, while 89 remained COVID-negative during follow-up. A total of 98 deaths (51.57%) were recorded: 55 among COVID-positive patients and 43 among COVID-negative ones. Cardiovascular disease was the most common comorbidity, affecting 122 (69.5%) patients, followed by diabetes mellitus in 58 (30.5%) patients. Logistic regression identified older age and cardiovascular disease as the strongest predictors of mortality, while gender and diabetes were not significantly associated with increased mortality. Vaccination status emerged as a powerful modifiable factor. Among the 133 vaccinated patients, survival was significantly higher compared to the unvaccinated .

The second cohort included 88 patients with PCR -confirmed COVID-19 infection. Patients were stratified by dialysis adequacy using Kt /V values: 34 (38.6%) had Kt /V <1.3, while 54 (61.4%) had Kt /V ≥1.3. The median age was 64 years (range 35–84), with 55 men (62.5%) and 33 women (37.5%). Kaplan-Meier survival curves showed a steeper early decline in Group A, although Cox regression did not identify statistically significant long-term differences.

The third analysis focused on 50 patients in whom dialysis adequacy was measured before and after COVID-19 infection. This subgroup included 20 women (40%) and 30 men (60%), with a mean age of 64 years. According to vascular access, patients were divided into: 23 (46%) with arteriovenous fistula, 22 (44%) with an indwelling catheter, and 5 (10%) with a temporary catheter. These results indicate that although COVID-19 itself did not impair dialysis adequacy .

After discussing the results obtained, the dissertation researcher establishes 8 basic **conclusions** :

The overall mortality rate in chronic hemodialysis patients is extremely high (over 50% for the entire follow-up period), which confirms the vulnerability of this population regardless of COVID-19 infection. Although SARS-CoV-2 infection is a significant stress factor, it is not established as the only predictor of mortality compared to major comorbidities . Cardiovascular diseases emerge as the strongest independent predictor of fatal outcome. They increase the risk of mortality more than fivefold and are a leading factor for cardiovascular death. Vaccination against COVID-19 is associated with significantly lower mortality and a reduction in the risk of cardiovascular fatal outcomes in COVID-19 positive patients. Advanced age increases the overall risk of death, but is not directly associated with a specific type of fatal outcome. Diabetes and gender have not been established as independent predictors of mortality. Lower dialysis adequacy was associated with more complications and higher mortality, but did not reach statistical significance as an independent predictor of survival.

- The author formulates four **contributions** of a theoretical nature, the underlying conclusions are: the high mortality in chronic hemodialysis patients during the COVID-19 pandemic is the result of a complex interaction between COVID-19 infection, age, cardiovascular diseases (CVD), vaccination status and dialysis adequacy, and that CVD is established as the strongest independent predictor of mortality, which emphasizes their dominant importance in the pathogenesis of lethal outcome in dialysis patients.

- Five **contributions** of a practical and applied nature, the basics of which are: immunization for COVID-19 has a strong protective effect and that the prevention, diagnosis and treatment of CVD and its complications in hemodialysis patients is appropriate to be the main component of the therapeutic approach.

The dissertation work is of practical and theoretical importance. For the first time in Bulgaria, the impact of the COVID-19 pandemic on patients with end-stage renal failure on chronic hemodialysis has been studied. The main modifiable factor for reducing mortality from COVID-19 infection during the pandemic in the studied group of patients is vaccination status. CVD complications and COVID-19 infection are the main causes of death in COVID-19 negative and positive patients, respectively.

Dr. Kiril Zhelyazkov has 4 publications related to his dissertation.

The dissertation is written in clear and precise language in a good scientific style.

CONCLUSION

ON THE BASIS OF THE MENTIONED DATA, I ACCEPT THAT THE DISSERTATION OF DR. KIRIL ZHELYAZKOV MEETS ALL THE REQUIREMENTS FOR AWARDING THE EDUCATIONAL AND SCIENTIFIC DEGREE "DOCTOR" DEGREE IN NEPHROLOGY. I VOTE POSITIVELY AND I SUGGEST THAT THE OTHER MEMBERS OF THE SCIENTIFIC JURY ALSO VOTE POSITIVELY.

05.02.2026 Dr. Kiril Nenov, MD

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