**REVIEW**

By Prof. Emil Paskalev Dimitrov, DM, PhD
Elected as a member of the scientific jury by Order № 15-05-169/11.08.2025
of the Executive Director and Procurator of UMHAT "Acibadem City Clinic Tokuda Hospital"
for the public defense procedure of the dissertation of
Dr. Dilyana Mihaylova Nikolova
for awarding the educational and scientific degree "Doctor"
on the topic:
**THE ROLE OF FIBROBLAST GROWTH FACTOR 23 IN THE DEVELOPMENT OF RENAL BONE DISEASE AND CARDIOVASCULAR COMPLICATIONS IN PATIENTS WITH CHRONIC KIDNEY DISEASE**
Acibadem City Clinic Tokuda Hospital
Scientific supervisor: Assoc. Prof. Aleksandar Osichenko, DM

Biographical Data:
Dr. Dilyana Mihaylova Nikolova was born on August 22, 1971, in Sofia. She graduated from the 91st German Language High School in 1990 and from the Medical University of Sofia in 1996. From 1996 to 2005, she worked at the 5th City Hospital. In 2005, she obtained her specialization in Internal Medicine and that same year began working as an assistant in the Clinic of Nephrology and Transplantation at UMHAT "Alexandrovska," Sofia. In 2011, she specialized in Nephrology. In 2014, she worked in Germany as a nephrologist at the City Hospital of Wittenberg Medical University. Since 2022, she has served as Head of the Nephrology Department at the Internal Medicine Clinic of Tokuda Hospital, where she currently works. Dr. Nikolova has extensive experience in Internal Medicine and Nephrology. She has substantial experience as a nephrologist and a specialist in Internal Medicine.

All of these qualifications provide the basis for Dr. Nikolova to summarize her experience in a dissertation.

Dissertation Focus:
In her dissertation, Dr. Nikolova aims to study the role of the laboratory marker FGF-23 in the diagnosis and treatment of renal bone disease and cardiovascular complications in patients with Chronic Kidney Disease (CKD). CKD is a socially significant medical condition with an increasing prevalence worldwide, including Bulgaria. Patients often reach end-stage CKD requiring replacement therapy. All CKD patients experience secondary complications that significantly worsen quality of life and reduce survival, particularly cardiovascular diseases.

This significance led to the introduction of the term "Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD)", focusing on the role of calcium-phosphate metabolism, which increases fracture risk, including spontaneous fractures, severely affecting patients' functional status. These patients often experience cardiovascular, heart, neurodegenerative diseases, secondary anemia due to insufficient hematopoiesis, cognitive impairment, all contributing to disability.

Dr. Nikolova correctly targets the issue of hyperphosphatemia and the significance of its association with increased FGF-23, making the dissertation topic current and practically oriented.

Dissertation Structure:
The dissertation comprises 106 standard pages. The literature review provides sufficient

information on the topic. Dr. Nikolova has optimally described the clinical, laboratory, and statistical methods used in the study. The results are presented convincingly. She emphasizes the practical benefits of laboratory tests for patients in diagnosing and monitoring CKD.

The bibliography includes over 120 references, eight of which are by Bulgarian authors. More than 25 of the cited sources are from the last five years. The material includes a sufficient number of figures (36) and tables (8).

Applied Contributions:

1. The measurement of FGF-23 in CKD diagnosis is an excellent screening tool for patients at risk of developing severe hyperparathyroidism and serious bone-mineral disorders within two years.
2. Screening patients at risk for rapid CKD progression.
3. Laboratory marker for assessing the effectiveness of diet in CKD patients.
4. Laboratory marker for evaluating hemodialysis efficiency regarding phosphate removal.
5. Laboratory marker for patients at high risk of cardiovascular complications with CKD-MBD.
6. Laboratory marker for persistent hypophosphatemia and muscle weakness in post-renal transplant patients.

Scientific-Theoretical Contributions:

- For the first time in Bulgaria, FGF-23 was studied in pre-dialysis and dialysis-stage CKD patients.
- First presentation of data on changes in FGF-23 and PTH levels in CKD stages 3–5.
- Patients are analyzed in the context of the new CKD-MBD concept and its relationship to cardiovascular disease.
- The relationships of FGF-23 with phosphorus, PTH, and eGFR are confirmed.
- The effect of Calcitriol treatment on PTH levels, and its lack of effect on FGF-23, is confirmed.
- Analysis provides new directions for diagnosis and therapy of CKD patients.

The dissertation is written clearly, understandably, and logically leads to relevant conclusions. The findings have pronounced clinical significance for nephrology practice.

Critical Notes: None

Reviewer:
Prof. Emil Paskalev Dimitrov, DM, PhD