

# **REVIEW**

**by Prof. Dr. Boryana Deliyska, PhD, DSc.**

**of dissertation for awarding the scientific and educational  
degree "Doctor"**

**"MONITORING AND EVALUATION OF NUTRITIONAL  
STATUS AND MARKERS OF THE INFLAMMATORY  
PROCESS IN PATIENTS WITH CHRONIC KIDNEY DISEASE"**

**of Dr. PETAR PLAMENOV PETROV**

**Scientific adviser: Prof. Dr. Svetla Vasileva Staykova, PhD, DSc**

**Scientific consultant: Assoc. Prof. Dr. Lili Slavcheva Grudeva, PhD**

I was elected as a member of the scientific jury, voted by the Faculty of Medicine "Faculty of Medicine" at MU - Varna (Protocol № 57 of 21.12.2021) and appointed by order of the Rector № R-109-596 / 31.12.2021. for the acquisition of degree "Doctor" in the field of higher education 7.0 Health and sports, professional field 7.1 Medicine and specialty "Nephrology". The dissertation was discussed and directed to the defense at Second Department of Internal Medicine at the Medical University "Prof. Dr. Paraskev Stoyanov"- Varna.

## **Brief biographical data of Dr. Petar Petrov**

He graduated medicine in Varna in 2015, after which he began working as a nephrologist at the University Hospital "St. Marina EAD, Varna. Since 2017 he has been an assistant at the Medical University of Varna, teaching 5th year medical students. In 2020 acquires the specialty "Nephrology". He speaks English and German. There are courses for raising the qualification: 2016 and 2021 - Ultrasound of abdominal organs, and in 2019 - Providing temporary vascular access and percutaneous needle biopsy of the kidney in patients with renal disease under imaging control.

## **Analysis of the dissertation**

The literature review is based on a bibliographic reference, including 183 literature sources, of which 2 in Cyrillic and 181 in Latin, most of them from the last 5 years. The literature review examines in detail the epidemiology, major changes in CKD, biomarkers in renal structure, diagnosis of renal impairment, progression of CKD, endothelial dysfunction and oxidative stress, the relationship of CKD with CVD, new trends in the diagnosis of chronic kidney disease, nutritional status and quality of life in patients with CKD. Based on an in-depth and critical analysis of the literature, the aim of the dissertation was determined, namely to establish a correlation between the new non-invasive biomarker (Visfatin) and nutritional status / inflammatory process, given the prognostic value of the biomarker in CKD. The chosen topic is relevant due to the social significance of CKD, which is growing worldwide and leads to its progression to end-stage renal disease and permanent disability of patients. New biomarkers are constantly being sought in the world, which would have diagnostic and prognostic significance for patients in the predialysis and dialysis stages. One of them is Visfatin, also known as pre-B-cell colony enhancing factor-1 (PBEF-1) or nicotinamide phosphoribosyltransferase (NAMPT). It is adipokine, secreted by activated lymphocytes, monocytes and neutrophils and stimulates the secretion of IL-6, induces the expression of inflammatory mediators in humans on endothelial cells by nuclear factor (NF) -  $\kappa$ B. According to some authors, it can be considered as a marker of endothelial dysfunction.

From the set goal in the doctoral dissertation 5 main tasks are formulated, which include determining the importance of the modern non-invasive biomarker (Visfatin) related to the inflammatory process and its diagnostic value, as well as assessing its practical significance determined by the relationship between Visfatin and nutritional status of patients with CKD, comparing its levels with indicators characterizing the inflammatory process, as well as monitoring changes in individual quality of life depending on nutritional status and the accompanying inflammatory process.

The dissertation contains 149 standard pages and is illustrated with 6 tables, 42 figures and 3 appendices.

The object of the study are a total of 80 patients with CKD in predialysis (30 patients) and hemodialysis treatment (50 patients) from the Clinic of Nephrology and dialysis at the University Hospital "St. Marina" - Varna, followed clinically and examined by routine methods. They are defined according to clearly defined inclusion and exclusion criteria.

The laboratory methods used in the development are described in detail, which include not only the routine parameters, but also the study of intact fibroblast growth factor -23 (iFGF-23), Human EPOR, Visfatin. Determining the quality of life with a questionnaire of 36 questions (Kidney Disease Quality of Life - Short Form - 36, KDQOL-36) after modification of Prof. Dr. S. Staykova, Ph.D (2018) for its adaptation to the conditions in the country. The use of 7 statistical methods determines the reliability of the results obtained.

The study was conducted with the permission of KENI of MU-Varna with Protocol / Decision № 101 / 24.03.2021, and each participant filled out a declaration of informed consent. The results are analyzed in detail in various aspects concerning the development of the set goals. In the discussion, the data obtained from the present study are thoroughly compared with those from the literature review.

Circulating concentrations of Visfatin have been reported to be significantly elevated in CKD. Due to the lack of uniform reference limits for Visfatin, a threshold value of 16.92 ng / ml (AUC = 0.612 (0.485-0.739);  $p < 0.05$ ) was established, at which a distinction was made between patients in the predialysis and dialysis groups. Gender differences in the levels of the indicator were also observed. Of interest is the fact that low serum iron levels are associated with higher levels of Visfatin. The study of the relationship

between CRP and Visfatin levels found that the two markers correlated inversely in the dialysis group. The indicator is positively correlated with IL-6 and CRP, but negatively with serum albumin in CKD, which confirms the association of Visfatin with the inflammatory process and hypoalbuminemia. There was a significant difference in BMI values according to Visfatin levels between the two groups. Dialysis patients have lower BMI values and lower Visfatin values.

Quality of life was studied in 50 dialysis patients. Low levels of Visfatin have been found to correlate with lower scores on patients' health, and patients who feel tired have significantly higher levels of Visfatin.

As a summary of his material, Dr. Petar Petrov draws five main conclusions, which include the place of Visfatin as a non-invasive marker of inflammation in dialysis patients, Visfatin levels are significantly lower in the inflammatory process in patients on dialysis, there is no correlation between nutritional status and Visfatin, levels of the indicator are negatively correlated with the duration of dialysis treatment, and that low levels of Visfatin are associated with poorer quality of life and poor health.

The dissertation has significant theoretical and practical significance. Scientific contributions are of original nature. For the first time in Bulgaria the diagnostic and prognostic value of Visfatin is determined as a new non-invasive biomarker in patients with different stages of CKD, as well as its relationship to other biomarkers. Visfatin is a new and non-invasive marker for the country that is not routinely studied among nephrologically ill patients. The dissertation provides an opportunity to clarify its role in the diagnosis of the inflammatory process. An algorithm for disease progression and quality of life assessment in dialysis patients based on the use of modern non-invasive biomarkers has been developed and proposed.

The dissertation contains 149 standard pages and is very well illustrated with 6 tables, 42 figures and 3 appendices.

The dissertation has 3 publications related to the present study.

The dissertation is written clearly and accurately, with a good scientific style. I do not know any evidence of plagiarism.

### **Conclusion**

**Based on the above, I accept that the dissertation of Dr. Petar Plamenov Petrov meets the requirements for the award of degree "Doctor" of Nephrology and I invite the esteemed members of the scientific jury to vote positively.**

**Prof. Dr. Boryana Deliyska, PhD, DSc**

02/02/2022

