

OPINION

by Assoc. Prof. Iliyan Todorov, MD, PhD

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regarding a dissertation for the award of the educational and scientific degree "Doctor"

Field of higher education: 7. Healthcare and Sports,

Professional field: 7.1. Medicine

Doctoral program: "Infectious Diseases"

Author: *Ekaterina Lyutsova, MD*

Form of doctoral study: *full-time*

Department: *Infectious Diseases, Parasitology and Dermatovenereology*

Title: *"Fecal calprotectin as a diagnostic and prognostic marker in acute intestinal infections in children"*

Scientific supervisor: *Prof. Margarita Gospodinova, MD, PhD, Department of Infectious Diseases, Parasitology and Dermatovenereology, MU-Varna*

In accordance with Order No. P-109-125/11.03.2026 of the Rector of the Medical University of Varna, **I have been appointed** as a member of the Scientific Jury, and basing to Protocol No. 1/23.03.2026, **I have been assigned** to prepare an opinion (in Bulgarian and in English) within the procedure for awarding the educational and scientific degree "Doctor" to the candidate Dr. Ekaterina Lyutsova at the Medical University of Varna.

1. General presentation of the procedure

The submitted set of materials, in both printed and electronic format, **complies with the requirements** of the Law on the Development of the Academic Staff in the Republic of Bulgaria, its implementing regulations, as well as the Regulations for the Development of the Academic Staff at the Medical University of Varna, and includes all necessary documents.

2. Presentation of the PhD candidate

Ekaterina Lyutsova was born in 1983 in Tashkent, Uzbekistan. In 2006, she graduated with honors in Medicine from Yaroslavl State Medical University. Until 2009, she practiced as an internist, after which she obtained a specialty in Internal Medicine ("Therapy") and worked as a physician in the Moscow region until 2014.

In 2015, she successfully passed the state examinations for recognition of her professional qualification in the Republic of Bulgaria and, following a competitive selection process, was appointed as an Assistant Physician at the Department of Infectious Diseases, Parasitology and Dermatovenereology at the Medical University of Varna, as well as at the Clinic of Infectious Diseases at the University Hospital "St. Marina." In 2020, she acquired a specialty in Infectious Diseases. Since 2023, she has been enrolled in a Master's program in "Artificial Intelligence in Healthcare," and during the period 2024–2025, she has been undertaking training at Burgas Free University in the specialty "Healthcare Management."

In her teaching activities, Lyutsova, MD conducts practical training sessions in infectious diseases for students from various specialties and participates in the training of medical interns. She actively takes part in both national and international scientific forums and conferences. Her research interests are in the field of diagnosis, treatment, and control of infectious diseases, particularly intestinal infections presenting with diarrheal syndrome, with a focus on the implementation of modern and intelligent technologies in medical practice. She is an author and co-author of publications in Bulgarian and international journals.

3. Relevance of the topic

Acute intestinal infections presenting with diarrheal syndrome represent a leading cause of morbidity and mortality among children under 5 years of age. The etiological agents include a wide range of bacteria and viruses, and less commonly parasites, which result in clinical presentations with similar symptomatology but varying severity and prognosis. Timely orientation toward the probable etiological agent is essential for establishing an appropriate therapeutic approach in each individual patient.

Traditionally, the presence of pathological admixtures such as blood and mucus in the stool has been considered an indicator of bacterial etiology in intestinal infections. However, these manifestations are subjective and do not always represent a reliable early discriminative marker. On the other hand, standard stool cultures require technological time for the detection of microbial growth and for determining antibiotic susceptibility of the isolate. They are not the method of choice in the diagnostic algorithm of viral intestinal infections, which are identified by modern multiplex immunochromatographic methods that are not universally available across all laboratories.

In this context, there is a need to introduce into clinical practice modern, cost-effective, easily accessible, and reliable markers that allow timely etiological differentiation of cases. One such promising indicator is fecal calprotectin /FC/ — a calcium-binding protein localized in the cytoplasm of neutrophil leukocytes, whose concentration in feces is directly proportional to the degree of neutrophil influx into the intestinal lumen. At present, it is routinely used in patients with Crohn's disease and ulcerative colitis, with its levels correlating both with the degree of inflammatory activity and with the response to treatment.

Contemporary international studies emphasize its role in infectious disease practice as a discriminative marker for differentiating bacterial from viral intestinal infections. To date, there is a lack of systematic studies in the Republic of Bulgaria evaluating its clinical value in children with intestinal infections presenting with diarrheal syndrome.

In this context, the submitted dissertation is characterized by high relevance from a theoretical perspective, presenting up-to-date data on FC within the field of infectious pathology. In addition, it has significant practical potential, contributing to improved diagnostic and therapeutic efficiency in this group of diseases.

4. Knowledge of the problem

The literature review is comprehensive, competently developed, and demonstrates in-depth knowledge of the main clinical and epidemiological characteristics of intestinal infectious diseases presenting with diarrheal syndrome in childhood. It is logically structured, with individual sections consistently and coherently connected, presenting in a chronological manner both the historical development of knowledge and the contemporary advances related to the etiology, epidemiology, and pathophysiology of these conditions.

Key aspects related to the most common etiological agents and the mechanisms of their transmission in the national context are thoroughly examined. The author emphasizes contemporary approaches to the clinical assessment of children with acute intestinal infections, providing a logical transition to the role of laboratory investigations, and in particular to FC as a marker for assessing disease severity, therapeutic response, and prognosis.

The stated aim of the dissertation logically follows from the conducted literature analysis, while the tasks formulated for its achievement are clearly defined, methodologically sound, and oriented toward obtaining results of high practical significance.

5. Research methodology

The research methodology is appropriately selected and fully aligned with the stated aim and the formulated tasks of the dissertation. The applied clinical, laboratory, and statistical methods provide an opportunity for objective assessment of the investigated parameters and for obtaining reliable results. The study design is logically structured and allows for the identification and analysis of the key relationships underlying the research concept. The applied approaches create the conditions for accurate data analysis and interpretation, ensuring the formulation of valid, scientifically grounded conclusions with practical significance.

6. Characterization and evaluation of the dissertation and its contributions

The dissertation comprises 183 pages and is illustrated with 23 figures and 26 tables. Its content framework includes the main sections: "Introduction," "Literature Review," "Aim and Objectives," "Materials and Methods," "Results and Discussion," "Conclusion," "Findings," and "Contributions of Original and Applied Scientific Value." The bibliography includes 159 references, 17 of which are in Bulgarian. More than half of the cited publications are from the last decade, and approximately 20% reflect the most recent scientific achievements on the topic, published between 2023 and 2025. The text demonstrates high linguistic quality, stylistic coherence, and grammatical correctness. In the introduction, the author convincingly argues the relevance and scientific significance of the research problem. The structural components are logically sequenced, with each section concluding with a summary synthesizing the most important practical conclusions derived from the critical analysis of the presented data.

In accordance with the stated aim—to investigate the diagnostic and prognostic value of FC as a non-invasive marker in acute infectious diarrhea in childhood, as well as its role in etiological differentiation, severity stratification, monitoring therapeutic response, and predicting clinical outcomes – six research objectives are logically formulated. Using established methodological approaches, including modern statistical analyses, a thorough study was conducted on a carefully selected patient cohort. The obtained results are presented precisely and illustrated with appropriate tables and figures. They have been subjected to in-depth critical analysis and interpreted in the context of current epidemiological and clinical research on the topic. The dissertation concludes with a summary that systematizes the main findings and convincingly emphasizes the significance of studying FC in the relevant pathology.

The conclusions (six in total) logically follow from the stated aim and objectives, being clearly, precisely, and argumentatively presented based on the obtained results. Clinically significant correlations have been identified, including statistically significant relationships between FC levels and the etiology of intestinal infections, disease severity, therapeutic response, and prediction of clinical outcomes. Reference and cut-off values with specific clinical relevance have been determined.

The contributions of the dissertation are presented in a synthesized form and encompass both original and applied scientific aspects. The role of FC in the early clinical monitoring of children with acute intestinal infections has been demonstrated. For the first time in Bulgaria, a prospective analysis of this kind has been conducted, adding further scientific and practical value to the study.

7. Assessment of publications and the personal contribution of the PhD candidate

For participation in the current competition, Ekaterina Lyutsova, MD submitted two scientific publications thematically related to the dissertation, in which she is the first author—an evident indicator of her substantial personal contribution to the research. Both works are peer-reviewed and indexed in reputable international databases. According to the Regulations for the Development of the Academic Staff at the Medical University of Varna, the presented publication activity fully meets the minimum scientometric requirements for obtaining the educational and scientific degree “Doctor.” Data regarding citations, impact factor, h-index, and other indicators were not provided.

I have no critical remarks regarding Lyutsova’s scientific output. I recommend expanding her publication activity on the topic in the international scientific arena, as well as active participation in scientific forums to present the achieved results, which would contribute to their broader dissemination. In the future, the research could be further developed by including additional markers for acute intestinal inflammation that are easily applicable, rapid to assess, and widely accessible.

8. Abstract of the dissertation work

The presented by the author abstract of the dissertation work is prepared in accordance with the established guidelines and, in a concise form, includes all main sections of the dissertation. The research methods, the most clinically relevant results, conclusions, and contributions of both original and applied scientific value are accurately presented.

CONCLUSION

The dissertation **contains** scientific and applied scientific results that constitute an original contribution to the field and **fully comply** with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, its implementing regulations, and the Regulations of the Medical University of Varna for obtaining the educational and scientific degree “Doctor.”

The work convincingly demonstrates that the PhD candidate, Ekaterina Lyutsova, MD possesses in-depth theoretical knowledge and professional competencies in the scientific specialty of Infectious Diseases, as well as the skills and qualities necessary for conducting independent scientific research.

Based on the above, **I confidently give a positive assessment** of the dissertation, the author's abstract, and the achieved results and contributions, and **I recommend** to the esteemed Scientific Jury the award of the educational and scientific degree "Doctor" to Ekaterina Lyutsova, MD in the doctoral program in Infectious Diseases.

01.04.2026

Varna, Bulgaria

Prepared by:

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Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
2016/679