

**TO  
THE CHAIRMAN OF THE SCIENTIFIC JURY  
APPOINTED BY ORDER No. P-109-440/05.12.2024  
OF THE RECTOR OF THE MEDICAL UNIVERSITY  
“PROF. DR. PARASKEV STOYANOV” - VARNA**

**REVIEW**

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**On the competition for the academic position of Associate Professor  
in the field of higher education 7. Health and Sport, Professional drive 7.4.  
Public Health, Scientific specialty „Public Health Management  
(Clinical Microbiology)”**

**For the needs of the Department of Microbiology and Virology, Faculty of  
Medicine, Medical University “Prof. Dr. Paraskev Stoyanov” - Varna**

In the competition for the academic position of Associate Professor announced in Official Gazette No. 85/08.10.2024, one candidate has applied - Senior Assistant Professor Dr. Denis Sunay Niyazi, PhD.

Dr. Niyazi was born on 17.07.1993. He graduated in medicine at Medical University - Varna in 2018 with excellent grades. In 2018 he started working at the Department of Microbiology and Virology of Medical University - Varna as an assistant professor and since 2023 and currently he is a senior assistant professor. In 2023 he acquired the medical specialty “Microbiology”. In 2022 he defended his dissertation on the award of educational and scientific degree “Doctor” in the scientific specialty “Microbiology” on the subject: “Investigation of bacteremia and invasive fungal infections in patients following autologous and allogeneic hematopoietic stem cell transplantation”. In 2023, he graduated with a Master's degree in Public Administration with a specialization in Health Management.

Dr. Niyazi presented 43 research works in this competition, which I accept for review as follows:

- Thesis summary of a dissertation on the award of educational and scientific degree «Doctor»
- Habilitation work – monography
- Publications in scientific journals, refereed and indexed in world-renowned databases of scientific information – 20
- Publications in non-refereed peer-reviewed journals – 4
- Participation in scientific forums – 17, including 5 international and 12 national with international participation.

It should be noted that Dr. Niyazi's research results have been published in prestigious journals with high IF. The total IF of scientific output is 17.57. The individual h index of the author is 4 (Google Scholar). Dr. Niyazi's works have received considerable attention from the scientific community. They have been cited 49 times, with 16 citations in scientific journals, refereed and indexed in world-renowned databases of scientific information, evidence of the high scientific value of the publications. Taken together, these scientific metrics present the candidate as an established and respected scientist with a significant contribution to the development of clinical microbiology.

The analysis of the publications according to the author's participation shows that Dr. Niyazi is the sole or first author in 11 of the publications and the second author in 5, which indicates his leading and significant role in the research.

The research activity of Dr. Niyazi is distinguished by a clear concentration on the problems of clinical microbiology in the following main areas:

1. Infectious complications and antimicrobial resistance in patients with hematological malignancies and hematopoietic stem cell transplantation.
2. SARS-CoV-2 and COVID-19
3. Mycotic infections

In his work in the above scientific areas, Dr. Niyazi has achieved significant original and confirmatory scientific-theoretical and practical contributions, which can be presented in the following summarized form.

1.1. A systematic study of bloodstream infections in patients with hematologic malignancies covering a 6-year period (2015-2020) and 298 patients with laboratory-confirmed bloodstream infections has been performed. Gram-negative bacteria were shown to dominate (54.7%) as etiological agents, with *E. coli* (14.5%), *Enterobacter* spp. (12%) and *Klebsiella* spp. (10.1%). A high relative proportion of ESBL producers was found among *Enterobacter* spp. and *Klebsiella pneumoniae* isolates (over 50%) and over 15% in *E. coli*. The results were compared with a previous study covering the period 2011-2014. There was a persistent trend of Gram-negative bacteria dominance in the etiological spectrum of bloodstream infections, a persistently high level of ESBL producers among the members of *Enterobacteriaceae* family and a high proportion of carbapenem-resistant *Acinetobacter baumannii*. A new negative trend associated with the emergence of invasive carbapenem-resistant *Enterobacteriaceae* isolates in the period 2015-2020 has been demonstrated.

1.2. Bloodstream infections in patients after hematopoietic stem cell transplantation (HSCT):

1.2.1. For the first time in Bulgaria, a study was conducted on the incidence, risk factors and outcome of bloodstream infections in patients after HSCT, with 74 patients followed up after HSCT. A 35% cumulative incidence of bacteraemias was found in this group. The mean time period from transplantation to the onset of bacteremia was 8 days. The study identified intestinal colonization with multidrug-resistant microorganisms and occurrence of bacteremia before transplantation as statistically significant risk factors for bloodstream infection after HSCT. The survival rate to day 30 after HSCT was 23% and the four-month survival rate was 86.5%. The type of underlying disease (leukemia and lymphoma) and previous HSCT were the identified factors with a negative effect on survival.

1.2.2. The species identification and antibiotic susceptibility of staphylococci causing catheter-associated bloodstream infections in patients after HSCT were studied. Coagulase-negative staphylococci (CoNS) were found to play the leading etiologic role (85.7%), with *Staphylococcus epidermidis* predominating (57.1%). The relative proportion of *Staphylococcus aureus* was 14.1%. All CoNS were identified as methicillin-resistant, while *S. aureus* had preserved susceptibility (MSSA).

1.2.3. The *in vitro* activity of a new combined antibacterial agent (ceftazidime/avibactam, CZA) against isolates resistant to third-generation cephalosporins and/or carbapenems isolated from haemocultures and/or faecal samples of patients undergoing HSCT was studied. Multidrug-resistant bacteria carrying *bla*<sub>ESBL</sub>, *bla*<sub>VIM</sub>, *bla*<sub>OXA-23</sub>, *bla*<sub>OXA-24/40</sub>, and *bla*<sub>OXA-48</sub> were identified in 30.7% of patients studied. CZA activity was confirmed against ESBL isolates and was absent in isolates carrying *bla*<sub>OXA</sub> and *bla*<sub>MBL</sub>.

2.1. A large-scale hospital-based study was conducted on the dynamics of COVID-19 during the first year of the pandemic (May 2020-April 2021) and on the role of certain demographic factors in disease development. 40% of samples tested were positive, with the most affected age group being 60-79 years. Male sex was confirmed as a risk factor in the 20-59 age group, and in the under 19 group, female sex was identified as a predisposing factor for infection.

2.2. It was found that the relative proportion of SARS-CoV-2 positive samples among patients from Northeast Bulgaria for a two-year period (2020-2021) covering the first four waves of the pandemic was 33.6%. The seasonal and regional prevalence of COVID-19 in Northeastern Bulgaria was studied and compared with those in other European countries. The lack of seasonality was confirmed, as well as a variable regional distribution during the first two years of the pandemic. Differences in the prevalence of infection in both sexes and in relation to age during the different periods were also demonstrated.

2.3. The significance of so-called "suspicious" results when using the PCR method for the diagnosis of COVID-19 (detection of only one gene in the clinical sample) was evaluated and recommendations for their interpretation were made in relation to the clinical symptoms and the patient's history.

2.4. The reliability of rapid immunochromatographic assays for the diagnosis of COVID-19 was investigated by evaluating results obtained from over 2500 hospitalized patients. A sensitivity of 60% and a specificity of 98% were found, results confirming the place of this rapid method in the diagnostic process, especially in a setting of rapidly increasing patient numbers, the need for specialized equipment and trained personnel to operate the PCR method.



2. 5. A study was conducted on carbapenem-resistant *Enterobacterales* isolated from clinical materials of patients hospitalized in COVID-19 and intensive care clinics of St. Marina University Hospital - Varna in the first year of the pandemic (2020-2021). Carbapenem-non-susceptible *Klebsiella* spp. were found to dominate, with resistance mediated predominantly by *bla*<sub>KPC</sub>. The study also demonstrates within-hospital dissemination of MDR *K. pneumoniae* and *Enterobacter cloacae* complex clones.

3.1. A pivotal place in the scientific field of Mycotic Infections is occupied by Dr. Niyazi's monographic work entitled "Invasive aspergillosis in patients after hematopoietic stem cell transplantation". Dr. Niyazi provides comprehensive scientific information regarding both the etiologic agent and the epidemiology, clinical presentation and risk factors for the disease in this high-risk group of patients, diagnostic approaches, treatment and prevention. The scientific information presented on the problem is based on more than 500 references as well as the author's own clinical and laboratory experience. Systemic mycotic infections, including invasive aspergillosis in severely immunosuppressed patients, are difficult to diagnose and present a real challenge to clinical and laboratory professionals. This monograph discusses in detail the diagnostic options in the light of a comprehensive approach, combining both classical and established methods in practice and newer, modern and innovative methods, commenting on their capabilities, sensitivity, specificity, limitations and advantages. In addition to a comprehensive presentation of the modern diagnostic approach to this invasive mycotic infection, all groups of antimycotic drugs (including newly developed ones) are presented in detail with information on microbial spectrum, mechanism of action, dose regimens, inter-drug interactions, etc., as well as methods for determining susceptibility to them, sharing the most important and common practical difficulties and approaches to their interpretation and resolution. Particular attention is also given to the problem of emergence of resistance to the major groups of antimycotics, a phenomenon that is increasingly encountered in practice and that holds serious potential to compromise the treatment of this life-threatening infection.

3.2. For the first time, a Bulgarian case of mucormycosis after COVID-19 was described in a 66-year-old man presenting with rhino-orbito-cerebral form (ROC). The role of viral infection and elevated blood glucose levels as risk factors for ROC

mucormycosis was confirmed, as well as the need for a prompt and adequate multidisciplinary diagnostic process.

3.3. The importance of invasive mycotic infections (mucormycosis, aspergillosis, pneumocystosis) in the etiological spectrum of infectious complications in patients with hematologic malignancies and after HSCT has been demonstrated. The role of hematologic malignancies, consecutive HSCT as significant risk factors for the development of invasive mycotic infections was confirmed.

3.4. The effectiveness of molecular genetic techniques such as PCR in the diagnosis of invasive mould infections has been demonstrated, as has the effectiveness of a multidisciplinary approach (microbiological, imaging, histological examination) for their early diagnosis given the high disease burden with which these infections are associated.

3.5. The role of combined therapeutic approach (etiological and surgical) for rapid control of the infectious process accompanying invasive mycotic infections (mucormycosis) in patients with oncohematological diseases is confirmed.

3.6. The role of allogeneic transplantation as a factor in reactivation of latent herpesvirus infections has been confirmed.

3.7. The aggravating role of combined infectious complications (mycotic and viral) on disease outcome in patients with hematologic malignancies and after HSCT has been demonstrated.

For the implementation of his intensive scientific activity in the period 2019-2024, Dr. Niyazi is involved in three scientific projects at the Science Fund of MU - Varna, in one of which he is the main investigator.

In addition, Dr. Niyazi is an active participant in the teaching and educational activities of MU - Varna. His total teaching workload for the last 5 academic years is 1308 hours, which exceeds the norm, with 60% of the hours in the English-language program. He actively participates in conducting exercises and seminars in the specialty "Medical Microbiology" for students of the specialties of Medicine, Dentistry and Pharmacy. Since 2024, he has also been involved in the delivery of courses to postgraduate doctors in Clinical Microbiology.

## **Conclusion**

Dr. Niyazi is known as a respected and highly skilled specialist in the field of clinical microbiology, especially infectious complications in immunocompromised patients. The overall analysis of the scientific metrics, the contributions of his scientific production and his teaching activities testify to a categorical compliance with the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria, the Regulations for its implementation and the Regulations of MU - Varna for holding the academic position of Associate Professor. All this gives me grounds to confidently support with my positive judgment the election of Dr. Denis Sunay Niyazi to the academic position of "Associate Professor" in the specialty "Public Health Management (Clinical Microbiology)" for the needs of the Department of Microbiology and Virology at the Medical University - Varna.

14.02.2025

Reviewer:

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/ Prof. Stefana Sabcheva, MD, PhD /