To the chairman of the scientific jury appointed

by Order No. 524 from 19. 12. 2022 of the Director of the NCIPD

REVIEW

for competition for the academic position "Associate Professor"

at the National Center for Infectious and Parasitic Diseases

by Professor Todor Vesselov Kantardjiev, MD, PhD, DSc, MHM

with only candidate *Maria Angelova Pishmisheva-Peleva, MD, PhD*

I have no common publications or conflict of interest of any other matter with the sole candidate in accordance with the normative documents. The review was prepared in accordance with *Order No. 524/19. 12. 2022* of the Director of the NCIPD for the appointment of a scientific jury for this competition. In addition, it complies with the requirements of the national normative documents regulating the development of the academic staff.

Professional and career development of the candidate

Dr. Maria Pishmisheva-Peleva graduated higher medical education in 1989 at MU Plovdiv and started working as a general practitioner until 1992, when she started working at the Department of Infectious Diseases / Multiprofile Hospital for Active Treatment, Pazardzhik. Consecutively,

she held the positions of resident physician in infectious diseases (until 1999), senior physician (from 1999 to 2013) and head of department (from 2013 to date). From 1997 she is an Infectious Diseases specialist.

She was a volunteer doctor in Turkey after the earthquake in Adapazari, 1999.

In 2019, the candidate defended a dissertation -"Clinical-epidemiological aspects of acute hepatitis E virus infection"- and gained the educational and scientific degree''Doctor" – (Doctor of Philosophy – PhD).

Dr. Pishmisheva-Peleva actively participates in scientific events in the country and abroad. She is the organizer of the national conference of Infectious Diseases / Pazardzhik, 2011. The candidate regularly participates in the annual congresses of the ECCMID with reports and posters - in 2016 she presented 6 posters in this forum; participation in the international conference "Emerging and Returning Infectious Diseases", Sofia, 2009, and in the international conference "Hantavirus Infections", Athens, 2010. At national level, Dr. Pishmisheva-Peleva participates in the congresses and conferences organized by the Bulgarian Society of Infectious Diseases; South Bulgarian Society of Infectious Diseases, Epidemiology and Parasitology, and Bulgarian Association of Microbiology.

From 2022, Dr. Pishmisheva-Peleva is a part-time assistant professor at the Faculty of Biology of Plovdiv University "Paisii Hilendarski", conducting training with third-year students of the "Microbiology and Virology" specialty.

Dr. Pishmisheva-Peleva is a member of the Ethics Committee of Multiprofile Hospital for Active Treatment, Pazardzhik; Committee on Nosocomial Infections, and Committee on the Hospital's antibiotic policy.

Analysis of publication activity and research activity

The general direction of Dr. Pishmisheva-Peleva's publications can be defined as "clinical-epidemiological aspects of infectious diseases that are currently relevant to the country and specifies the modern global epidemic process".

One of the main highlights in her publications is directly related to the problem of Hepatitis E. The title of her dissertation "Clinical-epidemiological aspects of acute hepatitis E virus infection" indicates an interdisciplinary approach, and in this sense, Dr. Pishmisheva-Peleva's doctoral work could be classified as "integration of knowledge from the clinic of infectious diseases in classical epidemiology". The dissertation was successfully defended in the early 2019 with very good assessment from both clinicians and epidemiologists. The literature review gives sufficient information about the causative agent and the historical data on the knowledge of the HEV infection nature from different times and geographical regions. It also includes description of indicative epidemic situations among different population groups in Asia and current data on the understanding of the epidemic risks and source of infection. In view of this, the source of infection can be not only humans, but also some domestic animals, especially domestic and wild pigs. For this purpose, pigs of different age from four farms in the region were studied. To support the zoonotic nature of hepatitis E infection, a number of demonstrative epidemiological examples have been described, specifically – those directly related to pork consumption preferences. The clinic presentations in the risk group of pregnant women and newborns are also described in details. A series of epidemiological studies conducted in the course of the dissertation preparation (2014 – 2017), present the demographic characteristics of the patients of the Department of Infectious Disease of the Multiprofile Hospital for Active Treatment, Pazardzhik in an epidemiological style, as well as the seasonality of HEV-infection manifestations in regional conditions, morbidity, mortality and lethality. The statistical data

processing is at a very high level, and for this purpose appropriate methods and modern programs were used for the indicators calculations. Visualization with tables and charts is also at a high level. The cited references, presented conclusions, summaries, and images are sufficient and correctly given according to the accepted bibliographic requirements. In the dissertation of Dr. Pishmisheva-Peleva, a significant amount of clinical and laboratory information on the HEV-infection is outlined. This corresponds to one of the objectives of this work – to study the clinical and paraclinical characteristics, clinical forms, complications in patients with acute hepatitis E. Another objective was to study the extrahepatic manifestations in patients with acute hepatitis E and the influence of accompanying diseases on the disease course and outcome. The next objective was to clarify the serological profile of patients in different stages and people that were in contact with the infected ones. The information is important not only for clinicians, but also for epidemiologists. Apart from the immediate diagnostic and treatment, today the information from the dissertation appears to be necessary and useful for the structures that practically conduct health control - Regional Health Inspection. HEV-infection might also be obscured when it is combined with some non-infectious diseases, and similar is the co-infections issue. Among the coinfected, coinfection with hepatitis A outstands. Regarding the "Algorithm for diagnosis of acute HEV infection" developed by Dr. Pishmisheva-Peleva, its name indicates that the algorithm is mainly clinically oriented, however, of key importance for surveillance - in perspective, this algorithm has a direct relationship with the epidemiology and registration of the disease, because its implementation will help to elucidate the human reservoir of this relatively poorly understood liver infection; therefore, it also directly relates to the strategic epidemiology of viral hepatitis. Based on the research and experience gained during her doctoral studies, Dr. Maria Pishmisheva-Peleva published a monograph entitled "Hepatitis E - exotic or silent availability". In general, this title highlights the need to clarify the place, role and signficance of the disease in modern human

society and in Bulgaria in particular. I appreciate it as a contribution to our epidemiological science. It can be said that the conclusions and generalizations made during the studies in Pazardzhik region are valid for our country and other geographical regions and have practical significance.

The other areas of research activity of Dr. Maria Pishmisheva-Peleva are related to the epidemiology and clinics of infectious diseases: Mediterranean spotted fever, viral hemorrhagic fevers - Crimean Congo hemorrhagic fever and Hemorrhagic fever with renal syndrome (HFRS), as well as other diseases of public importance: Chickenpox, Legionnaires' disease, West Nile fever. In recent years, during the COVID pandemic, targeted studies have also been conducted on the detection of SARS-CoV-2-specific antibodies and pro-inflammatory cytokines, which explain certain aspects of the course of this infection. For this purpose, a significant number of hospitalized patients with a confirmed diagnosis of COVID-19 were examined.

It is also worth noting the participation in the monograph "Contemporary State of the Rickettsioses in the World and in Bulgaria", 2007. In addition to the clinical aspects of Mediterranean spotted fever in children, there are also data on the spread of this disease in Pazardzhik region and our country. As for the other publications, the article in the Journal "Social Medicine", dedicated to the history of healthcare in Pazardzhik region, is worth noting. Dr. Pishmisheva-Peleva is one of the co-authors of the Encyclopedia of the city of Pazardzhik.

Contributions

The main contributions of Dr. Pishmisheva-Peleva, achieved in her research activities, are related to Hepatitis E virus infection. They are related to different extend to the individual elements/units of the epidemic process and can be classified as follows:

- For the first time in our country, the prevalence of HEV-infection among healthy individuals was studied (in the general population from Pazardzhik region, in closed groups and people who were in contact with patients with acute HEV- infection).
- The study of the spread of HEV infection among inmates in a men's prison in the city of Pazardzhik - is a pioneering one.
- For the first time data on the HEV infection prevalence in pigs of different age groups and from several different pig farms are presented.
- Specific anti HEV IgM was detected for a long time (24 months) after acute hepatitis E.
- For the first time, a comparative analysis of the course of acute hepatitis E among different groups of patients is presented (according to the accompanying diseases - Diabetes mellitus, Liver diseases, Alcohol abuse).
- An algorithm for the diagnosis of acute viral hepatitis E is presented.

Of the studies on the other thematic areas, the following contributions of epidemiological importance can be emphasized:

- For the first time in Bulgaria, *RNA* of *Puumala hantavirus* was isolated from a patient with HFRS treated in the Department of Infectious Diseases, Pazardzhik. The contribution is related to the first unit of the epidemic process - the source of infection.

- The viral load, the dynamics of specific antibodies and the levels of the main cytokines were studied depending on the clinical severity of COVID 19. The contribution is also related to the first unit of the epidemic process - the source of infection, and to some extent to the second unit - the transmission mechanism of the infection.

- Anti-vaccine sentiment and facts are examined considering the post-2020 mass vaccination campaign aimed at limiting the spread of COVID 19 through high immunization coverage. The

contribution is related to the third unit of the epidemic process - the susceptibility of the population.

The problem "History of Healthcare in Pazardzhik region" was developed. The contribution is related to the use of the historical method for tracking the development of public healthcare in one region in the country. One of the elements of public health is anti-epidemic activity, which is described chronologically; therefore, this contribution is also important for the history of Bulgarian epidemiological science.

The remaining contributions in the scientific developments of Dr. Maria Pishmisheva-Peleva concern entirely the diagnosis, clinic, and therapy of infectious diseases. For these reasons, I do not take them into account in the analysis of the current competition for awarding the academic position of associate professor of epidemiology and accordingly do not evaluate them.

Teaching activity

Teaching activity at a university: Dr. Maria Pishmisheva-Peleva teaches third-year students from the "Microbiology and Virology" specialty at the Faculty of Biology of Plovdiv University "Paisii Hilendarski". From 2022 Dr Pishmisheva-Peleva delivers lectures and training as a part-time assistant and participates in the term examination.

Mentoring of specialist doctors at Multiprofile Hospital for Active Treatment, Pazardzhik: for the last 5 years, Dr. Maria Pishmisheva-Peleva supervised the postgraduate training of three residents in infectious diseases. Two of them have successfully graduated, the third is to finish residency.

Awards and prizes

In 2016, Dr. Pishmisheva-Peleva was awarded by the Bulgarian Medical Association with the "Doctor of the Year" prize, also in 2020, when she was nominated in the category "Fighting the

Covid-19 pandemic" - "Contribution to the development and strengthening of the authority of the medical organization" (Bulgarian doctors, gave their contribution to the fight against Covid-19).

In 2020, she was awarded with the Presidential Badge of Honour by the President of the Republic of Bulgaria.

The same year, Dr. Maria Pishmisheva-Peleva was awarded a Diploma for Special Merits of Public Significance by the Pazardzhik Municipality.

Conclusion

The materials submitted by Dr. Maria Pishmisheva-Peleva for the competition reflect research and teaching activities that correspond to the academic position of "Associate professor" in the scientific field and professional direction of the competition and the criteria of the law and the rules of the NCIPD. Her achievements have a contributing character, that expand and elaborate scientific and theoretical knowledge in the field of Epidemiology of Infectious Diseases.

Based on the above, I firmly believe that she is fully worthy to occupy the academic position "Associate professor" in the scientific specialty of Epidemiology, for which the competition has been announced.

April 03, 2023

Prepared the review: Kantardjiev

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