

## **Review**

**By Associate Professor Dimitar Ivanov Vutchev, MD, PhD,**

**Department of Parasitology and Tropical Medicine, Medical University – Plovdiv**

on the dissertation work for the Doctor of Science Doctor of Philosophy) (in Scientific and Technological Sciences

on the topic: "**Characteristics of imports and assessment of the possibility of malaria recovery in Bulgaria in the face of global climate change**"

Author: Dr. Iskren Tzvetkov Kaftandjiev,

Doctoral student: self-study at NCIPD-Sofia

Field of higher education: **4. Sciences, mathematics and informatics, professional field 4.3. Biological Sciences**

Specialty: Parasitology and helminthology

Scientific adviser: Assoc. Prof. Rumen Harizanov, MD, PhD, NCIPD-Sofia

### **1. General presentation** of the procedure and the PhD student

- dissertation
- abstract
- list of the publications on the topic
- list of participations on scientific forums
- declaration of originality and authenticity of the attached documents
- IF /of 2 publications on the topic/ - 2.522

### **2. Short biography** of the PhD student /in connection with the procedure/

Dr. Iskren Tzvetkov Kaftandjiev was born on 14.06.1962 in Sofia. After completing his medical education at the Medical Academy - Sofia in 1990, he initially worked as an intern at the Children's ward of the Municipal Hospital in Srednogorie until 1991. From 1991 to 1993 he was a resident at the National Center for Diabetic Children at the Scientific Institute of Pediatrics at the Medical Academy - Sofia and from 2007 until now he has been a resident at the Parasitology and Tropical Medicine Department at the National Center for Infectious and Parasitic Diseases (NCSPB) - Sofia. In 2012 he acquired the medical specialty Medical Parasitology. He speaks fluently English language both written and spoken.

### **3. Relevance of the topic developed in the dissertation**

Following the irradiation of the local malaria in Bulgaria (1965, WHO), the import of this parasitic disease with Bulgarian and foreign nationals coming from endemic countries continues with varying intensity. In the peer-reviewed dissertation, the relevance of the studied clinical and epidemiological data on malaria imported in the 2000-2015 interval, as

well as the possibility of recurrence of actual local endemicity, against the background of global warming, is indisputable and objective. The introduction and overview of the work contains numerous data on the prevalence and prevalence of malaria in the world, mainly in tropical countries, incl. about the existing specific vulnerability and susceptibility of countries in southern Europe as well as Bulgaria. In this regard, a new risk factor is the emigration flows from the Middle and Middle East and from Sub-Saharan Africa passing through the country. The work undoubtedly concerns and touches upon a particularly important medico-social problem facing national healthcare in the field of medical parasitology. The topic, defined and accepted for scientific research, according to the purpose and tasks, is based on a long-term study of the main epidemiological characteristics and their dynamics (16-year period), essential clinical data, incl. complications, lethality, chemo prophylaxis, and mathematically valid prognostic studies. It is theoretically established in certain areas of the country to significantly reduce the time for malaria parasites sporadic and accordingly to accelerate and increase the speed of malaria transmission, respectively. raising the level of epidemiological risk. Logically, the end of the studies is followed by concluding synthetic conclusions, which are clearly formulated, are theoretically practical and with a certain prognostic purpose, respectively. promotional value.

The Defined Purpose of the Thesis / “Determining the Clinical and Epidemiological Consequences of Imports under Climate Change and the Possibility of Recovering Actual Malarial Endemicity” / Includes an up-to-date study structured by problem-related two main sections related to vulnerability and susceptibility to malaria in regional contemporary climates. The aim is subordinated to six specific tasks that correspond to the mentioned sections and end with an exemplary working template of the "Map for epidemiological study of malaria and malaria outbreaks" to be used by parasitologists in the country.

#### **4. Knowledge of the problem**

Degree of knowledge of the status of the problem and of the literary material.

The PhD student is familiar with basic modern and classic specialized literature on the epidemiology and malaria clinic in the world, as well as in our country. The researched and used scientific sources testify to the clarity of the specific theoretical and applied problems defined for development and solving.

The other authors cited for the literature review and the main text in the sections of the dissertation are listed in the Literature Section. Cyrillic has been published in 71 titles of scientific publications - separate publications and monographs by Bulgarian and Russian authors, and the remaining 144 - in Latin, mainly by foreign researchers. A total of 215 titles were cited, among them by authors with outstanding international authority and by WHO working groups.

#### **5. Research methodology**

The research methods are adequate to the main purpose and make possible the consistent and systematic solution of the formulated operational tasks in the dissertation. Extensive medical documentation from HEI, RIOCOS and RHC, LZ, OPTM - NCIPD was examined for 175 persons (2000-2016), and a card was used to study patients with malaria - clinical and epidemiological data.

The National Institute of Meteorology and Hydrology has borrowed data on average monthly temperatures of the districts in the country (1916-1975, according to P. Petrov and 2000-2016, BAS) within a 100-year interval. Unique for the country is the application of a specific mathematical formula / adapted, according to Sh. Moshkovsky / for the time of the sporogony of *Plasmodium vivax*, *P. falciparum* and *P. malariae* at different temperature parameters. The forecast data for the expected temperature elevations for the earth's surface were borrowed from the International Commission on Climate Change / 2013 /.

The dissertation (204 pp.) Is illustrated in detail. The quantitative data and other graphical indicators are documented and reflected in 43 tables, 86 chart figures and 1 appendix (malaria and malaria outbreak surveillance map). The essential components are processed by modern medical-statistical methods, using specialized computer programs.

## **6. Characterization and evaluation of dissertation work**

Generally speaking, the two sections of the dissertation are characterized by the main clinical and epidemiological features of malaria introduced in the country in 2000-2015 and theoretical studies have been made on the possibilities of reintroduction of epidemic spread of malaria in the country, with the available climate changes. in the past years.

First Section (Malaria Vulnerability): Malaria imported cases - 175 individuals, were tracked by year and habitat (total 19), with major administrative and economic centers such as Sofia, Plovdiv, Varna and Burgas.

Patients with all anthropogenic types of malaria were reported, with significant mortality (4.32%) of tropical malaria. Among the patients, about 2/3 of them are Bulgarian citizens (sailors, aviation technicians, pilots, tourists, merchants, etc.) and the remaining cases are mainly migrants from Asia and Africa. The most active working age population is between 20-50 years old.

The author draws attention to the geographical factor of origin of the disease. Sub-Saharan Africa is 80% of the cases, with predominant cases of Malaria tropica (Nigeria, Equatorial Guinea, Angola, etc.). Asia accounts for 19% of cases, with *M. tertiana* predominant (from Afghanistan, Pakistan and India). Anofeline mosquito species on our continent are known to be vectors adapted to the Asian strains of *Plasmodium vivax*, more commonly imported from countries in Asia.

Particular attention is also paid to the possible delayed (incorrect or missing) diagnosis of *M. tropica*, which threatens with severe clinical complications (cerebral coma, acute renal failure, pulmonary edema, etc.) - to death. With the same diagnostic gaps for *M. tertiana* in the country's potential epidemic period (April - October), it carries the maximum risk of a local malaria outbreak (example - in the Sandanski region, 1995/6).

The author draws on misdiagnosis of malaria, ignoring the epidemic risks of all visits to endemic tropical countries by our citizens, as well as the failure to perform specific chemoprophylaxis. A similar, long-term and large-scale study on imported malaria has not been conducted in the last 40 years and is an extremely important and necessary information for public health and parasitologists in the country.

Section Two (Malaria susceptibility): The original studies on temperature changes and their impact on malaria transmission in current climate change are original. It finds that in the

period 2000 - 2015 the average monthly temperatures in Bulgaria increased on average by more than 0.5 ° C compared to the period 1916-1975, a total of 19 regions, most pronounced in Blagoevgrad (1 ° C), Plovdiv (2 ), Smolyan (2.5 ° C).

Under these conditions, it is projected to reduce the sporogony period of all malaria parasites, respectively. accelerating and increasing the number of revolutions of the parasitosis. This shows that the country's receptivity has increased. which in the event of a resumption of local transmission and an epidemic outbreak would result in more intensive transmission and impact on more populations.

Changes in average temperatures do not yet appear to be so significant, but the author cites prognostic scenarios from the International Commission on Climate Change, which are not soothing but worrying enough for the foreseeable future.

For the purpose of forecasting, a mapping territorial analysis of the registered cases of malaria imported / Poisson method / was made, as well as a higher risk of new cases occurring in some specific regions of the country.

Applying methods of quantitative epidemiology, the author tried to make a mathematical model of malaria transmission. He has applied, for example, two methods for digital simulation. According to Ross-McDonald's model, he used a certain multicomponent mathematical formula, and Sh. Moshkovsky's model is based on a known loymopotential. These mathematical models are intended to reflect the dynamics of the epidemic process and are of particular situational and prognostic significance.

At the end of the discussion it is undoubtedly emphasized that in addition to the above mentioned parameters in malarial transmission, temperature elevations in global climate warming extend the calendar and the potential malaria season for the country - an important epidemiological factor for malaria such as vector-transmissible, transmissible, transmissible.

At the end of the comprehensive study, the author Dr. I. Kftandjiev gives his conclusions in a synthetic way to maintain a strict monitoring of vulnerability, as well as respect for the considerable level of susceptibility by the medical organization as a result of global climate change and some social processes. In order to limit the effects of imports and prevent malaria return, a high level of malaria surveillance should be systematically maintained.

## **7. Contributions and importance of the work to science and practice**

The contributions are grouped appropriately into two sections, summarized respectively:

### **I. Original theoretical contributions.**

Particularly interesting and original are the doctoral student's achievements, such as: developing a territorial epidemic model on the level of risk of malaria outbreaks by districts across the country; subject to a reported rise in average daytime temperatures during the malarial season / April-October / followed by a shortening of the sporadic period and an increase in the malaria transmission rate; application of a computational module for predictive prediction of the number of malaria affected in the event of possible reintroduction of malaria in our country.

## II. Scientific and applied contributions

A study of the dynamics of imported malaria and its major epidemiological characteristics also outlined the regional nosoareas most frequently exposed (Sofia, Plovdiv, Blagoevgrad, Ruse, Burgas, Varna, etc.). The clinical implications and complications, as well as the causes of their occurrence, were also examined. The main "importers" of malaria in our country - occupational groups and geographical origin - have been identified. The main risk contingents are migrant groups from Asia, frequent carriers of *M. tertian*, as well as from Sub-Saharan Africa (often Bulgarians) - *M. tropica*. The results of the clinical and epidemiological analysis of imported malaria are the basis for drawing up the cited specific map for epidemiological study and activation of specific promotional measures for the control and surveillance of imported malaria, incl. systematic information on the prevention of Bulgarian citizens leaving for endemic countries, respectively. at regional and national level.

The dissertation concludes with eight specific conclusions concerning the author's scientific and practical results, which are reflected in the dissertation text and are synthetically presented in the contribution section.

### **8. Dissertation publications**

In the section Publications and reports in scientific forums on dissertation work. Five scientific publications were published, two of them - in foreign magazines with a total IF of 2,522 and three publications in Bulgarian journals. In addition, five participations in scientific forums are listed, one of them abroad, with abstracts of the reports presented.

### **9. Doctoral student's personal participation**

The studies reflected in the dissertation, with formulated results and contributions, adequately meet the set goals and objectives. They are done and processed formally and statistically, and the results achieved are from the personal participation of the doctoral student.

### **10. Abstract**

It has been carefully prepared and constructed according to the content of the dissertation, contains representative data from the sections of the research studies, is sufficiently illustrated. Essentially - it provides synthetically the content of the presented work, with the conclusions, contributions and additional information required.

**11. Critical notes and recommendations.** The dissertation work is planned, carefully prepared, successfully completed and I have no significant comments. I recommend that the author use the thesis database to publish a monograph on the problem.

### **12. Personal impressions**

In his dissertation, the author has used and developed comprehensive information material from the Rapid Reports, Epidemiological Surveys and Epicrises for cases diagnosed throughout the country with malaria in 2000-2016 (all, without exception, are registered with OPTM). The reported results, reflected synthetically in the conclusions drawn, are of complete theoretical and practical relevance. The development is purposeful and precisely implemented. The results are important for the anti-epidemic, clinical and preventive practice (respectively in RI and LZ). The applied mathematical methods in parasitology are impressive, as well as targeted prognostic studies towards such an important branch of

medical parasitology / malariology /. The work presented for review leaves the impression of a thorough, at the same time complex and integrated approach to research and research and shows the creative potential for successful future work of the doctoral student in OPTM - NCIPD, the only highly specialized complex structure of medical parasitology in the country.

### **13. Recommendations for future use of dissertation contributions and results**

The formulated conclusions from the developed work are objective, substantiated and necessary grounds for directing the attention of management bodies to maintain strict epidemiological control and surveillance of imported malaria, taking into account the different level of climatic and social risk factors in certain regional regions of the country.

### **CONCLUSION**

The dissertation contains scientific, scientifically applied and practical results, which represent a significant actual contribution to parasitological science and practice in our country and meet all the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB) and the Regulations for its application, as well as and the requirements of NCIPD-MH. The data and the results of the study presented in the dissertation are in full compliance with the specific provisions of the law.

The dissertation shows that Dr. Iskren Tzv. Kaftandjiev has extensive theoretical and practical knowledge and professional qualifications, with outstanding research achievements.

Because of the above, I am convinced of my positive assessment of the research, reflected in the peer-reviewed dissertation, the results achieved and the contributions, with the proposal to award the candidate's scientific and educational degree "Doctor" to Dr. Iskren Tzvetkov Kaftandjiev.

12/26/2019

Reviewer:



Assoc. Prof. Dr. Dimitar Vuchev, MD, Medical University - Plovdiv

Head. Section Parasitology and Tropical Medicine