

STRUCTURE AND DYNAMICS OF IMPORTED PARASITIC DISEASES IN BULGARIA (2014-2020): CHALLENGES AND RISKS FOR THE PUBLIC HEALTH SYSTEM

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ABSTRACT

The aim of this study is to analyze data on the structure and dynamics of imported parasitic diseases and the potential risk of local spread of already eradicated diseases, and of those that do not have local spread so far, but there are environmental conditions for their occurrence.

Material and Methods. This is a retrospective cross-sectional analysis of imported parasitic diseases in the country for a seven-year period. We used data from the annual analyzes of parasitic morbidity developed by the NCIPD, data from the diagnostic and reference activity of the National Reference Laboratory for Diagnosis of Parasitic Diseases, and data from the annual reports of the Regional Health Inspectorates.

Results. During the period 2014-2020, 22 862 persons were studied, of whom 896 (3.9%) were Bulgarian citizens and 21 966 (96.1%) were foreigners. Imported parasite diseases were found in 794 people (prevalence 3.47%). Different types of parasites causing pathology of

the gastrointestinal tract accounted for 87.53% (n = 695) of the identified pathogens, while the relative share of vector-borne parasitic diseases was 12.47% (malaria 11.09%, visceral and cutaneous leishmaniasis 1.38%).

Conclusion. There are favorable climate and fauna conditions in the country for the local spread of a number of parasitic diseases. Control measures with respect to this pathology are associated with timely detection and remediation of the source of infection. In the country, there is an algorithm for diagnosis, hospitalization, treatment, prevention and control of imported parasitic diseases, but it is difficult to be applied to migrants entering in the country illegally. The deficiencies in the surveillance and control of imported parasitic diseases pose a real danger for a local spread of already eradicated parasitic diseases, such as malaria, and from outbreaks of diseases that do not have local spread till the present moment.

Keywords: *imported parasitic diseases; potential risk; local distribution; prevention; control*

INTRODUCTION

Migration is an intrinsic phenomenon of the dynamics of human population driven by socio-economic, political and environmental factors (1). Each year, millions of people travel abroad exposing themselves to the risk of various diseases. The circulation of microorganisms, vectors, infected humans and animals in different parts of the globe poses a global threat to public health and requires attention at national and international level (2). The import of parasitic diseases in non-endemic countries around the world is increasing due to the growing number of travellers. Increased migration flows to Europe in recent years raise concerns about the effectiveness of surveillance and control of imported pathology and the potential health risk to the local population (1). Migrants' health is receiving increasing attention in Europe and is a priority for ECDC (3). Current flow of migrants to Europe follows two main routes: from Africa to

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Italy and from the Middle East to Greece, which increases the apprehensions that the usual epidemiological pattern of infectious diseases observed in Europe, may change (1). Although the main migration flow is directed to Great Britain, Germany, Spain, France and Italy, such also exists to other EU member states, including Bulgaria. Parasitic diseases are not vaccine preventable ones and the issue for their import is significant as the major measure for their control is timely diagnosis and treatment.

MATERIAL AND METHODS

Data collection system

In Bulgaria, the system for surveillance and control of imported parasitic diseases is regulated by Ordinance № 17 of July 30th, 2008 issued by the Ministry of Health (MoH) and defining the terms and conditions for diagnosis, prevention and control of imported parasitic diseases. It is based on three levels. At a regional level, it is carried out by the Regional Health Inspectorates (RHI), which perform research according to epidemic, prophylactic and clinical indications and further epidemiological studies of cases that are subject to registration and notification. The Department of Parasitology and Tropical Medicine (DPTM) at the National Center for Infectious and Parasitic Diseases (NCIPD) is the reference diagnostic and consultative structure for Bulgaria in the field of parasitic diseases, both, indigenous and imported. It performs routine and confirmatory diagnosis of parasitic diseases, and clinical activities with patients in outpatient settings. The DPTM staff prepares annual analyzes of parasitic morbidity, on the basis of which MoH plans measures for surveillance and control

of the parasitic diseases. There are also four parasitological offices in the country, where travellers going to tropical countries, can get advice on disease prevention and prophylaxis.

Study design

The study covers a seven-year period (2014-2020) and represents a retrospective analysis of parasitic diseases imported into the country. Data from the annual analyzes of parasitic morbidity prepared by the NCIPD, and from RHI annual reports on the local and imported parasitic diseases registered in the country, were used. The primary data were analyzed in the following directions: etiological characteristics of the imported diseases in the country and analysis of the possibility for autochthonous transmission of some of them in Bulgaria.

Methods

Parasitological methods of examination were applied for diagnosis: morphological (staining, culture, concentration techniques), serological (ELISA, Western blot), and immunochromatographic methods.

Epidemiological analysis

The epidemiological analysis included determination of certain parameters, such as prevalence, relative share, mortality and analysis of the risk of local spread of some of the parasitic species imported into the country.

RESULTS

During the period 2014-2020 a total of 22668 persons were examined for imported parasitic diseases in Bulgaria, and data on their number, distribution by year and nationality along with data for the positive cases are presented in Table 1.

Table 1. *Data of examined for imported parasitic diseases persons by year.*

Year	Total No of examined persons	Total No of infected	Prevalence (%)	No of examined Bulgarian citizens	No of infected	Prevalence (%)	No of examined Foreign citizens	No of infected	Prevalence (%)
2014	4209	121	2.87	162	11	6.79	4047	110	2.72
2015	3982	131	3.26	194	0	0	3982	131	3.3
2016	5235	251	4.79	76	9	11.84	5159	242	4.69

Year	Total No of examined persons	Total No of infected	Prevalence (%)	No of examined Bulgarian citizens	No of infected	Prevalence (%)	No of examined Foreign citizens	No of infected	Prevalence (%)
2017	1908	51	3.67	105	4	3.81	1803	47	2.61
2018	3173	53	1.2	227	8	1.76	2946	45	1.15
2019	1890	101	5.4	96	4	4.17	1794	98	5.46
2020	2271	85	3.74	36	4	11.11	2235	81	3.62
Total	22862	794	3.47	896	40	4.46	21966	754	3.43
Mean	3238	113.3	3.56	128.0	5	5.64	3138	106	3.36
Std. Deviation	1292	68.07	1.36	68.35	3.67	4.51	1295	69	1.42
Mean of prevalence in Bulgarian citizens vs. Mean of prevalence in Foreign citizens Mann Whitney test P value = 0,3829 Bulgarian citizens vs. Foreign citizens Odds ratio = 1.3									

The most commonly imported parasitic diseases in the country are malaria and intestinal parasitic infections.

Malaria

For the studied period a total of 87 cases of imported malaria, of which 41 (47%) in Bulgarian citizens and 46 (53%) in foreign citizens were recorded in the country. . According to the type of the causative agent tropical malaria and vivax malaria were with the highest relative share. Cases of imported malaria caused by other members of *Plasmodium spp.* were registered relatively rarely (Table 2).

Table 2. Cases of imported malaria by year and species of causative agent.

Year	Species			
	<i>P. falciparum</i>	<i>P. vivax</i>	<i>P. malariae</i>	<i>P. ovale</i>
2014	9	1	0	0
2015	14	5	1	0
2016	10	17	1	0
2017	6	1	1	0
2018	4	3	0	1
2019	3	5	0	0
2020	5	0	0	0
Total	51	32	3	1
Percent (%)	59	37	3	1

The distribution of persons with imported malaria by sex, age groups and nationality is presented in Table 3.

Table 3. Cases of imported malaria by age group, gender and nationality of infected people.

Age group	Gender		Bulgarian citizens	Foreign citizens
	Male	Female		
0	0	0	0	0
01-05	0	0	0	0
05-09	0	0	0	0
10-14	2	0	0	2

Year	Species			
	<i>P. falciparum</i>	<i>P. vivax</i>	<i>P. malariae</i>	<i>P. ovale</i>
20-24	14	1	3	12
25-29	7	1	4	4
30-34	10	2	8	4
35-39	9	1	4	6
40-44	2		2	
45-49	5	2	4	3
50-54	7	0	7	0
55-59	3	0	3	0
60-64	5	0	5	0
65+	1	0	1	0
Total	80	7	41	46
Percent (%)	92	8	47	53

During the study period, two of the cases of imported malaria were fatal (in 2014 and 2016). The deceased were Bulgarian citizens, in one case a person working in Africa, while in the other, the disease occurred after blood transfusion with a blood product from a foreign donor, who has been an asymptomatic parasite carrier.

Leishmaniasis

From this group of protozoan diseases a total of 11 imported cases were registered for the period, three of which were visceral leishmaniasis among Bulgarian citizens living and working in European countries endemic for the disease (Greece, Spain, and Portugal), and the other eight cases were of cutaneous leishmaniasis imported by foreigners who arrived in the country from the Middle East (Syria and Afghanistan).

Intestinal parasitic infections

For the seven years studied, 695 imported intestinal parasitic infections caused by 11 parasitic species were registered in the country (Table 4).

Table 3. Cases of imported intestinal parasitic infections.

Causative agent / No of cases	Year							Total (%)
	2014	2015	2016	2017	2018	2019	2020	
<i>Blastocystis spp.</i>	56	28	51	19	8	30	23	215 (30.9%)
<i>Giardia intestinalis</i>	29	57	83	17	11	20	22	239 (34.4%)
<i>Entamoeba coli</i>	7	0	2	0	0	22	7	38 (5.5%)
<i>Enterobius vermicularis</i>	5	1	6	2	7	1	4	26 (3.7%)
<i>Hymenolepis nana</i>	4	2	17	2	9	8	7	49 (7.2%)
<i>Ascaris lumbricoides</i>	6	19	55	1	2	6	10	99 (14.1%)
<i>Trichuris trichiura</i>	1	2	3	1	1	4	4	16 (2.3%)
<i>Taeniarhynchus saginatus</i>	0	0	1	1	2	0	0	4 (0.6%)
<i>Iodamoeba butschlii</i>	0	0	2	0	0	0	2	4 (0.6%)
<i>Ancilostoma duodenale</i>	0	0	0	0	0	2	1	3 (0.4%)
<i>Dicrocoelium lanceatum</i>	0	0	0	0	2	0	0	2 (0.3%)

Discussion

The issue of imported parasitic diseases is becoming increasingly important for Bulgaria, especially in recent years in connection with the large number of migrants who arrive in the country. According to

the Bulgarian Refugee Agency, more than 62000 people were registered for the study period, mostly from sub-Saharan Africa, Syria, Algeria, Afghanistan, Iraq, Iran, Pakistan and stateless persons (4). They are initially accommodated in reception centers located on the territory of the districts of Haskovo, Stara Zagora and Sofia. Measures for surveillance and control of introduced parasitic pathology are carried out in an organized manner by RHI and are regulated by law. These measures have been in place since the 1960s, when Bulgaria was recognized by WHO as a country free of malaria (5).

Tropical parasitic infections imported into the country by foreign and Bulgarian citizens arriving from endemic regions can be divided into four groups:

Parasitic diseases with local transmission, such as some soil-transmitted helminth infections (ascariasis, trichocephaliasis) and community-acquired diseases as enterobiasis, hymenolepiasis, giardiasis, blastocystosis. In the country, sporadic cases of amoebic cysts carriers have been described, as well as an amebic liver abscess in a traveler returning from India, some anthroponoses, such as taeniarhinos, zooanthroponoses, such as visceral leishmaniasis and dicrocoeliasis. This group includes over 93% of the imported parasitic pathogens, registered among Bulgarian and foreign citizens arriving in the country from endemic areas during the period studied by us. The presence of large groups of people with such parasitic diseases in potentially endemic regions of the country can lead to the formation of new foci of parasitic transmission, and/or increasing intensity of the existing ones.

Parasitic diseases that are not autochthonous in Bulgaria, but studies have shown that the existing climate conditions and the established presence of appropriate intermediate hosts and vectors may allow local transmission. This group includes hookworms, lymphatic filariasis, loiasis, paragonimosis. Experimental studies conducted in the country (6) showed that the local populations of *Culex pipiens molestus* were successfully infected

with microfilariae of *Wuchereria bancrofti* and on average in 12-13 days at a temperature of 25-27°C reached invasive stages. The results indicate the possibility of local transmission of *W. bancrofti*. Experimental data displayed that in the fields of the upper Thracian lowland the hydrothermal conditions on the surface and in depth of the soil create suitable conditions for the development of eggs and larvae of *Ancylostoma duodenale* and *Necator americanus* to an invasive stage during 6 months of the year (April to October) (7). For the seven-year study period, no imports of lymphatic filariasis were recorded in the country, although rare cases of hookworm disease were found ($n = 3$, 0.4%). Given the fact that most reception centers for refugees and migrants are located in potentially endemic areas of the country, there is a real chance for local outbreaks in case of a control gaps. This group also includes amoebiasis, which is not registered annually as a local disease but has been diagnosed in cysts carriers (8).

Parasitic diseases that have been indigenous in the country in the past, but through epidemic control measures and surveillance have been irradiated. Such diseases are malaria, amoebiasis and strongyloidiasis. Malaria is especially relevant from the epidemiological and clinical aspect. By 1965, the disease had spread over 2/3 of the country, and endemicity was recorded for three species of plasmodia, *P. vivax*, *P. falciparum* and *P. malariae* as the most prevalent was *P. vivax*. In some settlements, hyperendemicity or holoendemicity have been registered in the past. There is a malariogenic potential in the country, which includes a susceptible non-immune human population, ubiquitous anophelism (*Anopheles maculipennis*, *An. Superpictus*, *An. Sacharovi*) and suitable climate conditions from the beginning of April to the end of October on 2/3 of the country (9). Studies have shown that the season for possible malaria transmission is longest in the districts of Burgas, Varna, Plovdiv, Blagoevgrad, Vidin, Ruse, Silistra and Haskovo, and the shortest is in the district of Smolyan (6). The registered imported cases of malaria

from 1996 to 2013 are 267 (10), and for the period studied by us are 87, as the distribution by sex shows predominant involvement of males (92%) and the age group over 19 years. (80%). The cases of imported malaria according to the nationality of the patients are distributed almost evenly (Table 3), but it is noteworthy that 37% of the cases of foreign citizens are in children and adolescents, while among Bulgarian citizens there are no registered cases in this age group. This could be explained by the profile of travellers. While Bulgarian citizens travel the endemic areas mostly for business and work, most of the foreign citizens were refugees and/or economic migrants arriving in the country with their families.

The majority of the cases was recorded during the summer months when they may become an effective source for infection of the mosquitoes. An alarming fact is that 37% of the cases included in our study, were cases of tertiary malaria (for which the vectors in the country are more susceptible), and in over 90% of them they were registered among persons who have entered the country illegally. In this regard, the emphasis should be placed on the fact that an outbreak of 18 cases of local from imported malaria caused by *P. vivax* was recorded in the Sandanski region in 1995 (11, 12) The source of the disease was a group of illegal immigrants from Asia (Afghanistan and Pakistan) who spent several days in the Struma River valley. The disease was registered on the territory of three municipalities: Sandanski municipality (Sandanski and Valkovo), Strumyani municipality (Drakata village, Mikrevo village, Strumyani village) and Petrich municipality (Petrich town and Novo Delchevo village). The outbreak was registered in the months of August to September. Efforts were then focused on rapid diagnosing and treatment of the patients. For this purpose, all persons with a febrile condition from the region were examined, as a result of which 18 cases were diagnosed, and in the following year another 5 cases of relapse were found (11, 12).

Parasitic diseases, that are imported, but the country lacks climate and fauna conditions for local transmission. Such are the zoonotic cutaneous leishmaniasis, which is imported most often from Syria, Sudan and Afghanistan, the schistosomiasis and some types of (subcutaneous) filariasis. This is not the case for the anthroponotic variant of cutaneous leishmaniasis, in which three epidemiological prerequisites are required for local spread: presence of a source (sick person), presence of a specific vector (phlebotomies of the species *Ph. Papatasi* and *Ph. Sergenti*) and susceptible population. The second and third factors of the epidemiological chain are present in the country and in the presence of a source, serious preconditions will be present for the occurrence of local cases of the disease (13). Therefore, the medical professionals must be familiar with the symptoms of tropical diseases to be able to refer the patient to specialized settings for timely diagnosis and treatment.

Challenges for the public health system

The country has favorable climate and fauna conditions for local spread of a number of parasitic diseases. Control measures are related to the timely detection and remediation of the source. While such control is feasible for traveling foreigners and legal immigrants, it is practically impossible for illegal migrants who arrive in the country in order to reach other European countries. These are mainly people arriving from regions endemic for a number of parasitic diseases in sub-Saharan Africa and the Middle East. An example of this is the outbreak of local malaria with a source of illegal immigrants from Afghanistan and Pakistan in Bulgaria in 1995. Similar cases are registered almost annually in Greece, where the main source for local transmission of vivax malaria are illegal immigrants.

Allowing local spread of vector-borne diseases would lead to serious economic losses in view of the need to take eradication measures, such as mass screening of the population in

affected areas, large-scale insecticide treatment, measures against animal reservoir hosts. Losses can also be expected in the field of tourism. In this regard, there are issues concerning border control, access to medical care for immigrants and the ability of the health system to deal with unfamiliar to the country pathology. There is also an issue with the supply with effective antiparasitic drugs in Bulgaria. This problem also exists in a number of other European countries, because many of them lack specific medicines, as they are not officially licensed and are not available in pharmacies. Few health centers can afford access to medicines for neglected tropical diseases due to complex bureaucracy and high costs associated with importing or providing them through the WHO (14).

Providing knowledge about the recommended prophylactic measures is of particular importance to people who plan to visit tropical countries. Unfortunately, many travellers to endemic areas do not have the opportunity to consult themselves on the preventive measures before departure. As a result, some of them become infected during their stay, and some may develop life-threatening conditions, especially in cases of tropical malaria, which could be fatal. Indicative of this is the fact that for the period studied by us, two deaths from tropical malaria were registered (mortality 2.3). Another factor confirming the above is the value of the odds ratio, which shows that the risk of disease for Bulgarians returning from endemic areas is 1.3 times higher than that for foreigners arriving in the country.

CONCLUSIONS

Today, one of the most important assignments for the country's healthcare is the maintenance of the achieved success in interrupting local transmission of malaria, regardless of its import from endemic territories.

The training of medical specialists in parasitology in postgraduate education should guarantee competencies in the analysis of parasitic

morbidity, the diagnosis of urgent and life-threatening conditions caused by parasites and in the complex anti-epidemic measures in the outbreaks of parasitic diseases.

There is an algorithm for prevention, diagnosis, hospitalization, treatment and control of imported parasitic diseases in the country, but it cannot be applied to illegal immigrants. Many of the imported helminthiasis can increase the intensity of existing indigenous outbreaks. There is a real danger of the spread of already eradicated diseases, such as malaria, and the emergence of outbreaks of diseases that never before had local transmission.

Failures in the surveillance and control of tropical parasitic diseases can lead to severe economic and social losses.

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