

IMPORTOVANA MALARIJA NA PODRUČJU BEOGRADA U PERIODU OD 2014. DO 2018. GODINE

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SAŽETAK

Uvod/Cilj: U bivšoj Jugoslaviji eradikacija malarije zvanično je potvrđena od strane Svetske zdravstvene organizacije 1974. godine. Od tada u Srbiji se registruju samo importovani slučajevi malarije. Cilj ovog rada je da se analiziraju epidemiološke karakteristike importovane malarije na području Beograda u periodu od 2014. do 2018. godine.

Metode: Primenjena je deskriptivna epidemiološka studija. Podaci o broju novoobolelih od importovane malarije po polu, uzrastu i regionu odakle je malarija importovana, za navedeni period, preuzeti su iz Gradskog zavoda za javno zdravlje Beograd. U analizi podataka korišćene su proporcije, sirove i uzrasnospecifične stope incidencije.

Rezultati: U periodu 2014-2018. godine, na području Beograda registrovano je 77 novoobolelih od importovane malarije, a prosečna sirova stopa incidencije iznosila je 0,9 na 100.000 stanovnika. Najveći broj obolelih (28) i najveća sirova stopa incidencije (1,7/100.000) importovane malarije zabeleženi su u 2017. godini, a najmanji broj obolelih (7) i najmanja sirova stopa incidencije (4,0/100.000) u 2014. i 2018. godini. Muškarci (89,6%) su češće oboljevali od importovane malarije nego žene (10,4%). Najveća uzrasno specifična stopa incidencije importovane malarije registrovana je u uzrasnoj grupi od 10 do 19 godina (3,5/100.000). *P. vivax* (45,4%) i *P. falciparum* (37,7%) su bili najčešći uzročnici importovane malarije u Beogradu. Oko 88% importovanih slučajeva malarije činile su osobe koje su boravile u endemskim područjima Azije i Afrike. Najveći broj obolelih od importovane malarije navodi migraciju (44,2%) i odlazak zbog posla (39,0%) kao razloge putovanja u endemska područja. Oboljenje se registruje tokom čitave godine, sa pikom oboljevanja u mesecu avgustu (19,5%).

Zaključak: Neophodno je kontinuirano zdravstveno vaspitanje stanovništva, u cilju edukacije stanovništva o načinu prenošenja malarije i neophodnosti primene mera prevencije tokom boravka u zemljama gde se endemski održava malarija.

Ključne reči: importovana malarija, incidencija, endemski regioni

Uvod

Malarija je oboljenje uzrokovano parazitima koji pripadaju rodu *Plasmodium* (*P.*). Čovek se inficira ubodom zaraženih ženki komaraca roda *Anopheles*. Poznato je preko 250 vrsta roda *Plasmodium* koje mogu parazitirati kod različitih životinja, uključujući primat, glodare, ptice i gmizavce. Uzročnici malarije kod ljudi su *P. falciparum*, *P. malariae*, *P. vivax*, *P. ovale*, a od nedavno i zoonotska vrsta *P. knowlesi*, zbog pojava epidemija u jugoistočnoj Aziji. Malarija je vezana za vodena staništa vektora, pre svega tropskih i suprotropskih regiona sveta, gde visoke

temperature pogoduju vektorima i obezbeđuju razvoj plazmodijuma u ženki komaraca (1,2).

Klinička slika malarije zavisi uglavnom od obrasca i intenziteta prenosa malarije u mestu prebivališta, što određuje stepen stečene zaštite i profil kliničkog oboljenja. Malariju karakteriše groznica i simptomi slični gripu, uključujući jezu, glavobolju, bol u mišićima i slabost. Navedeni simptomi se mogu javiti u intervalima (3). Najveći broj slučajeva malarije se klasifikuje kao umerena ili nekomplikovana malarija. Međutim, malarija može dovesti do anemije, uvećane slezine, trombocitopenije,

IMPORTED MALARIA ON THE TERRITORY OF BELGRADE FROM 2014 TO 2018

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SUMMARY

Introduction/Aim: In the former Yugoslavia, malaria eradication was officially confirmed by the World Health Organization in 1974. Since then, only imported cases of malaria have been recorded in Serbia. The aim of this study was to analyze epidemiological characteristics of imported malaria on the territory of Belgrade from 2014 to 2018.

Methods: A descriptive epidemiological study was applied. Data on the number of newly diagnosed patients with imported malaria by gender, age and region from which malaria was imported, for the specified period were taken from the Institute of Public Health of Belgrade. Proportional, crude and age-specific incidence rates were used in the data analysis.

Results: There were 77 cases of imported malaria registered on the territory of Belgrade from 2014 to 2018, and the average crude incidence rate was 0.9/100,000. The highest number of patients (28) and the highest incidence rate (1.7/100,000) of imported malaria were registered in 2017, and the lowest number of patients (7) and the lowest incidence rate (0.4/100,000) were registered in 2014 and 2018. This disease was more common among men (89.6%) than among women (10.4%). The highest age-specific rate of imported malaria was registered in the age group of 10-19 years (3.5/100,000). *P. vivax* (45.4%) and *P. falciparum* (37.7%) were the most frequent causative agents of imported malaria in Belgrade. About 88% of imported malaria cases were from people living in endemic areas of Asia and Africa. The largest number of newly diseased cases of imported malaria stated migration (44.2%) and work (39.0%) as the reason for their stay in endemic regions. The condition is registered throughout the year, with the peak of the disease in August (19.5%).

Conclusion: It is necessary to continuously improve the health education of the population, in order to educate population about the manner of transmission of malaria, and to apply measures of prevention during their stay in endemic countries.

Key words: imported malaria, incidence, endemic regions

Introduction

Malaria is a disease caused by parasites, which belong to the genus *Plasmodium* (*P.*). People get infected when they are bitten by an infected female mosquito of the *Anopheles* genus. There are more than 250 species of the *Plasmodium* genus, which can infect different animals, including primates, rodents, birds and reptiles. Causative agents of malaria in humans are *P. falciparum*, *P. malariae*, *P. vivax*, *P. ovale*, and recently zoonotic species *P. knowlesi* has been recognized, due to the occurrence of epidemic in Southeastern Asia, as the fifth

causative agent of malaria in humans. Malaria vectors are associated with water habitats, in the tropical and subtropical regions of the world, where high temperatures favor vectors and ensure the development of plasmodium in female mosquitoes (1,2).

The clinical picture of malaria depends mainly on the pattern and intensity of malaria transition at the place of residence, which determines the degree of the acquired protection and the profile of clinical illness. Malaria is characterized by fever and symptoms similar to influenza, including chills, headache,

blage žutice, uvećane jetre, ubrzanog disanja, ali i težih komplikacija i smrtnog ishoda. Za pojavu ozbiljnih oštećenja organa u kratkom periodu, kao i za većinu smrtnih slučajeva odgovoran je *P. falciparum*. Inkubacija obuhvata vreme od uboda komarca do početka ispoljavanja bolesti i varira od 7 do 30 dana, ali može biti i znatno duža. Najkraća inkubacija, sa retkim izuzecima, vezuje se za *P. falciparum*, dok *P. malariae* može imati dugu inkubaciju, merenu i decenijama (1).

Tehnika mikroskopskog pregleda razmaza periferne krvi i dalje predstavlja zlatni standard u dijagnostici malarije. Pored mikroskopije, dijagnostika malarije uključuje: brze dijagnostičke testove (engl. *Rapid Diagnostic Test* - RDT), serologiju i molekularne metode zasnovane na reakciji lančane polimeraze (engl. *Polymerase Chain Reaction* - PCR) (1,2).

Dve ključne mere u prevenciji malarije su: hemioprofilaksa i borba protiv komaraca (4). Svetska zdravstvena organizacija, u saradnji sa Vladom Malavija, pokrenula je u Malaviju 23.04.2019. godine pilot program za prvu vakcinu protiv malarije u svetu. Malavi je prva od tri zemlje u Africi, u kojoj će „moskiriks” vakcina (engl. *Mosquirix*), poznatija kao RTS,S vakcina, biti dostupna deci starosti do 2 godine. U Gani i Keniji je planirana primena RTS,S vakcine krajem 2019. godine. Vakcina se daje u četiri doze, tri doze između 5. i 9. meseca života, a četvrta doza oko druge godine (5). Do sada, RTS,S je jedina vakcina protiv malarije koja je bila u trećoj fazi ispitivanja u Africi od 2009. do 2014. godine, i koja se pokazala efikasnom i do 36% u prevenciji malarije (6).

Cilj ovog rada je da se analiziraju epidemiološke karakteristike importovane

malarije na području Beograda u periodu 2014 – 2018. godine.

Metode

Primenjena je deskriptivna epidemiološka studija. Podaci o broju novoobolelih od importovane malarije po polu, uzrastu, datumu dijagnostikovanja, endemskom regionu odakle je malarija importovana, razlogu boravka u endemskom području, i dužini vremena koje protekne od boravka u endemskom području do pojave simptoma malarije, su preuzeti iz Gradskog zavoda za javno zdravlje Beograd. Kao izvor podataka korišćene su pojedinačne prijave zaraznih bolesti, epidemiološke ankete i informacije iz Centra za kontrolu i prevenciju bolesti Gradskog zavoda za javno zdravlje Beograd.

U analizi podataka korišćene su proporcije, sirove i uzrasno specifične stope incidencije. Za izračunavanje stopa incidencije, kao brojilac korišćen je broj novoobolelih od importovane malarije za posmatranu godinu, a za imenilac broj stanovnika Beograda sredinom posmatranog perioda, a prema podacima popisa stanovništva iz 2011. godine.

Rezultati

U periodu 2014-2018. godine, na području Beograda registrovano je 77 novoobolelih od importovane malarije, a prosečna sirova stopa incidencije je iznosila 0,9/100.000. Najveći broj novoobolelih (28) i najveća sirova stopa incidencije (1,7/100.000) importovane malarije je zabeležena u 2017. godini, a najmanje novoobolelih (7) i najmanje sirove stope incidencije (0,4/100.000) registrovane

Tabela 1. Broj novoobolelih i uzrasno specifične stope incidencije (na 100.000) za importovanu malariju, Beograd, 2014 – 2018. godina

Uzrasne grupe (Age groups)	≤ 9	10-19	20-29	30-39	40-49	50-59	60+	Ukupno (Total)
	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	
Godina (Years)								
2014	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)	3 (1.2)	0 (0.0)	7 (0.4)
2015	0 (0.0)	0 (0.0)	3 (1.3)	4 (1.5)	0 (0.0)	4 (1.6)	2 (0.5)	13 (0.8)
2016	0 (0.0)	11 (6.9)	4 (1.8)	2 (0.7)	3 (1.3)	2 (0.8)	0 (0.0)	22 (1.3)
2017	0 (0.0)	17 (10.7)	2 (0.8)	4 (1.5)	1 (0.4)	2 (0.8)	2 (0.5)	28 (1.7)
2018	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.7)	2 (0.9)	2 (0.8)	1 (0.2)	7 (0.4)
2014-2018	0 (0.0)	28 (3.5)	10 (0.8)	13 (0.9)	8 (0.7)	13 (1.0)	5 (0.2)	77 (1.0)

*Stopa incidencije

pain in muscles, and weakness. These symptoms can appear in intervals (3). The greatest number of malaria cases is classified as mild or uncomplicated malaria. However, malaria can lead to anemia, splenomegaly, thrombocytopenia, mild jaundice, enlarged spleen, fast breathing, but also to complications and deathly outcome. *P. falciparum* is responsible for the appearance of severe organ damage in a short period of time and for most of deathly outcomes, as well. The incubation period includes the time following the mosquito bite until the first symptoms appear and it varies from 7 to 30 days, but it can be much longer. The shortest incubation period, with rare exceptions, is associated with *P. falciparum*, whereas *P. malariae* can have a long incubation period, lasting even decades (1).

The technique of viewing the peripheral blood smears under the microscope is the golden standard diagnosis test for malaria. Beside the microscopy, malaria diagnosis includes: Rapid Diagnostic Tests (RDT), serology testing and molecular testing based on Polymerase Chain Reaction – PCR (1,2).

Two key measures regarding the prevention of malaria are: chemoprophylaxis and combating mosquitoes (4). The World Health Organization, in cooperation with the government of Malawi, launched the pilot program for the first vaccine against malaria in the world on the 23rd of April, 2019. Malawi is the first of the three countries in Africa, in which the Mosquirix vaccine, known as RTS,S vaccine, will be made available to children up to two years of age. The application of RTS,S vaccine was planned in Ghana and Kenya near the end

of 2019. The vaccine is given in four doses, three doses between 5 and 9 months of age, and the fourth around two years of age (5). RTS,S has been the only vaccine against malaria so far, which was in the phase three trial in Africa from 2009 to 2014, and which proved to be efficient in up to 36% regarding malaria prevention (6).

The aim of this study was to analyze the epidemiological characteristics of imported malaria on the territory of Belgrade from 2014 to 2018.

Methods

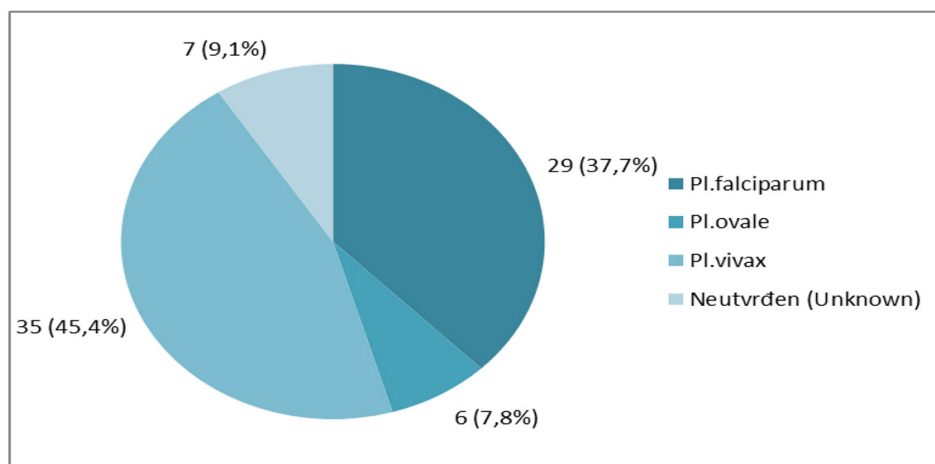
A descriptive epidemiological study was applied. Data on the number of newly diagnosed patients with imported malaria regarding gender, age, date of diagnosis, endemic region, where malaria was imported from, the reason for staying in endemic regions, and the time which passed from their stay in endemic region to the first symptoms of malaria were taken from The Institute of Public Health of Belgrade. Individual reports on contagious diseases, epidemiological survey and information from the Centre for Disease Control and Prevention of The Institute of Public Health of Belgrade were used as a source of data.

Proportions, crude and age-specific incidence rates were used for the analysis of data. In order to calculate the incidence rates, the number of new cases of imported malaria for the observed year was used as a numerator, while the mid-year population number of Belgrade, according to the Census from 2011, was used as a denominator.

Table 1. Number of new cases and age-specific incidence rates (per 100,000) for imported malaria, Belgrade, 2014 – 2018

Uzrasne grupe (Age groups)	≤ 9	10-19	20-29	30-39	40-49	50-59	60+	Ukupno (Total)
	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	Broj (Stopa*) No (Rate*)	
Godina (Years)								
2014	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)	3 (1.2)	0 (0.0)	7 (0.4)
2015	0 (0.0)	0 (0.0)	3 (1.3)	4 (1.5)	0 (0.0)	4 (1.6)	2 (0.5)	13 (0.8)
2016	0 (0.0)	11 (6.9)	4 (1.8)	2 (0.7)	3 (1.3)	2 (0.8)	0 (0.0)	22 (1.3)
2017	0 (0.0)	17 (10.7)	2 (0.8)	4 (1.5)	1 (0.4)	2 (0.8)	2 (0.5)	28 (1.7)
2018	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.7)	2 (0.9)	2 (0.8)	1 (0.2)	7 (0.4)
2014-2018	0 (0.0)	28 (3.5)	10 (0.8)	13 (0.9)	8 (0.7)	13 (1.0)	5 (0.2)	77 (1.0)

*Incidence rate



Grafikon 1. Distribucija novoobolelih od importovane malarije prema vrsti prouzročivača, Beograd, 2014 – 2018. godina

su 2014. i 2018. godine (tabela 1). Muškarci (89,6%) su češće obolevali nego žene (10,4%). Najviša uzrasno specifična stopa incidencije importovane malarije je zabeležena u uzrasnoj grupi od 10 do 19 godina (3,5/100.000), a najniža u najstarijem uzrastu (60 i više godina) (0,25/100.000).

U posmatranom periodu kod najvećeg broja obolelih uzročnici importovane malarije su bili *P. vivax* (45,4%) i *P. falciparum* (37,7%), a najmanje *P. non specificata* (9,1%) i *P. ovale* (7,8%) (grafikon 1).

Najviše obolelih od importovane malarije je boravilo u endemskim područjima Azije (44,2%) i Afrike (44,2%), a najmanje je bilo sa područja Centralne Evrope (1,3%) (grafikon 2).

Kao razlog boravka u endemskom području, najveći broj novoobolelih od importovane malarije je naveo migraciju (44,2%) i posao (39,0%), a najmanji privatne razloge (2,6%) i

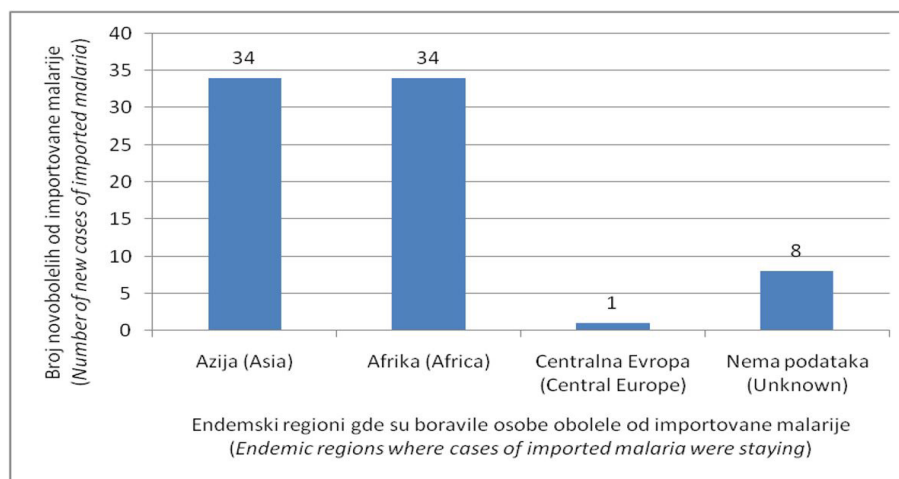
turizam (1,3%) (grafikon 3). Za deset osoba sa importovanom malarijom nije bio poznat razlog boravka u zemljama gde postoji endemska malarija.

Interval između dolaska u Srbiju i pojave simptoma malarije je bio poznat za 77% ispitanika (grafikon 4). Kod najvećeg broja obolelih (42,8%) od importovane malarije je došlo do pojave simptoma u periodu do 30 dana od povratka u Srbiju, a najmanje (3,9%) nakon godinu dana od dolaska u našu zemlju.

Oboleli od importovane malarije se registruju tokom cele godine. Najveći broj novoobolelih od importovane malarije je bio zabeležen u avgustu (19,5%), a najmanji u januaru (2,6%) (grafikon 5).

Diskusija

Iako je u poslednjih 50 godina značajno smanjena geografska teritorija zahvaćena



Grafikon 2. Broj novoobolelih od importovane malarije prema endemskom regionu gde su osobe boravile, Beograd, 2014 – 2018. godina

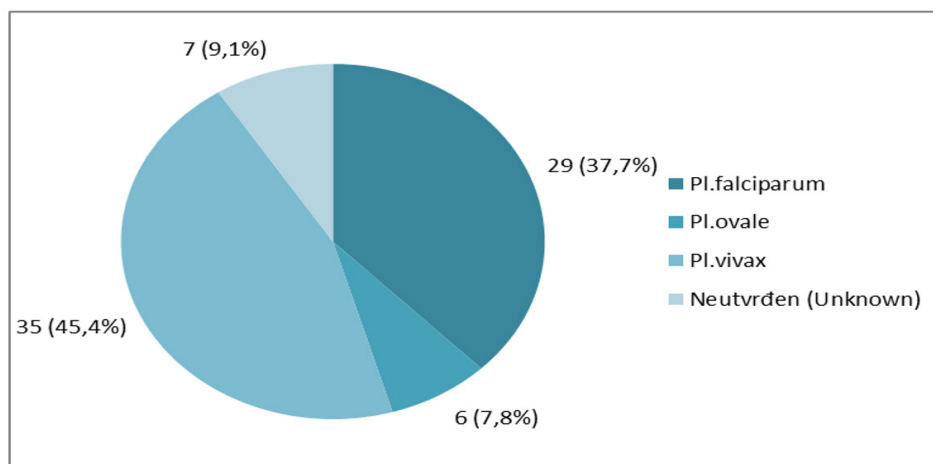


Figure 1. Distribution of new cases of imported malaria by species, Belgrade, 2014 – 2018

Results

There were 77 cases of imported malaria registered on the territory of Belgrade from 2014 to 2018, and the average crude incidence rate was 0.9/100,000. The largest number of newly diseased (28) and the highest crude incidence rates (1.7/100,000) of imported malaria were noted in 2017, whereas the smallest number of newly diseased (7) and the lowest crude incidence rates (0.4/100,000) were registered in 2014 and 2018 (Table 1). This disease was more common among men (89.6%) than among women (10.4%). The highest age-specific incidence rate of imported malaria (3.5/100,000) was noted in 10 to 19 age group, and the lowest rate (0.25/100,000) was in the oldest age group (60 years and older).

In the observed time period, the largest number of cases of imported malaria was caused by *P. vivax* (45.4%) and *P. falciparum* (37.7%), whereas the smallest number was caused by

P. non specificata (9.1%) and *P. ovale* (7.8%) (Figure 1).

Of 77 imported cases of malaria, 44.2% were from Asia, 44.2% from Africa, 1.3% from Central Europe, while for 10.4% cases it was not known where malaria was imported from (Figure 2).

The largest number of newly diseased cases of imported malaria stated migration (44.2%) and work (39.0%) as the reason for their stay in endemic regions, and the smallest number stated private reasons (2.6%) and tourism (1.3%) (Figure 3). The reason for staying in countries with endemic malaria was not known for ten people with imported malaria.

The interval from their arrival in Serbia and the first symptoms of malaria was known for 77% of examinees (Figure 4). In most cases of malaria patients (42.8%), the first symptoms appeared within 30 days after their arrival in Serbia, while the smallest number of patients

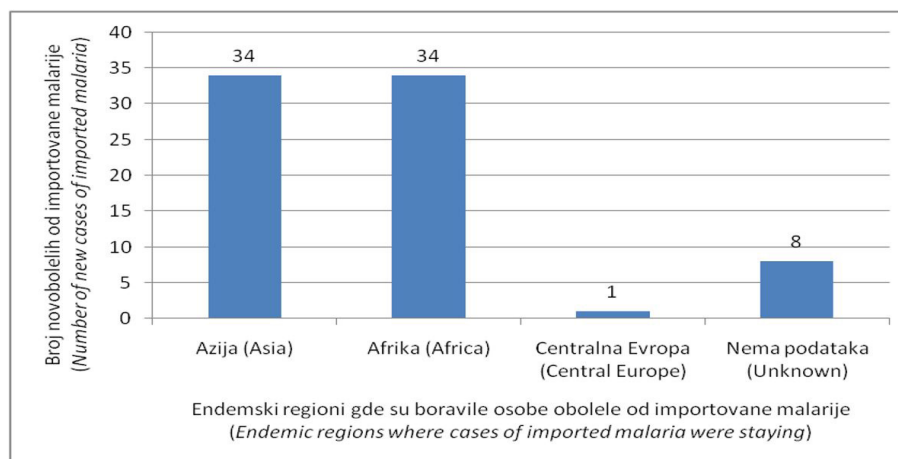
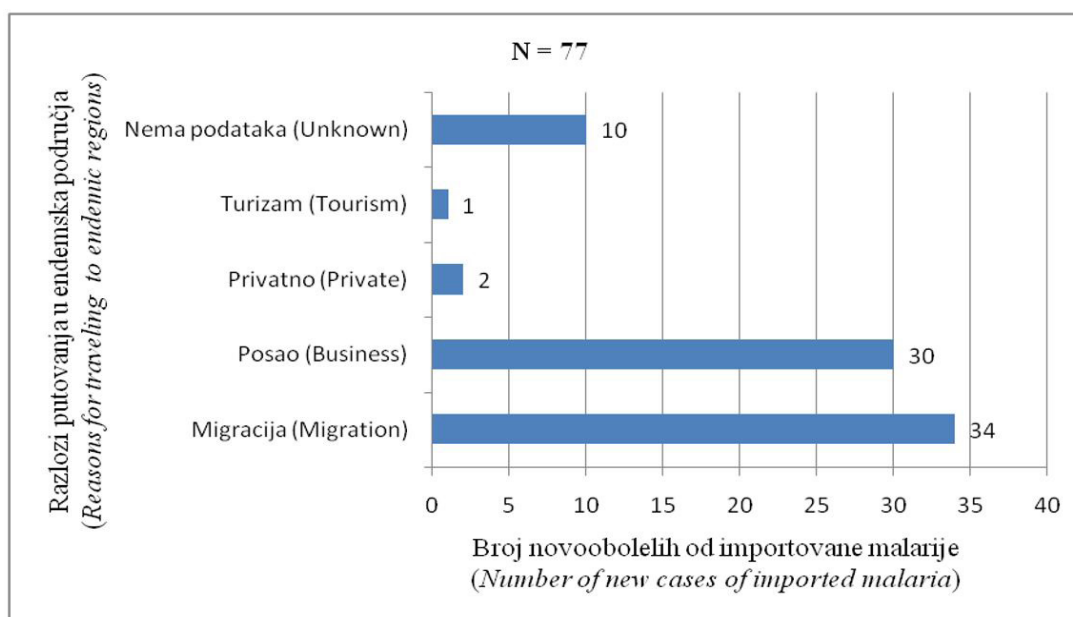


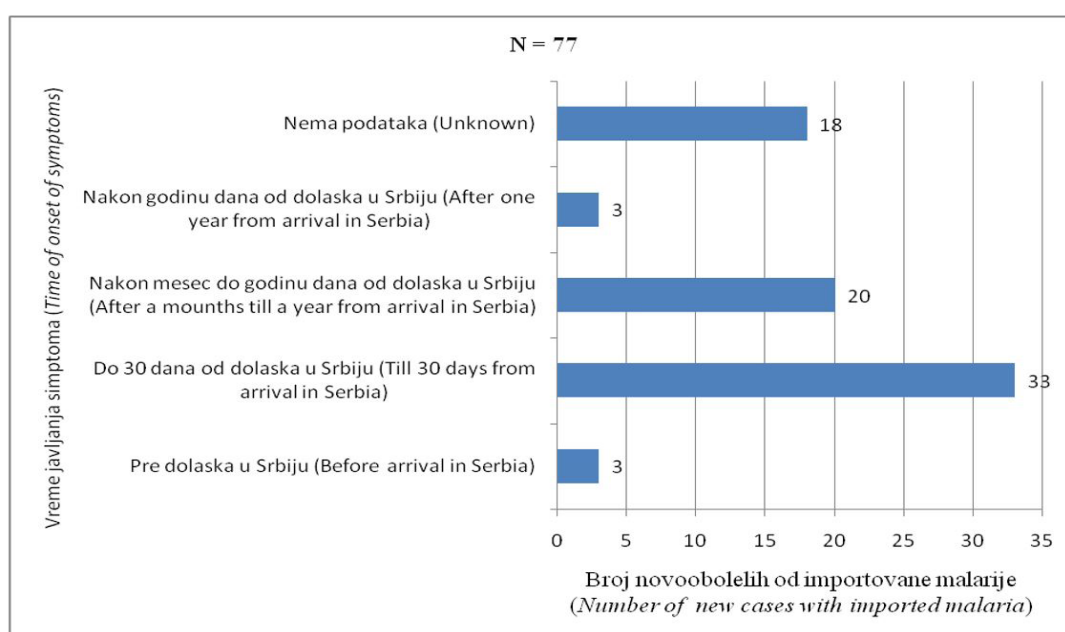
Figure 2. Number of new cases of imported malaria according to endemic region where they were staying, Belgrade, 2014 – 2018



Grafikon 3. Broj novoobolelih od importovane malarije prema razlozima putovanja u endemska područja, Beograd, 2014 – 2018. godina

malarijom, malarija i dalje predstavlja veliki javno-zdravstveni problem. Na globalnom nivou, u 2018. godini, prema podacima Svetske zdravstvene organizacije (SZO), od malarije je obolelo oko 228 miliona ljudi i umrlo 405 hiljada, što je manje nego u 2017. godini kada je bilo 231 milion obolelih i 416.000 umrlih (7-9). U pet država supsaharske Afrike (Nigerija, Demokratska Republika Kongo, Uganda, Mozambik i Obala Slonovače) prisutno je 50% svih slučajeva malarije. Trudnice i deca mlađa od pet godina u supsaharskoj Africi su

pod najvećim rizikom od malarije. Trudnoća smanjuje imunitet, čineći trudnice podložnijim infekciji i povećavajući rizik od obolevanja od malarije, teške anemije i smrti. U 2017. godini bilo je procenjeno da je čak 29% svih trudnica u supsaharskoj Africi inficirano malarijom, što je negde oko 3,2 miliona trudnica (7,9). Takođe, 67% svih smrtnih ishoda usled malarije na globalnom nivou je kod dece mlađe od 5 godina. Pored supsaharske Afrike, u riziku od malarije su jugoistočna Azija, istočni Mediteran, zapadni Pacifik i obe Amerike.



Grafikon 4. Vreme javljanja simptoma kod novoobolelih od importovane malarije nakon boravka u endemskom području, Beograd, 2014 – 2018. godina

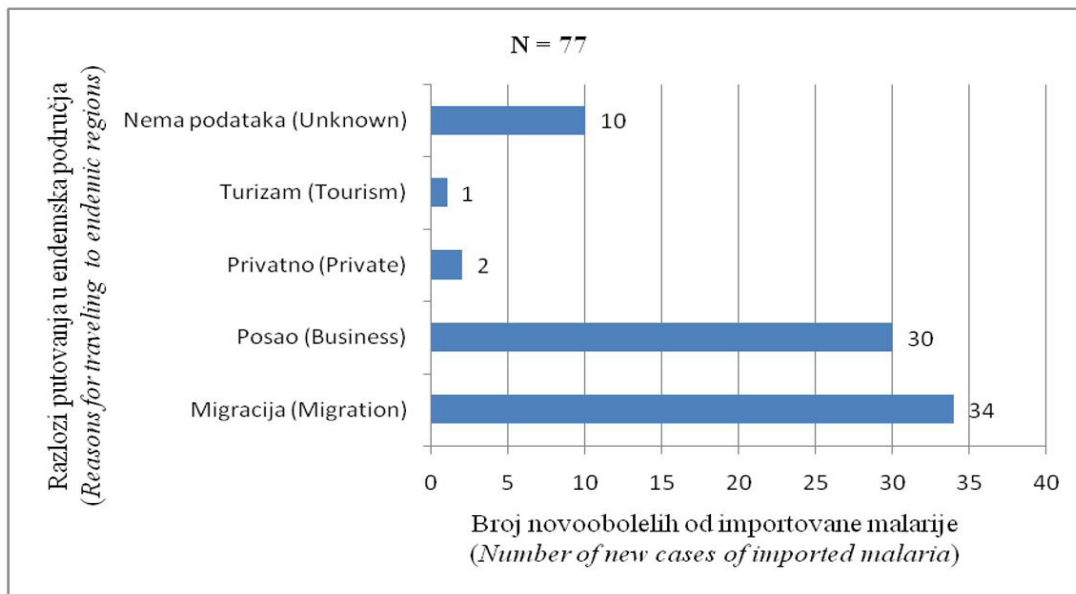


Figure 3. Number of new cases of imported malaria by reasons for traveling to endemic regions, Belgrade, 2014 - 2018

(3.9%) had symptoms one year after their arrival in Serbia.

Patients with imported malaria are registered during the whole year. The largest number of patients was registered in August (19.5%), and the smallest in January (2.6%) (Figure 5).

Discussion

Although geographic territory exposed to malaria has been significantly reduced during the last 50 years, malaria still presents a big public

health problem. In 2018, according to the World Health Organization, there were around 228 million cases of malaria around the world and 405,000 deathly outcomes, which is less when compared to 2017, when there were 231 million cases and 416,000 malaria deaths (7-9). 50% of all malaria cases are present in five Sub-Saharan African countries (Nigeria, the Democratic Republic of Congo, Uganda, Mozambique and Ivory Coast). Children younger than five years and pregnant women in Sub-Saharan Africa are at the greatest risk of malaria. Pregnancy lowers

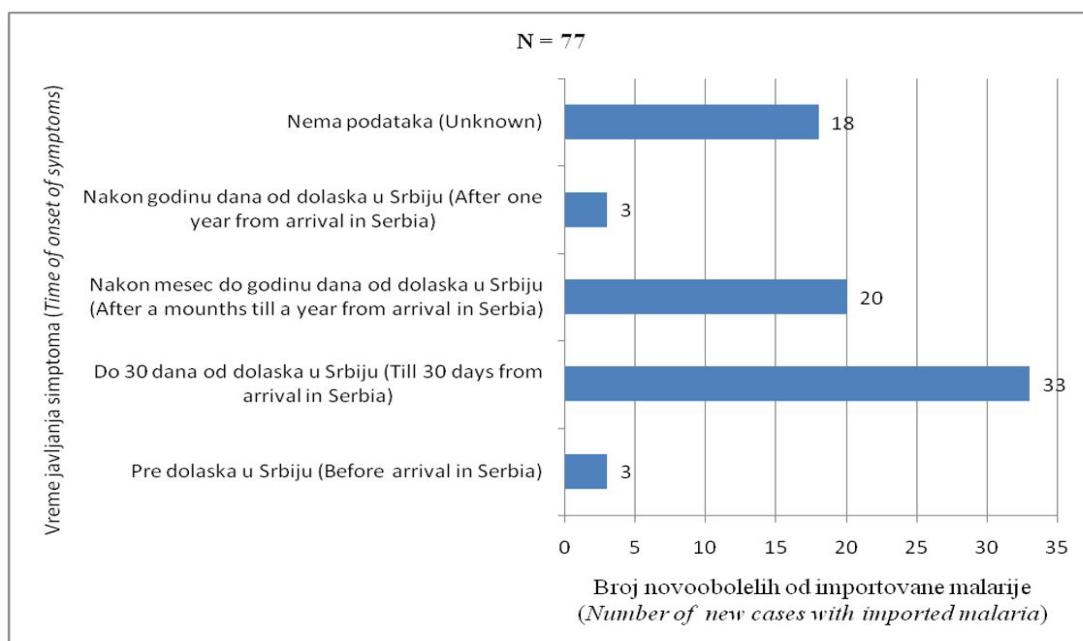
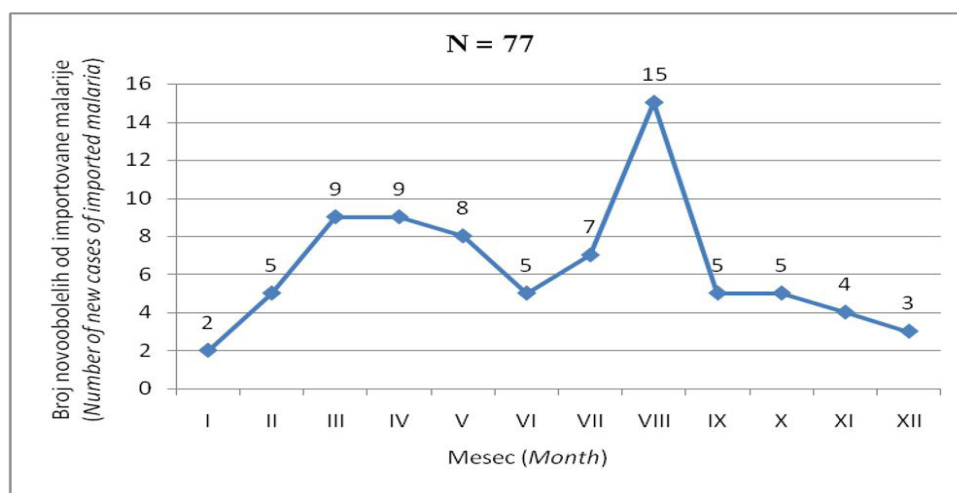


Figure 4. Time of onset of symptoms in newly diagnosed patients with imported malaria after staying in the endemic area, Belgrade, 2014 - 2018



Grafikon 5. Distribucija novoobolelih od importovane malarije po mesecima, Beograd, 2014 – 2018. godina

Mreža eliminacije malarije se svake godine širi i sve više zemalja ide ka cilju nulte malarije. Povećava se broj zemalja gde je broj autohtonih slučajeva manji od 100, sa 17 zemalja u 2010. godini na 27 zemalja u 2018. godini.

Malaria se održava endemski u 31 zemlji sveta, ali je u period od 2015. do 2018. godine došlo do značajnog smanjivanja obolelih što bi doprinelo redukovanju obolelih za 40% i više do 2020. godine.

Ponovno javljanje malarije je sve učestalije u regionima gde je malaria eradikirana ili u kojima je incidencija bila značajno smanjena. Razlozi su mnogobrojni i uključuju globalne klimatske i ekološke promene nastale pod uticajem čoveka, koje favorizuju održavanje i širenje populacije komaraca, multirezistenciju parazitskih vrsta, kao i masovne migracije, izazvane konfliktima ili porastom turističkih i poslovnih putovanja u područja gde ima malarije (1).

Prema rezultatima naše studije, prosečna sirova stopa incidencije importovane malarije, u periodu od 2014. do 2018. godine, u Beogradu se kretala od 0,4/100.000 do 1,7/100.000 stanovnika. U Srbiji, tokom istog perioda, sirova stopa incidencije importovane malarije je bila od 0,14/100.000 do 0,40/100.000 stanovnika (10), a u Evropskoj uniji (EU) od 1,2/100.000 do 1,3/100.000 stanovnika (11). Podaci Evropskog centra za sprečavanje i kontrolu bolesti pokazuju da su, u 2018. godini, skoro svi slučajevi (99,8%) malarije u zemljama EU importovani (11). Posebno zabrinjava činjenica da je u EU registrovano 14 slučajeva autohtone

malarije (deset u Grčkoj, dva u Španiji, po jedan u Francuskoj i Italiji), što ukazuje da su i druge zemlje EU, kao i naša zemlja pod rizikom i od autohtone malarije (11).

U Beogradu je broj obolelih od importovane malarije bio 8,6 puta veći kod muškaraca nego kod žena. Kao i u našoj studiji, u zemljama EU, u 2018. godini, stopa potvrđenih slučajeva malarije je bila 1,9 puta veća za muškarce (1,6 na 100.000) nego za žene (1,6 na 100.000) (11).

Posmatrajući obolevanje od importovane malarije po uzrasnim grupama u Beogradu, uočeno je da je uzrasno specifična stopa incidencije malarije najviša u uzrasnoj grupi od 10 do 19 godina, a najniža kod osoba uzrasta 60 i više godina. Ovo se može objasniti boravkom u Beogradu velikog broja mladih ljudi, migranata, koji dolaze iz zemalja Azije, gde je malaria autohtona. Epidemiološka ispitivanja importovane malarije u Australiji, pokazuju da je uzrasno specifična stopa incidencije malarije najviša u dobnoj grupi od 25 do 29 godina (12).

Najveći broj obolelih od importovane malarije u Beogradu je boravio u endemskim područjima Azije i Afrike, a razlozi boravka su bili najčešće migracija i posao. U zemljama EU u kojima se prijavljuje najveći broj importovanih slučajeva (npr. Francuska, Velika Britanija i Nemačka) uočeno je da one imaju istorijske, ekonomske i kulturne veze sa endemskim područjima u Africi i Americi (11). Među 7.338 potvrđenih slučajeva importovane malarije u EU, čak 99,8% je bilo povezano sa putovanjima. Interesantno je da je četrnaest slučajeva autohtone malarije registrovano u

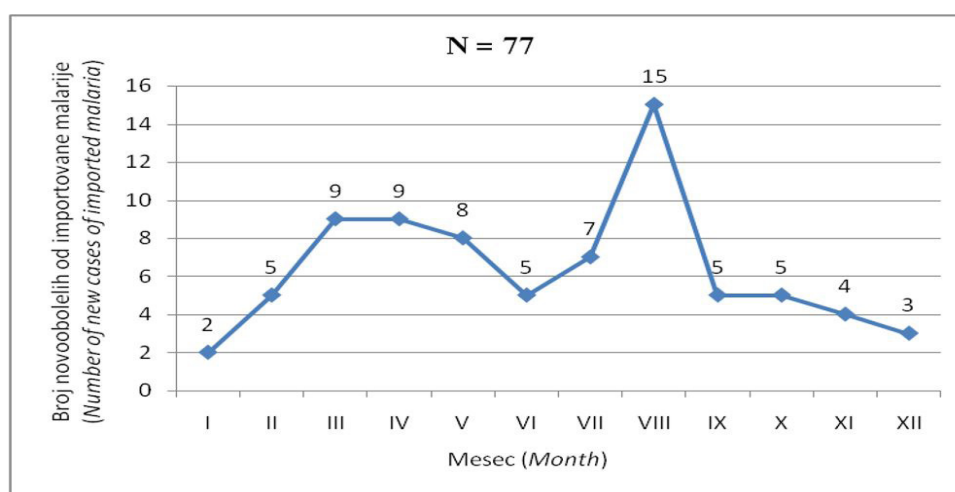


Figure 5. Distribution of new cases of imported malaria by months, Belgrade, 2014 – 2018

immunity, making pregnant women more susceptible to the infection, and increasing the risk of being infected with malaria, severe anemia and death. It was estimated that 29% of pregnant women in Sub-Saharan Africa were infected with malaria in 2017, that is, around 3.2 million pregnant women (7,9). Also, 67% of all deathly outcomes due to malaria at the global level were in children younger than five years. Beside Sub-Saharan Africa, Southeast Asia, the Eastern Mediterranean, Western Pacific and Americas are at risk of malaria.

The network of malaria elimination spreads every year, while more and more countries are reaching the zero malaria. The number of countries, where the number of autochthonous cases is lower than 100, increased from 17 countries in 2010 to 27 countries in 2018.

There are 31 malaria-endemic countries, but during the period 2015-2018 there came to the significant decrease of patients, which will contribute to the decrease of the number of patients for 40% and more until 2020.

Recurring malaria is all the more frequent in regions, where malaria has been eradicated, or in which incidence has significantly decreased. The reasons are numerous, including global climate and ecological change, which appeared due to the human influence, and which favor the maintenance and spread of the mosquito population, multi-resistance of parasitic species, as well as mass migrations, caused by conflicts or rise in touristic and business travels (1).

According to the results of our study,

the average crude incidence rate of imported malaria for the period 2014-2018 ranged from 0.4/100,000 to 1.7/100,000 people in Belgrade. In Serbia, during the same time period, the crude incidence rate of imported malaria ranged from 0.14/100,000 to 0.40/100,000 residents (10), and in the European Union from 1.2/100,000 to 1.3/100,000 residents (11). Data of the European Centre for Disease Prevention and Control show that in 2018, almost all cases (99.8%) of malaria in EU countries were imported (11). The fact that 14 cases of autochthonous malaria were registered in the EU is especially worrying (ten in Greece, two in Spain, one in France and Italy), which points to the fact that the other EU countries, as well as our country, are at risk of autochthonous malaria (11).

In this study, imported cases of malaria were 8.6 times more common among men than among women. As in our town, in EU countries in 2018 the rate of confirmed malaria cases was 1.9 times higher among men (1.6/100,000) than among women (1.6/100,000) (11).

By observing the disease of imported malaria in relation to age groups in Belgrade, it was noted that the age-specific incidence rate was highest in the age group 10 to 19 years, while the lowest rate was in people who were 60 and older. This may be explained with the fact that a lot of young people, migrants stayed in our town, and they came from Asian countries, where malaria is autochthonous. Epidemiological investigation of imported malaria in Australia showed that age-specific

samoj EU (deset slučajeva uzrokovanih *P. vivax* u Grčkoj, jedan nepoznate vrste plazmodijuma u Francuskoj, jedan slučaj uzrokovan *P. falciparum*, jedan slučaj mešovite infekcije uzrokovane *P. malariae* i *P. ovale* u Španiji, i jedan slučaj uzrokovan *P. falciparum* u Italiji) (11).

Prema rezultatima studije sprovedene u Australiji u periodu od 2014. do 2015. godine najviše registrovanih obolelih od malarije je bilo iz regiona Afrike (23%) i sa Pacifičkih ostrvskih zemalja (20%) (12). Međutim, u zemljama Ujedinjenog Kraljevstva tokom 2017. godine, najveći broj obolelih od importovane malarije je kao razlog bolesti naveo putovanje rođacima/prijateljima 814 (80%), potom turizam 108 (11%) i posao 98 (10%) (13).

Importovana malarija kod obolelih u Beogradu najčešće se javljala do 30 dana (43%), a najređe nakon godinu dana od dolaska u zemlju (4%). Prema rezultatima studije sprovedene u Sjedinjenim Američkim Državama (SAD), tokom 2015. godine, kod najvećeg broja obolelih od malarije došlo je do pojave simptoma tokom prvih mesec dana od povratka (76,5%), a najmanje nakon godinu dana od povratka u zemlju (0,8%) (14).

U Beogradu, najčešći prouzrokovali importovane malarije su bili *P. vivax* i *P. falciparum*. Suprotno našim rezultatima, epidemiološka istraživanja importovane malarije u zemljama Ujedinjenog Kraljevstva ukazuju da dominira serotip *P. falciparum*, a zatim *P. vivax* (13). Od 4.516 potvrđenih slučajeva malarije u EU za koje je bio poznat uzročnik, čak u 84,0% slučajeva uzročnik je bio *P. falciparum* (11).

U periodu 2014-2018. godine, na području Beograda, oboleli od malarije su se registrovali tokom cele godine. Najveći broj obolelih je bio u mesecu avgustu, a najmanji u mesecu januaru. Slično je zabeleženo u SAD-u, gde se malarija registruje tokom cele godine, sa pikom u avgustu mesecu (8). U EU zabeležen je izražen sezonski trend u svim zemljama, a broj obolelih je povećan tokom i neposredno nakon leta (od jula do septembra) (11).

U održavanju eradikacije malarije u Beogradu, kao i u drugim zemljama, glavnu prepreku predstavljaju importovani slučajevi malarije i prisustvo komaraca roda *Anopheles*. Neke od mera koje treba sprovoditi za održavanje stanja bez malarije su: suzbijanje

komaraca, praćenje vrsta komaraca, hemioprofilaksa putnika koji putuju u endemska područja, nadzor nad osobama koje dolaze iz endemskih područja, nadzor nad migrantima, dobra snabdevenost lekovima za lečenje i hemioprofilaksu malarije, laboratorijska dijagnostika i dr. Realizacija održavanja eradikacije malarije nezamisliva je bez saradnje svih odgovornih za detekciju i nadzor iste, a u cilju boljeg razumevanja gde i kako se malarija kreće, koje mere se preduzimaju, kao i šta se dešava sa brojem importovanih slučajeva malarije tokom vremena.

Zaključak

Broj novoobolelih od importovane malarije na području Beograda osciluje u periodu 2014-2018. godine i kreće se od 7 do 28. Neophodno je raditi na kontinuiranom zdravstvenom vaspitanju stanovništva u cilju informisanosti o načinu prenošenja malarije, primeni preventivne mere tokom boravka u zemljama gde se malarija održava endemski, kao i na podizanju svesti o značaju blagovremenog javljanja zdravstvenoj službi prilikom pojave prvih simptoma bolesti. U cilju daljeg smanjenja broja obolelih od malarije od značaja bi bio pronalazak efektivne vakcine. Zbog prisustva malaričnih komaraca na teritoriji Beograda, pogodnoj za održavanje komaraca roda *Anopheles* usled prisustva velikih vodenih površina, kao i zbog povećanog broja slučajeva importovane malarije, postoji rizik ponovnog javljanja autohtone malarije.

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incidence rate of malaria was highest in the age group 25 to 29 years (12).

The largest number of patients (around 88%) with imported malaria in Belgrade stayed in the endemic regions of Asia and Africa, while the reasons for their stay were most frequently migration (44.2%) and work (39.0%). In EU countries, in which the largest number of cases was registered (e.g. France, Great Britain, and Germany), it was noticed that they have historical, economic and cultural bonds with the endemic regions in Africa and America (1). Among 7,338 of confirmed cases of imported malaria in the EU, even 99.8% were connected with travels. It is interesting that fourteen people got this infection in the EU itself (ten *P. vivax* in Greece, one of the unknown species of plasmodium in France, one *P. falciparum*, one mixed case of *P. malariae* and *P. ovale* in Spain, one *P. falciparum* in Italy) (11).

According to the results of one study conducted in Australia for the period 2014-2015, most of the registered cases were from the region of Africa (23%) and from Pacific Islands (20%) (12). However, in the countries of the United Kingdom during 2017, the largest number of patients stated traveling to cousins/friends 814 (80%), tourism 108 (11%) and work 98 (10%) as their reasons (13).

Imported malaria in patients in Belgrade appeared most frequently within 30 days from their arrival in the country (43%), and most rarely one year after their arrival in the country (4%). According to the results of studies conducted in The United States during 2015, in most malaria cases symptoms appeared within the first month from their return to the USA (76.5%), and the smallest number of cases had symptoms one year after return to the USA (0.8%) (14).

P. vivax and *P. falciparum* were the most frequent causative agents of imported malaria in Belgrade. Contrary to our results, epidemiological investigation of imported malaria in the United Kingdom pointed that serotype *P. falciparum* was dominant, and then *P. vivax* (13). Of 4,516 confirmed cases of malaria in the EU, for whom the causative agent was known, in 84% of cases the causative agent was *P. falciparum* (11).

Patients with malaria are registered during

the whole year. The largest number of patients is registered in August, and the smallest number in January. Similar situation was recorded in the USA, where malaria is registered throughout the entire year, with the peak in August (8). In the EU, the pronounced seasonal trend was recorded in all countries, and the number of cases was increased during and immediately after summer (from July till September).

Imported malaria cases and the presence of mosquitoes of the *Anopheles* genus present the main obstacle to maintaining the eradication of malaria in Belgrade, as well as in other countries. Some of the measures, which should be taken in order to maintain the absence of malaria, are: repelling mosquitoes, following mosquito species, chemoprophylaxis of passengers who travel to endemic regions, surveillance of people who come from endemic regions, surveillance of migrants, good supplies of medicines for the treatment and chemoprophylaxis of malaria, laboratory diagnostic tests etc. The realization of the maintenance of malaria eradication is unimaginable without the cooperation of all the people responsible for its detection and surveillance, in order to understand better where and how the parasites move, what measures are taken, as well as what happens with the number of imported malaria cases over time.

Conclusion

The number of new cases with imported malaria on the territory of Belgrade varies from 7 to 28 for the period 2014-2018. Continuing health education of population is necessary, aimed at informing them about the ways in which malaria is transmitted, applying the preventive measures during the stay in malaria endemic-countries, as well as raising awareness of the significance of timely notification of healthcare service when the first symptoms appear. In order to further decrease the number of patients with malaria, the efficient vaccine discovery would be of great significance. Due to the presence of malaria-transmitting mosquitoes on the territory of Belgrade, suitable for the maintenance of the *Anopheles* genus due to the great water areas, and because of the increased number of cases of imported malaria, there is a risk of autochthonous malaria appearance.

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