Annual epidemiological surveillance report

Malaria in Greece, 2021

Introduction

Malaria is a parasitic infection, transmitted through the bite of an infected female *Anopheles* mosquito. Five species of Plasmodium cause disease to humans: *Plasmodium falciparum, P. vivax, P. ovale, P. malariae,* and *P. knowlesi* (zoonotic malaria). *P. falciparum* and *P. vivax* are the most common.

The most common symptoms of malaria (high fever, chills, sweating, malaise, headache and muscle aches) manifest usually 1-4 weeks after infection with the parasite, while relapses of the disease are usually observed in short intervals but up to more than five years after *P. vivax* and *P. ovale* infections (if not properly treated). A number of effective anti-malarial drugs are available to treat the infection; starting the treatment promptly is essential in avoiding complications and interrupting the transmission of the disease in the community.

Ongoing transmission of malaria is currently recorded in 85 countries around the world (WHO, World Malaria Report, 2021), mainly in sub-Saharan Africa, Asia and Latin America. Until the mid-twentieth century, several countries in Europe and North America were also malaria endemic, but -after intense malaria control programs- it was eliminated.

Malaria surveillance in Greece

Data are derived from the reports of laboratory-confirmed malaria cases and the enhanced malaria surveillance systems of the Hellenic National Public Health Organization (NPHO). The NPHO's Vector-borne Diseases Department undertakes investigation of every reported case, through communication with the treating physician and the patient, and assesses the transmission risk. Re-active case detection and environmental investigation are undertaken by the staff of the Vector-borne Diseases Department, with the collaboration of local public health authorities, for every locally acquired/ introduced malaria case throughout Greece. In addition, in specific areas with recorded cluster of locally acquired malaria cases over the last years, systematic pro-active detection of malaria cases, door-to-door, is implemented (see below).

Malaria surveillance data in Greece, 2009 - 2020

Malaria was eliminated from Greece in 1974, following an intense control program (1946-1960). Since then and up to 2020, several (20-110 cases) imported cases were reported annually to the NPHO referring to patients infected abroad (returning travelers or migrants from malaria endemic countries). Increasing numbers of imported malaria cases are expected due to the increase of travels and population movements worldwide, a phenomenon that is observed in all developed countries. According to the European Centre for Disease Control and Prevention (ECDC), in 2018 more than 8,000 imported malaria cases were recorded in EU/EEA countries (ECDC, Malaria, Annual Epidemiological Report for 2018).

Additionally, since 2009 a number of locally acquired/introduced *P. vivax* malaria cases have been recorded in some areas of the country (i.e., among patients without travel history to a malaria endemic country),

mainly as sporadic introduced cases (1st generation transmission) but also in clusters (in 2011-2012). Regarding these *P.vivax* introduced cases, the *Plasmodium* transmission was mosquito-borne, through mosquitoes that got infected from imported cases. Most areas where *P.vivax* locally acquired/introduced cases were recorded over the last years were rural close to wetlands with high number of persons from malaria endemic countries. In addition, in the previous years, two sporadic locally acquired *P.falciparum* malaria cases were recorded (one in 2017 and one in 2020), for which the most likely place of exposure was a heath care facility (the exact mode of transmission was not possible to be defined). Since 2009, no malaria transmission through blood transfusion has been recorded.

The number of malaria cases in Greece reported to the NPHO by year of symptom onset (for imported cases) or infection (for locally acquired cases) and by epidemiological case classification (imported or locally acquired) is presented in Table 1. Table 2 presents locally acquired/ introduced *P. vivax* malaria cases by probable Region and Regional Unit of exposure, years 2009-2020.

Table 1: Reported malaria cases by year of symptom onset[1] (for imported cases) or infection (for locally acquired cases) and by epidemiological case classification (imported or locally acquired), Greece, 2009 - 2020[2].

Year	Case classification	
	Imported cases	**Locally acquired/ introduced cases[3]**
2009	44	7
2010	40	4
2011	54	42
2012	73	20
2013	22	3
2014	38	0
2015	79	8
2016	111	6
2017	100	7
2018	44	11
2019	38	1
2020	21	2

1. Cases with no information regarding symptom onset were classified according to the year of hospitalization or notification to the NPHO.
2. Known reported relapses, two locally acquired *P.malariae* cases (2012), that were attributed to former transmission periods, and three malaria cases "of undetermined classification" (two in 2016 and one in 2018) are not included.
3. All were *P.vivax* cases, except two hospital-acquired *P.falciparum* cases, one in 2017 and one in 2020 (included in the Table).

Table 2: Locally acquired/ introduced *P. vivax* malaria cases by probable Region and Regional Unit of exposure and year of infection, Greece, 2009 - 2020.

Region	Regional Unit	Locally acquired *P.vivax* cases by year of infection											
		2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Peloponnese	Lakonia	6	1	36	10	0	0	1	0	0	0	0	0
Attica	East Attica	1	1	2	4	0	0	2	0	0	0	0	0
Sterea Ellada (Central Greece)	Boeotia (Viotia)	0	2	1	2	0	0	1	0	1	0	0	0
	Euboea (Evoia)	0	0	2	0	0	0	0	0	0	0	0	0
Thessaly	Karditsa	0	0	0	2	1	0	0	0	1	0	0	0
	Larisa	0	0	1	0	0	0	3	1	0	0	0	0
	Trikala	0	0	0	0	0	0	1	0	0	1	0	0
	Magnesia & Sporades	0	0	0	0	0	0	0	1	0	0	0	0
East Macedonia & Thrace	Xanthi	0	0	0	2	0	0	0	0	0	0	0	0
	Evros	0	0	0	0	2	0	0	0	0	2	0	1
Central Macedonia	Thessaloniki	0	0	0	0	0	0	0	2	0	8	0	0
	Pieria	0	0	0	0	0	0	0	0	0	0	1	0
Western Greece	Achaea (Achaia)	0	0	0	0	0	0	0	1	1	0	0	0
	Elis (Ileia)	0	0	0	0	0	0	0	1	2	0	0	0
	Aetolia-Acarnania	0	0	0	0	0	0	0	0	1	0	0	0
Total		**7**	**4**	**42**	**20**	**3**	**0**	**8**	**6**	**6**	**11**	**1**	**1**

This case classification is based on epidemiological criteria (e.g., history of travel within the last three years to a malaria endemic country). However, recent *Plasmodium* genotyping results suggested that a number of cases previously classified as "imported" were actually locally acquired. These cases concerned migrants from malaria endemic countries in 2011 (n=9) and 2012 (n=11), who were residing in the Municipalities of Evrotas Lakonia and Sofades Karditsa (Spanakos G, Snounou G, Pervanidou D, et al., 2018).

You can find more information regarding epidemiological malaria data at the NPHO website (https://eody.gov.gr/en/epidemiological-statistical-data/annual-epidemiological-data/).

Malaria surveillance data, Greece, 2021

In 2021, a total of thirty-two (32) laboratory diagnosed and confirmed malaria cases have been reported to the NPHO (Table 1): 28 cases were classified as imported (i.e., were infected abroad), and four malaria cases were classified as locally acquired (1st generation transmission).

Among the 28 imported cases, 18 were migrants/refugees from malaria endemic countries (17 from Africa and one from South Asia) and 10 cases were travellers (seven from Africa and three from the Indian subcontinent). More specifically, the countries of infection of the 28 imported malaria cases included: Nigeria (n=9), India (n=3), Cameroon (n=3), Democratic Republic of Congo (n=3), Ivory Coast (n=2), Burkina Faso (n=2), Afghanistan (n=1), Ghana (n=1), Uganda (n=1), Sierra Leone (n=1), Sudan (n=1), Tanzania (n=1).

Among the 18 cases in migrants/refugees from malaria endemic countries, 16 cases concerned migrants visiting friends and relatives at their country of origin. Among the 10 cases in travelers, eight cases had travelled to malaria endemic countries for professional reasons.

Four (4) cases were classified as locally acquired (1st generation of transmission). Case investigation of these cases suggested the following:

- Three (3) *P.falciparum* malaria cases, with symptom onset during the weeks 25-26/2021, were classified as locally acquired (1st generation of transmission). The most likely place of exposure of these patients was a hospital (where there was an epidemiological link with an imported malaria case), in Attica region. The most likely route of transmission of the hospital-acquired malaria was through nosocomial practices during patients' health care, which may contributed to the blood-borne transmission, while the exact mode of the nosocomial transmission was not possible to be confirmed; however, these practices did not include blood transfusion. During the re-active case detection, no more malaria cases were detected (among the other co-hospitalized patients). This event is considered a single and rare event. Similar events have been recorded in the literature, in Europe (including Greece, with two single cases previously recorded, one in 2017 and one in 2020), and worldwide. According to the consultation of the competent "Working Group for the designation of vector-borne disease (VBD) affected areas", the area was not defined as "malaria affected", given the very low possibility of ongoing malaria transmission.
- One (1) *P.vivax* case was classified as introduced (1st generation of transmission), with probable place of exposure at the Municipality of Delta, Regional Unit (RU) of Thessaloniki, in Central Macedonia Region. The patient had onset of symptoms in week 36/2021 (06-12/09/2021). No more malaria cases were detected in the area, during the field investigation (reactive case detection).

Table 3 presents the reported malaria cases in Greece by epidemiological case classification (imported or locally acquired), status (migrants/refugees or travellers) and *Plasmodium* species.

Table 3. Malaria cases by epidemiological classification, status and *Plasmodium* species, Greece, 2021 (n=32)

Epidemiological classification and status		***P.vivax***	***P.falciparum***	***P.ovale***	***P.malariae***	**Total**
Imported cases	**Migrants/refugees**	2	12	3	1	18
	Travelers	3	6	0	1	10
Locally acquired cases (1st generation transmission)		1	3	0	0	4

The number of imported malaria cases by status (migrants/refugees or travelers) and place of residence (for the imported cases) is described in Table 4.

Table 4. Imported malaria cases by status (migrants/refugees or travelers) and Regional Unit (RU) of residence, Greece, 2021 (n=28).

Regional Unit (RU) of residence	Imported cases		
	Migrants/refugees	Travelers	Total
Central Section of Athens	6	1	7
Southern Section of Athens	0	1	1
Piraeus	1	0	1
West Attica	1	0	1
Arcadia	1	0	1
Boeotia (Viotia)	1	0	1
Evros	0	1	1
Kavala	0	1	1
Kalymnos RU: Patmos Municipality	0	1	1
Lakonia	1	0	1
Larisa	1	0	1
Magnesia	0	1	1
Messinia	2	1	3
Preveza	0	1	1
Rhodes	1	0	1
Syros	0	2	2
Thessaloniki	2	0	2
Zakynthos	1	0	1
Total	**18**	**10**	**28**

Activities for the prevention and management of malaria

Since 2011, NPHO has developed and continuously implements an Action Plan for the Management of Malaria. In addition, in 2015 the Ministry of Health published the "National Action Plan for the Management of Malaria".

According to these plans, a series of activities are implemented nationwide for the prevention and management of malaria, with the collaboration of national, regional and local authorities:

I. **Risk assessment for the re-emergence of malaria:** All areas (Regions, Municipalities) are assigned a Risk Level from 0-3, taking into consideration the locally acquired/ introduced malaria cases reported since 2009, and other local risk factors (entomological, environmental and demographic data). The area Risk Level defines the activities to be implemented.

II. Enhanced malaria surveillance and intervention activities:

- **Case finding:** In order to promptly detect all malaria cases, awareness raising among health professionals nationwide and active case detection activities in high-risk areas are implemented, as well as support for the laboratory diagnosis of malaria.

- **Case investigation:** NPHO investigates all notified malaria cases. For locally acquired/ introduced cases, an in-depth interview with the patient is conducted, in order to identify the most likely place of exposure and mode of transmission, and the risk for further local transmission.

- **Immediate communication to stakeholders and health professionals** at national and local levels, after the reporting of each locally acquired/ introduced malaria case to the NPHO:
  i. Hierarchy of the Ministry of Health (MoH),
  ii. MoH Committee for the Prevention and Management of Tropical Diseases,
  iii. Working Group for the designation of vector-borne disease (VBD) affected areas (MoH),
  iv. Hellenic National Blood Transfusion Center, responsible for the relevant blood safety measures,
  v. Coordinating Centre for Haemovigilance and Surveillance of Transfusion of NPHO,
  vi. Regional public health authorities,
  vii. Municipalities,
  viii. Physicians practicing in the affected area, to raise their awareness for investigating suspect cases.

- **Focus investigation – re-active case detection**: NPHO investigation teams are deployed after the notification of each locally acquired/ introduced case to perform a "focus investigation", in an area indicated by the epidemiological, entomological and environmental investigation. In this activity, all individuals in the "focus" are screened for malaria compatible symptoms and tested for malaria accordingly.

  Following the reports of the introduced malaria cases in 2021, the NPHO, in collaboration -as applicable- with the hospital's infection control committee or the regional public health authorities, organized and performed reactive case detection: i) for the hospital-acquired *P.falciparum* malaria: testing for malaria of other patients linked/co-hospitalised in the same ward with the cases was performed, and ii) for the introduced *P.vivax* malaria case (mosquito-borne transmission): focus investigation was performed, including door-to-door field visits, screening for malaria compatible symptoms and testing for malaria of the local and migrant population accordingly, in the proximity of the case, as well as communication activities for health professionals and the public in the area.

- **Environmental and vector investigation** is performed in the area after the recording of each locally acquired malaria case (or imported case in a receptive area), in collaboration with regional and local authorities, in order to identify *Anopheles* breeding sites and other risk factors for local transmission.

- **Pro-active malaria case detection (PACD) in Evrotas Municipality, Lakonia** (where clusters of locally acquired *P.vivax* cases were recorded in 2011-2012): The NPHO, in collaboration with the Region of Peloponnese, the Municipality of Evrotas, the University of Thessaly and Doctors Without Borders (2012), supported from 2011-2014 a field team in the area for the pro-active detection of malaria cases. Since 2015, the field team -with staff from the University of Thessaly and field education from the NPHO- is supported by the Region of Peloponnese to continue the PACD programme, undertaking also the radical treatment and focus investigation of all recorded malaria cases. A significant number of migrants from malaria endemic countries (mainly Pakistan) live and

seasonally work in Evrotas. During the field visits, health promotion information is provided for protection against mosquitoes and fever screening and/or testing for malaria is performed regularly. During the mosquito circulation season, fever screening visits are performed every 7-15 days in migrants and other high-risk groups in the particular area.

- **Ad-hoc malaria surveillance reports** (uploaded on the NPHO website), following the recording and the investigation of each local malaria transmission event.

III. **Enhancing laboratory diagnosis of malaria:** Since 2012, NPHO has distributed Rapid Diagnostic Tests (RDTs) for malaria to Hospitals and Health Centers in areas with recently recorded malaria transmission, and in areas with large populations of migrants from endemic countries (i.e., large urban centers, in refugee/migrant camps and the nearby Health Units, areas hosting large travelers' populations), aiming at prompt diagnosis and treatment of malaria cases. In 2020-2021, NPHO provided RDTs to a total of >200 Health Units/facilities, nationwide. RDTs have contributed significantly to the early detection of malaria cases in our experience and have been proven a valuable field tool.

In addition, NPHO supports the Reference Malaria Laboratory (RML, School of Public Health, University of West Attica) for the (free-of-charge) testing for malaria of every suspected case, and recommends the transportation of samples from any laboratory in Greece to the RML for verification of diagnosis and further identification (and genotyping) of *Plasmodium* species.

IV. **Case management - Standardization of the malaria treatment in Greece,** according to treatment and management guidelines developed by the NPHO with the input of experts in infectious diseases. NPHO infectious diseases specialists are available for counseling. NPHO also maintains a stockpile of anti-malarial medicines (e.g., the national stockpile of artesunate for parenteral injection, for severe cases), for the timely distribution of the proper anti-malarial treatment to Health Units in cases of emergency.

V. **Increase awareness amongst health professionals** for the diagnosis and management of malaria. NPHO staff delivers presentations and organizes seminars -as necessary- for health professionals in Health Centers/Hospitals in areas with recently recorded locally acquired cases. The NPHO provides guidelines for the recognition and diagnosis of malaria and the recommended laboratory investigation and case management (mailings and website, https://eody.gov.gr/disease/elonosia/). NPHO communicates annually (through informative letters) to all Hospitals/Health Centers and Medical Associations of the country about malaria.

VI. **Communication to the public** on malaria and personal protection measures against mosquitoes:

- **Educational and informative material** on malaria and protective measures against mosquitoes is available on the NPHO website.

- **Information material** for the public (leaflets, posters) is distributed according to the needs. In June 2021, NPHO sent -via email- informative material to regional and local authorities, and sent informative leaflets for the protection against mosquito bites to all Regions of Greece, in order to be distributed to the public.

- In areas with introduced cases recorded, the NPHO field team informs the local population, raises awareness about malaria and the necessary protective measures against mosquitoes, during the focus investigations (door-to-door), and urgently provides informative leaflets.

VII. **Designation of affected areas - Blood safety and haemovigilance measures:** An inter-sectoral Working Group (WG) on the designation of VBD affected areas (under the MoH) considers all available epidemiological and laboratory data for each locally acquired/ introduced case and decides on the

characterization of malaria affected areas in Greece. This designation is then used by the Hellenic National Blood Transfusion Center to issue guidance on blood safety. The list of affected municipalities is published on our website (www.eody.gov.gr) and updated regularly according to recorded locally acquired cases. Post donation and post transfusion information to donors and other haemovigilance measures are in place following relevant guidance from the Coordinating Centre for Haemovigilance and Surveillance of Transfusion of NPHO.

VIII. Vector surveillance and control activities:

- **Raising awareness and guidance to Regional Authorities:** NPHO communicates regularly (meetings, letters and technical guidance) with all Regional Authorities in Greece recommending the timely planning, organization and implementation of integrated vector control programmes particularly in high-risk areas. NPHO sent relevant awareness letters in early February 2021 underlying the high risk areas, and recommending the intensification of vector control in areas with risk factors for local transmission. In addition, NPHO timely informs the regional and local authorities of areas with recorded malaria cases, and -after risk assessment- recommends prevention and response measures, including the urgent intensification of vector control in the area, in order to reduce the mosquito vector population.
- **Monitoring of the implementation of vector control programmes across the country** (through a structured questionnaire).
- **Distribution and placement of Long Lasting Insecticide-treated Nets (LLINs):** According to WHO and ECDC guidance, NPHO provided/ distributed (in 2013) LLINs to migrants, in the Municipality of Evrotas, Lakonia, under a special license from the Ministry of Rural Development and Agriculture. Since then, the distribution, placement and monitoring of the proper use of the nets is implemented by the PACD field team, which conducts the active case detection in the area.
- **Entomological surveillance**: For the 2021 period, NPHO organized/participated in/performed an active vector surveillance programme in various areas of the country, in collaboration with local/regional authorities, private mosquito control sub-contractors, the School of Public Health-University of West Attica and the Benaki Phytopathological Institute. MoH and NPHO recommends that local authorities should perform vector surveillance annually, especially in areas with risk factors for local malaria transmission (e.g., rural areas with large populations of migrants from malaria endemic countries) and tries to collect the available vector surveillance data.

IX. Communication with international public health stakeholders: The NPHO communicates frequently for exchange of knowhow and information on malaria cases and activities with the ECDC and WHO, as well as with a number of European and international agencies and networks.

In addition, due to the increased **migrant/ refugee population residing in the country** in reception and accommodation camps, a series of targeted activities have been organized in these camps, including: strengthening malaria surveillance and diagnosis, distribution of rapid diagnostic tests to the camp clinics and nearby Health Units, recommendation for systematic vector surveillance in the area, risk assessment (collection of available vector, environmental and demographic data) and, if necessary, intensification of mosquito control measures, personal protection measures against mosquitoes and communication activities (leaflets distribution) for the hosted migrants/ refugees.

Conclusions

As indicated by the malaria surveillance data of the last years, and despite the malaria elimination in Greece since 1974, the risk of re-introduction of the disease in specific vulnerable and receptive areas of the country exists, especially where the presence of adequate numbers of *Anopheles* mosquitoes (the competent vector of the disease) is combined with the presence of malaria patients coming from endemic countries. Following a peak of locally acquired *P.vivax* malaria cases in 2011-2012, their number declined steadily in the following years. This decrease is the result of a number of intense and costly public health interventions implemented since 2011, with the collaboration of various stakeholders at the national, regional and local level, which have contributed to the successful prevention of the re-appearance of malaria in Greece.

Sporadic events of *P.vivax* malaria introduction (single cases or small clusters, 1st generation of transmission) are still recorded over the last years in few vulnerable and receptive rural areas, with a mosquito-borne *P.vivax* transmission (through mosquitoes infected from imported cases from malaria endemic countries), indicating the need to sustain malaria prevention activities as a priority for the preparedness of public health authorities.

Additionally, the recording of rare events of hospital-acquired malaria transmission indicates the intense need for systematic and strict implementation of all recommended prevention measures during the health care of malaria patients, in order to minimize the possibility of further malaria transmission, through any possible route; either though mosquitoes, in areas with competent vectors, or though nosocomial practices during the patients' health care which may contribute to blood-borne transmission.

Early detection and **eradication treatment of malaria cases,** together with **appropriate investigation** and **effective integrated vector control measures** represent the main components of the public health strategy to prevent malaria reintroduction and re-appearance in high-risk areas of the country. In this context, high level of preparedness and awareness of health and public health services should be maintained. In addition, important determinants for the prevention of local malaria transmission in Greece include the migrants' health care and access to health services, for the timely diagnosis and treatment of malaria, the communication with the migrant population and achieving a minimum standard for their living conditions and well-being.

Advice for travelers in Greece:

The NPHO, based on the surveillance data available until now and the implemented prevention measures in the areas where locally acquired/ introduced malaria cases have been reported, maintains that **the risk to travelers for malaria infection in Greece is extremely low**. **Chemoprophylaxis for malaria is not recommended for visitors to any area in Greece** (including areas where locally acquired/ introduced malaria cases have been recently recorded). Nevertheless, personal protective measures against mosquitoes are encouraged during the mosquito circulation season (given also the seasonal circulation of West Nile virus in some areas in the country).

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