

# Malaria in pediatric age in the Piedmont Region

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## Abstract

**Introduction.** Pediatric malaria, even in countries considered as free as Italy, is an important problem of public health because children have a high variability of the clinical picture. The objective of this brief note is to determine the incidence of pediatric malaria in the Piedmont Region during the period 1989-2015.

**Materials and methods.** All cases of pediatric malaria notified were considered thanks to the regional information flow over the period 1989-2015. Cases of congenital malaria, unconfirmed malaria cases, and aged 14 and older were excluded of the study.

**Results.** In Piedmont in the period 1989-2015, pediatric malaria accounts for 8.8% of the total (172/1946 cases). 74% of patients are of foreign nationality, to which must be added the 14% represented by those born in Italy from foreign parents, while it is 100% the fraction of patients who have made a trip to the abroad. The notification of cases is greater in the autumn months. Only 7.6% of the sample carried out a complete chemoprophylaxis. In 79% of cases, the primary care physician advised chemoprophylaxis on trips to endemic areas.

**Conclusions.** At present, lacking an effective vaccine, the prevention and implementation of standard precautions such as chemoprophylaxis, represent the safest strategy to put into practice to eradicate the disease especially for the groups at greater risk as visiting friends and relatives.

## Key words

- malaria
- pediatric malaria

## INTRODUCTION

Malaria is a disease caused by Plasmodium protozoans (*Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae* and *Plasmodium Knowlesi*) transmitted to humans by the bite of some species of female mosquito of the genus Anopheles. *Plasmodium falciparum* is the most prevalent malaria parasite in sub-Saharan Africa (100%), the Western Pacific (72%), Eastern Mediterranean (69%) and South East Asia (63%), while *Plasmodium vivax* is the dominant malaria species in the Americas (74%) [1].

The symptoms, depending on the plasmodium species, appears 7-15 or more days after the bite of the infected mosquito. They are consistent in fever, often very high, headache, vomiting, diarrhea, sweating and shaking chills, all symptoms, at least existing, common to any flu syndrome or other infections.

Malaria cases are classified according to the terminology adopted by the WHO in 1963, as follows: a case of malaria is considered to be imported when the infection was contracted in a country other than that

in which it is diagnosed; autochthonous when it is locally contracted. Among the autochthonous cases are defined induced, those caused by transfusions or other form of parenteral inoculation (transplants, nosocomial infections, etc.); introduced the secondary cases locally contracted after the bite of an indigenous mosquito infected on an importation case (bearer of gametocytes) or contracted with the bite of an infected mosquito accidentally imported (malaria from luggage, from the airport). A cryptic case is an isolated case of malaria that after an adequate epidemiological investigation cannot be classified in any of the categories described above. In the period 2013-2017 in Italy there were 3805 cases of malarial cases, of which 12 cases were autochthonous, 4 induced and 8 cryptic, with a peak of 7 cases occurred in summer 2017 that created a great concern for public health [1].

WHO's World Malaria Report has estimated that in 2017 the number of total cases was around 219 million, with about 435 000 deaths [2]. Although it represents one of the most widespread diseases in the world, 92%

of cases and 93% of deaths occurred on the African continent.

However, in the latest years the spread of malaria has considerably reduced thanks to increasing fight and control plans and since 2016 WHO announced that the autochthonous transmission of malaria in European states was eradicated [3].

Yet, because of global migrator fluxes' increase and growing number of international travelers, in non-endemic countries malaria continues to be the most important import disease [4].

Worldwide, imported malaria is defined as a malaria infection acquired in an endemic area of malaria but diagnosed in no endemic country. Italy is included by WHO among malaria-free countries since 1970 but the attention remains very high because cases imported into areas that are no longer endemic may represent infection's sources due to the presence of competent vectors on the territory, allowing the reactivation of a local transmission, as recently happened in Greece [5].

In areas of high malaria transmission, children under the age of 5 are particularly vulnerable to infection and develop the disease in severe form. In 2017, 61% of deaths (266 000) affected this age group [2]. Pediatric malaria is an important public health problem because clinical picture is highly variable for children, and often not easily attributable to the disease. Children develop more severe disease's forms especially before the age of 5, with a greater probability of death than adults [6].

The objective is to determine the incidence of pediatric malaria in the region of Piedmont in the period 1989-2015. Secondary objectives are the determination of the incidence of malaria cases among European and Non-European citizens, the determination of the percentage of malaria cases despite chemoprophylaxis and the determination of the increase in notifications post holidays periods.

## MATERIALS AND METHODS

The study evaluated all cases of pediatric malaria notified and recovered through in Piedmont thanks to regional information flow in the period 1989-2015. The composition of the study sample included all confirmed cases of malaria in the age group up to 14 years, regardless of nationality and sex. The exclusion criteria applied were: unconfirmed cases of malaria, age over 14 years, congenital malaria cases. The analysis provided a quantitative stratification for some characteristics: nationality, notification month of malaria cases, travel destination and fulfillment prophylaxis. The notification forms analyzed did not allow us to describe the clinical course and the severity of the individual case. In fact it was not possible to consult the medical records. Furthermore, another aspect that could not be investigated was the possible diagnostic delay.

## CASE DEFINITION

The criteria adopted for the identification of the case are those provided by the Italian Ministry of Health [7]: a case of malaria is defined as a symptomatic, paucisymptomatic or asymptomatic individual in which there is the presence of malarial parasites with diagnostic methods

that have clinical, epidemiological or laboratory criteria. The classification offers the possibility of having a probable case, in which the clinical and epidemiological criteria are met, and a confirmed case, in which the laboratory criterion (microscopic confirmation) is also satisfied. Only confirmed cases were considered in this study.

## RESULTS

Among 1946 malaria cases notified in Piedmont in the period 1989-2015, pediatric malaria represents 8.8 % of total (n. 172), the case-fatality rate is 0.58 %, due to a single case of death in the study sample. The most represented species of *Plasmodium* protozoans was the *Plasmodium falciparum* (150 cases) *Plasmodium vivax* (3 cases), *Plasmodium ovale* (8 cases); there were also 3 cases of mixed forms and 9 cases in which the agent is not specified. The stratification of the sample by citizenship has shown that the largest share of patients is of foreign nationality. They represent 74% (n. 127) of the sample, while 12% (n. 21) of the sample is represented by Italian citizens and 14% (n. 24) by children born in Italy from foreign parents. The 100% of the sample is the share of patient who travelled abroad. The country of destination was North e West Africa for over 95% of cases, around 60% of the notifications, in fact, come from people who have visited the Ivory Coast and Nigeria. There were several reasons behind those travels, but in the most cases it was for returning to the country of origin, *Table 1* shows the destination and the reason for the trip and the use of chemoprophylaxis.

August, September and October and partly even November and January are the months in which the largest number of diagnosis occurred, as a consequence of people returning from journeys taken during school summer and winter breaks (*Figure 1*).

The notification forms analyzed starting from 2003 are enriched with some information: type of trip, type and method of chemoprophylaxis and operator who recommended chemoprophylaxis. Considering that the data is partial, related to 131 cases, the data we present are not to be considered general.

Only 7.6% of the sample received a complete chemoprophylaxis. Moreover, it should be considered that 26% of malaria cases are not preventable by a prophylaxis, as they concern that share of children reaching Italy via immigration. Mefloquine was the most used molecule in either complete or partial chemoprophylaxis. It was the family doctor (general practitioner/family pediatrician) that in most cases (79%) recommended a chemoprophylaxis before a trip to endemic areas.

## DISCUSSION

According to Surveillance Atlas of Infectious Diseases data of the European Center for Disease Prevention and Control (ECDC) for 2017, 8401 cases of malaria were reported in the EU/EEA, 8393 (99.9%) of which were confirmed and almost all cases of malaria reported by EU countries for 2017 have been imported [8].

France reported the highest number of cases, followed by the United Kingdom, Germany and Italy.

All countries that report the greatest number of cases have historical, economic, linguistic and cultural

**Table 1**  
Reason and destination of travel and use of malaria chemoprophylaxis\*

Destination		Reasons		Type of prophylaxis	
Benin	3	Immigration	26 (15%)	Atovaquone/Proguanil	2
Burkina Faso	16	Parental work	2 (1.2%)	Mefloquine	33
Cameroon	10	Residence	3 (1.7%)	Quinine	1
Congo	8	Return of origin country	102 (59.3%)	None	65
Ivory Coast	27	Tourism	20 (11.6%)	Not remember	30
Ghana	9	Other	2 (1.2%)		
Equatorial Guinea	3	Does not know	17 (9.9%)		
India	3			<b>Subdivision by citizenship</b>	
Kenya	2	<b>Percentage of sick people who have carried out chemoprophylaxis during travel*</b>		Italian	21 (12%)
Liberia	1	Complete chemoprophylaxis	10 (7.6%)	Foreign	127 (74%)
Madagascar	2	Missed doses	6 (4.6%)	Born in Italy from foreign parents	24 (14%)
Mali	4	Not executed	65 (49.6%)	<b>Clinicians who recommended chemoprophylaxis</b>	
Nigeria	73	Interrupted	12 (9.1%)	Travel medicine surgery	26 (20%)
Not reported	1	Late	3 (2.2%)	Family Doctor	103 (79%)
Senegal	9	Not remember	30 (22.9%)	Does not know	2 (1.5%)
Togo	1	Partial chemoprophylaxis	5 (3.8%)		

\*Reference period 2003-2015 131 cases.

links with endemic areas, particularly in Africa and the Americas. Most cases of malaria imported into France and the United Kingdom are linked to travel routes from West Africa [4]. Italy was the fourth country in terms of number of notifications, after France, United Kingdom and Germany, with 830 reported malaria cases, of which about 12% of pediatric malaria cases.

Although the Member States of the European Union have been free from malaria since 1975, the presence of the vector of the genus *Anopheles* is frequently documented [9]. Italy in particular seems to remain a risk zone due to the vector competence of some species of *Anopheles* (*Anopheles superpictus*, *A. sacharovi* and *A. labranchiae*) and the high malarious degree [10].

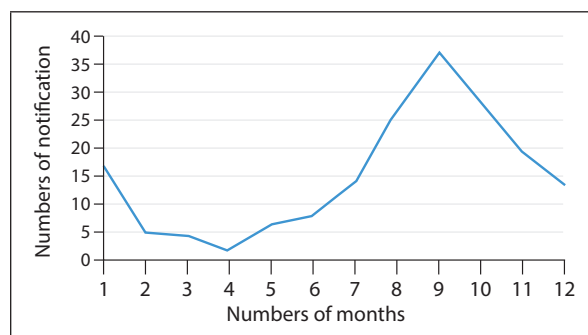
Over the last 10 years occasional cases of indigenous malaria were reported in several European countries. In almost all cases it was "airport malaria" [9]. However, malaria is more frequently introduced in Europe through importation, which has multiple variable: increased international travels, especially in tropical and subtropical areas, more immigrants from coun-

tries where malaria is endemic, and the role of visiting friends and relatives (VFRs).

VFRs are individuals from low-income countries who having settled in high-income countries periodically go back to their native country to visit relatives and friends. This population of immigrants alone counts for 50% of international travelers [10]. They represent a group of travelers particularly at risk with regard to travel-related diseases, more than other kind of travelers (tourists, business-travelers) [11].

VFRs visit rural areas more frequently and stay there longer than those who travel in risk area for tourism or business, and probably in healthier conditions. Furthermore, with regard to malaria, VFRs may have a lower perception of risk, believing that they have a permanent immunity to infection, acquiring with birth in the endemic country, without considering the potential for a relapse of the infection. This leads to a lower employment of available preventive measures: repellents, mosquito nets, air conditioning and chemoprophylaxis [12], and also for their children. Even the subpopulations belonging to the group of traveler VFRs, like pregnant women and pediatric individuals, seems to be slightly sensitive about preventive measures [13].

VFRs may represent up to 70% of imported malaria cases in developed countries [11]. Data analyzed in this study also show how the greater incidence of pediatric malaria occurs during periods corresponding to school summer holidays (August, September and October) and Christmas festivities (December and January), during which VFRs often go back to their native country (Figure 1).



**Figure 1**  
Diagnosis of malaria by month, cumulative 1989-2015 (n. 172 pediatric cases in the Piedmont Region, Italy).

## CONCLUSION

Imported malaria represents one of the most diagnosed diseases in developed countries, but at the same time one of the most preventable if standard precau-

tions were always adopted. VFRs are one of the group most at risk of contracting malaria and importing it in developed countries. This multiethnic and diverse category should represent the main target of awareness policies of the actors in charge of the purpose. However, there seems to be many implementation difficulties: VFRs often consider chemoprophylaxis as an almost exaggerated precaution for a disease that is been known since childhood [14]; furthermore, socio-economic difficulties, lack of knowledge of prevention tools and lack of knowledge of the correct and timely use of health and social services.

Prevention and awareness-raising strategy should thus be extensive and systematic, especially for VFRs individuals who are integrated into society in developed countries. Many actors shall be involved: general practitioner, family pediatrician, pharmacists, primary school teachers. Furthermore, an extensive information might be offered also in workplaces and places of entertainment.

In Europe, malaria chemoprophylaxis is recommended only for travelers in malaria endemic countries,

which are classified into different groups to determine the most effective drug regimen [15]. The choice of prophylactic drugs and prevention measures also depend mainly on the local epidemiology of malaria, on the duration of potential exposure to vectors, on the model of resistance to parasites, on the level and seasonality of transmission, on tolerance to prophylactic drugs, from age and pregnancy.

Currently, in the absence of an effective vaccine, prevention and implementation of standard precaution represent the safest strategy to put into practice to eradicate malaria.

#### **Conflict of interest statement**

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias the conduct and findings of this study.

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## REFERENCES

- Boccolini D, Menegon M, Di Luca M, et al. Malaria surveillance in Italy: a public health topic of relevance. XXX Congresso Nazionale SoIPa, Milano, 26-29 giugno 2018, Abstract: p. 35.
- World Health Organization. World malaria report 2018. Geneva: WHO; 2018.
- World Health Organization. History of malaria elimination in the European Region. Copenhagen: WHO; 2016. Available from: [www.euro.who.int/\\_\\_data/assets/pdf\\_file/0003/307272/Facsheet-malaria-elimination.pdf](http://www.euro.who.int/__data/assets/pdf_file/0003/307272/Facsheet-malaria-elimination.pdf).
- Tatem AJ, Jia P, Ordanovich D, et al. The geography of imported malaria to non-endemic countries: a meta-analysis of nationally reported statistics. *Lancet Infect Dis*. 2017;17:98-107.
- Andriopoulos P, Economopoulou A, Spanakos G, et al. A local outbreak of autochthonous *Plasmodium vivax* malaria in Laconia, Greece. A re-emerging infection in the southern borders of Europe? *Int J Infect Dis*. 2013;17:e125.
- Ladhani S, Aibara RJ, Riordan FA, et al. Imported malaria in children: a review of clinical studies. *Lancet Infect Dis*. 2007;7:349-57.
- Ministero della Salute, Direzione Generale della Prevenzione Sanitaria. Prevenzione e controllo della malaria in Italia. Roma; Ministero della Salute; 2017.
8. European Centre for Disease Prevention and Control. Malaria. In: ECDC. Annual epidemiological report for 2017. Stockholm: ECDC; 2019.
- ECDC. ECDC Meeting Report Consultation on *Plasmodium vivax* transmission risk in Europe. Stockholm, 17-18 January 2012. Available from: [www.ecdc.europa.eu/en/publications/Publications/MER-Malaria-meeting.pdf](http://www.ecdc.europa.eu/en/publications/Publications/MER-Malaria-meeting.pdf).
- Boccolini D, Romi R, D'Amato S et al. Sorveglianza della malaria in Italia e analisi della casistica del quinquennio 2002-2006. *Giornale Italiano di Medicina Tropicale*. 2007;12:1-4.
- Mascarello M, Gobbi F, Angheben A et al. Imported malaria in immigrants to Italy: a changing pattern observed in north eastern Italy. *J Travel Med*. 2009;16:317-21.
- Angell SY, Cetron MS. Health disparities among travelers visiting friends and relatives abroad. *Ann Intern Med*. 2005;142:67-72.
- Mali S, Kachur SP, Arguin PM. Division of Parasitic Diseases and Malaria, Center for Global Health; Centers for Disease Control and Prevention (CDC). Malaria surveillance-United States, 2010. *MMWR Surveill Summ*. 2012;61(2):1-17.
- Neave PE, Behrens RH, Jones CO. "You're losing your Ghanaianess": understanding malaria decision-making among Africans visiting friends and relatives in the UK. *Malar J*. 2014;13:287.
- World Health Organization. International travel and health. 15 November 2018. List of countries, territories, and areas. Vaccination requirements and recommendations for international travellers, including yellow fever and malaria. Geneva: WHO; 2018.